

Controversy Over the Diagnosis and Treatment of Hypothyroidism

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Lana Schwartz

Dr. Allison Leich-Hilbun

Table of Contents

1. Abstract
2. Introduction
 - a. What is Hypothyroidism
 - b. The Controversy Over Hypothyroidism
 - c. Aims
3. Stakeholders
 - a. The Medical System at Large
 - b. Patients
 - i. The Untreated Patient
 - ii. The Overtreated Patient
4. Grounds for Controversy
 - a. Psychosocial Grounds for Controversy
 - i. Psychosocial Grounds for Liberal Diagnosis and Treatment
 - ii. Psychosocial Grounds for Conservative Diagnosis and Treatment
 - b. Biological Grounds for Controversy
 - i. Biological Disagreement #1: Establishing a Healthy TSH Range
 - ii. Biological Disagreement #2: Subtypes of Hypothyroidism
 - iii. Other Biological Disagreements
5. Methods
6. Hypotheses, Results, and Inferences
 - a. Who Are Our Participants?
 - b. The Survey
 - i. Experience With the Controversy
 - ii. Evolution of Standards
 - iii. Opinions on Organizations' Standards
 - iv. Opinions on Arguments for Change
 - v. Which Hormones Do They Use?
 - vi. Importance of Hormones Other Than TSH
 - vii. Ranges of Hormones
 - viii. Patient Cases
 - ix. Psychosocial Factors
 - x. Conservative or Liberal Practices?
 - c. Statistical Inferences
7. Limitations
8. Conclusion
9. Sources

Abstract

This study surveys clinicians' hypothyroidism diagnosis and treatment practices and their opinions on current diagnostic standards. By distributing a redcap survey, the study ascertained whether practicing clinicians disagree with each other, where they stand on the debate over appropriate standards, and which standards they apply in practice. The survey garnered participants' opinions on seven primary aspects of hypothyroidism: organizations' differing recommendations, arguments for changing the standards, which thyroid hormones are worth testing, which ranges of thyroid hormones are appropriate, the psychosocial effects of the condition, their experience with clinical disagreements in practice, and their confidence in current standards. After asking for their opinions on these topics, participants were presented with nine fictional patient cases. Each patient case presented a fictional patient's age, BMI, thyroid hormone levels, and symptoms. Participants were asked to indicate whether they were "very likely," "likely," "moderately," "unlikely," or "very unlikely" to diagnose the hypothetical patients. The survey was distributed to 750 healthcare providers, including endocrinologists, GPs, PAs, and NPs that practice in the United States. 48 practitioners responded. The results of the survey indicated that clinicians consistently and drastically disagree over diagnostic and treatment standards for hypothyroidism. Clinicians recommended testing for different hormones, indicated different healthy ranges of hormones, sided with opposing organizations, valued the psychosocial effects of the disease differently, and indicated varying levels of confidence in modern standards. Notably, practitioners' likelihood of diagnosing and treating the fictional patients varied drastically. Qualitative responses provided the study with reasons for their answers. The qualitative results illustrated the polarizing nature of the disagreements; some practitioners deem clinicians of opposing opinions as committing "malpractice." In conclusion, current standards are not unambiguous enough to create near-unanimous agreement among clinicians regarding the diagnostic threshold.

Introduction

Hypothyroidism is a disease that prevents the thyroid gland from producing enough metabolic hormone, which leads to a systemic slow down of bodily functions. Symptoms include constipation, slowed heartbeat, impaired reproductive function, weight gain, chronic fatigue, increased risk of heart disease and diabetes, and more. It is diagnosed by testing the blood for thyroid hormone levels and is treated by oral ingestion of synthetic hormones.

Professional organizations of scientists and doctors provide different diagnostic and treatment criteria for the condition. Put simply, they disagree with each other about where the threshold for diagnosis should be. Patient coalitions, on the other hand, unanimously argue for a lower diagnostic threshold - they actively seek out treatment for those with debated or borderline cases. Presented with the controversy among professional associations and an unambiguous patient stance, one question remains unanswered: what do practitioners think?

This study aimed to garner clinicians' opinions on diagnostic and treatment criteria for hypothyroidism. By distributing a redcap survey, the study ascertained whether practicing

clinicians disagree with each other, where they stand on the controversy, and which standards they apply in practice.

Stakes of changing the diagnostic threshold are high for patients, practitioners, insurance providers and pharmaceutical companies. Biological, psychological, and sociological consequences of the condition render receiving proper treatment for hypothyroidism essential for patients' health. For that reason, patients hold the primary stake in the outcome of the debate. Changing the threshold could be expensive or profitable for different groups in the medical field.

What is Hypothyroidism?

The human body carries out millions of tasks per day - walking, thinking, digesting, eating, breathing - the list is infinite. Each of these processes is reducible to a set of chemical reactions that require energy, which we obtain from food. These energy-requiring reactions must occur at an optimal speed for survival. For example, the heart must beat fast enough to supply the body with oxygen when it needs it. Digesting food, muscle contraction, breathing, and nearly every other bodily function must occur at a specific rate. The body's "rate" of operation is called its metabolic rate, or metabolism.¹ An essential gland in the body sets the pace of this rate: the thyroid.

The thyroid gland releases thyroid hormones that work to conduct the body's metabolic rate.² Thyroid hormones are chemical compounds that instruct the body's cells to complete specific tasks - they act as messengers. The thyroid's rate of hormone production thereby controls the entire body's metabolic rate; it can be thought of as the body's pacemaker. If the thyroid does not send out enough of these hormones, some cells will not get the "message" until later. This delayed messaging causes the body's metabolic rate to slow down.

A healthy thyroid regulates the body's metabolism properly by producing an appropriate amount of metabolic hormones. A damaged or disrupted thyroid can not produce hormones appropriately, which causes the body's metabolism to become dysregulated. Depending on how the thyroid is diseased or damaged, it may manufacture too much or too little metabolic hormone.² Inappropriate levels of thyroid hormones cause a cascade of metabolic issues in the body. Hypothyroidism is a disease that prevents the thyroid from producing enough thyroid hormone, resulting in a slowing of the body's metabolic rate.² This slowing affects the body systemically, making patients' list of symptoms quite long:

- Slowed digestion → constipation
- Slowed reproductive processes → if female, irregular menstrual cycles and potential infertility, if male, erectile dysfunction and low sperm count
- Slow heartbeat (bradycardia)
- hair loss
- weight gain
- chronic fatigue
- insulin resistance, which may lead to type 2 diabetes
- depression

- cold intolerance
- swelling of the hands, feet, or face
- increased risk of heart attack
- miscarriage if pregnant

The severity of the patient's symptoms depends on the degree of thyroid hormone inadequacy.² If the thyroid produces only slightly lower levels of hormones than it should, the patient's symptoms will usually be mild. If the thyroid produces very little or no hormone, the symptoms may be severe. It can be fatal in rare cases.³ Extreme cases may lead to myxedema (coma), in which patients lose consciousness.² Bradycardia, slow heartbeat, can be dangerous if not fatal for patients in that it may cause frequent fainting.³

To diagnose hypothyroidism, clinicians will test a patient's blood for levels of thyroid hormones.² A "healthy" range of thyroid hormone levels has been established by the American Association of Clinical Endocrinologists, though the range has been disputed.^{4,5} If the patient's levels of thyroid hormones fall outside the healthy range, clinicians may choose to diagnose patients with the condition. Treatment usually consists of oral tablets of thyroid hormones. Ingesting these synthetic hormones is thought to replace the hormones the patient lacks.²

The Controversy Over Hypothyroidism

Healthcare professionals agree that hypothyroidism merits medical attention, but they disagree about where the diagnostic threshold should lie. The standard "healthy" range of thyroid hormones is disputed. Widening the healthy range would decrease diagnoses, raising the diagnostic threshold. Narrowing the healthy range would increase diagnoses, lowering the diagnostic threshold. Though critical, modifying the diagnostic threshold is not limited to altering the healthy range of thyroid hormones; subtypes of the condition and psychosocial implications for patients create additional grounds for controversy. These additional variables render consistent and equitable implementation of a diagnostic standard challenging to achieve.

Disagreements between professional associations provide a striking example of the controversy's polarizing character. Organizations like the American Association of Clinical Endocrinologists [AACE], the Institute for Quality and Efficiency in Health Care [IQEHC], and the American Association for Clinical Chemistry [AACC] recommend notably different diagnostic standards.^{4,6,7} The most apparent contention point between the organizations' recommendations is their varying standard healthy ranges for TSH, the primary hormone used to diagnose hypothyroidism. Some professionals believe the healthy TSH range should be narrowed, which would lead to an increase in diagnoses. Others argue the healthy range should remain as is or expand, which would decrease diagnoses.

AACE - arguably the most prominent professional association of endocrinologists - recently narrowed their recommendation for the healthy range of TSH slightly, from 0.5 - 4.5 mU/L to 0.5 - 4.12 mU/L, an alteration of only 0.38 mU/L.⁴ Some groups argue that this new range, 0.5 mU/L - 4.12 mU/L, should be narrowed further, including some AACE members, the AACC, and a study by NHANES.^{4,6,8} The AACC argues that this range should be much smaller,

asserting that a TSH level of over 2.5 mU/L is unhealthy.⁶ On the other hand, members of the Institute for Quality and Efficiency in Health Care disagree with narrowing it at all.⁷

Organizations also disagree about other physiological aspects of the condition. Though the standard TSH range is a core question in the debate, it is only one of several. Normal ranges of other thyroid hormones are also cause for disagreement. Subtypes of the disease, which are identified by measuring these other thyroid hormones, render diagnosis and treatment of hypothyroidism even more complex. Beyond that, treatment's mixed efficacy in subtypes of hypothyroidism provides another point of controversy regarding diagnostic thresholds. There is no shortage of biological details that offer opportunities for disagreement.

Unlike these clashing organizations, patient coalitions almost always stand in agreement.^{9,10} A bottomless pit "blogosphere" of hypothyroidism patient coalitions demonstrates that patients with debated or "borderline" cases go to great lengths to acquire treatment. These patient advocacy groups are in favor of lowering the diagnostic threshold. They advocate for the AACC's recommendation, which lowers the threshold for diagnosis significantly.⁹

Dr. Izabella Wentz is a pharmacist leading the movement to lower the diagnostic threshold.⁹ Her website provides a database of progressive-minded healthcare professionals who are willing to diagnose and treat borderline thyroid cases. That way, those who read her website can see practitioners they know will provide treatment. Her audience consults the database to find doctors that will treat them. She has a whopping 58,000 followers on Instagram and 16,000 subscribers on YouTube. Her book "Hashimoto's Protocol" (Hashimoto's is a subtype of hypothyroidism) was a #1 New York Times bestseller. In her blogs, she provides her readers - most of whom are hypothyroidism patients - with a pre-written letter for their doctor about the TSH controversy, imploring the doctors to treat their subclinical patients. She encourages patients to "take charge of your own health," to "learn as much as you can about your condition," and to "tell your doctor that you are not feeling well... and insist on getting better care." It seems that she and her community feel the need to fight for satisfactory treatment, hence the letter. Blogs like hers are not uncommon. Websites like "Stop the Thyroid Madness" and "HypothyroidMom" have thousands of monthly visitors as well.^{11,12} Existing sociological research and internet activity seems to exhibit that nearly all hypothyroidism patients believe the pros of diagnosis and treatment outweigh the cons.

One key question throughout the intricacies of the debate stands out: what is the appropriate diagnostic threshold? Where do we draw the line between "hypothyroidism" and "health"? Do mild or "borderline" cases merit diagnosis and treatment - and what do we define a borderline case to be? Should clinicians be more willing to diagnose and treat patients with borderline cases - a more "liberal" stance? Or should they be avoidant of diagnosing and treating borderline cases - a more "conservative" stance? Organizations' stances differ, but those of patient coalitions' do not.

With such prestigious associations at odds with one another and an unambiguous patient stance, one question is left outstanding: where do practicing clinicians stand? And which

standards do they apply in practice? An evaluation of practitioners' stances on the controversy has yet to be conducted.

Aims

This thesis does not aim to answer whether clinicians *should* be “conservative” or “liberal” in their practice. Instead, it seeks to answer whether they *are* more liberal or more conservative in practice. From there, it looks at how prevalent disagreement among them is. Do clinicians disagree about where the diagnostic threshold is, or do they stand in unison as patient coalitions do? Put simply: where do practicing clinicians stand, and which recommendations do they apply to their patients? This thesis aims to answer these questions.

To do so, we distributed a redcap survey that asked 48 healthcare professionals for their opinions about the disease's biological, psychological, and sociological characteristics. Participants were of all ages and from all regions in the United States. Most were endocrinologists, though some were generalist MDs or nurse practitioners. The survey included questions about their experiences with the controversy, whether they see themselves as more conservative or liberal regarding diagnosis and treatment, and their opinions on biological and psychosocial aspects of the condition. It also presented the participants with fictional patient cases. The cases presented fictional patients' blood thyroid hormone levels, symptoms, age, weight, and gender. In response, participants were asked how likely they would be to diagnose and treat the fictional patients.

The study's primary goal was to find out whether practitioners disagree with each other. Beyond that, we inferred whether the clinicians tended to follow ACE's recommendations, ACC's recommendations, or another set of recommendations. We were also able to discern common attributes among participants that make similar clinical decisions, such as age, geographical region, and type of degree. Our quantitative results exhibited that the participants significantly disagreed about nearly every facet of the condition. Our qualitative results provided us with their grounds for disagreement.

Stakeholders

Disagreement regarding the condition suggests the possibility of two issues. Firstly, the current standard for diagnosis and treatment may be wrong; some clinicians and scientific organizations suggest it is. Secondly, diagnostic criteria may be applied inconsistently throughout the country. Inconsistent diagnostic criteria could mean that patients would receive different diagnoses and treatments depending on the clinician they see.

If the standards for hypothyroidism diagnosis are wrong - whether it is too stringent or too loose - patients may be diagnosed and treated inappropriately. As the American Medical Association's Journal of Medical Ethics explains, identifying medical standards is essential to physicians' credibility and patients' wellbeing. They explain that “only by applying medical standards of care and evidence-based medicine can inappropriate care be identified in a manner that is credible to physicians and patients... physicians maintain that standard-setting is

necessary for high-quality medical care.”¹³ According to the AMA, if the hypothyroidism standard of care is incorrect, physicians would not have the ability to identify and implement appropriate care in a credible manner.

If the “healthy” range of thyroid hormones used to diagnose the condition is too broad, patients currently deemed healthy may merit diagnosis and treatment for hypothyroidism. This scenario would mean patients are currently underdiagnosed and are living through hypothyroidism’s biopsychosocial consequences without help. If the “healthy” range of thyroid hormones is too narrow, patients currently receiving diagnoses and treatments may not truly need them. This situation would mean patient populations are overdiagnosed and overtreated, which may also impose biopsychosocial consequences. Establishing a precise standard of care for hypothyroidism patients is key to physicians’ success and patients’ wellbeing.

Defining the accurate diagnostic standard is necessary, but applying it uniformly throughout populations of patients is just as critical. If patient populations are receiving different standards of care, some populations must be receiving the wrong one. Though the medical community has not yet identified a diagnostic threshold conclusive enough to garner near-unanimous agreement and patient satisfaction, it will do so one day. It will be essential to identify which populations were receiving inappropriate treatment in the future.

Answering this question of diagnostic criteria and then working to standardize its application is critically important for patients’ physiological, psychological, and sociological well-being. It is also financially relevant to the medical system at large; altering diagnostic criteria would result in a sizable influx or efflux of hypothyroidism patients in need of diagnoses and treatments. Providers, insurance companies, and the government have either lots of money to lose or lots of money to gain as a result.

The Medical System at Large

Changing diagnostic criteria for patients would result in either an influx or an efflux of patients needing diagnosis and treatment for hypothyroidism. If the diagnostic threshold lowers, more patients will need diagnosis and treatment. Providers would have more patients to diagnose and treat, hospitals and clinics would have to schedule more patients, insurance companies and government-sponsored insurance programs would have to support more patients financially, and pharmaceutical companies would have more customers. Alternately, if the threshold rises, providers would have fewer patients to treat, hospitals and clinics would see a free up of scheduling space, insurance companies and programs would not have to support as many patients as they currently do financially, and pharmaceutical companies’ customer base would shrink. The consequences this threshold imposes on the medical system could be gravely expensive for some and massively opportunistic for others.

Patients

The Untreated Patient

Untreated hypothyroidism patients face high biological, psychological, and sociological stakes. Biological consequences can be categorized into five classes of symptoms: lethargy, pain, long-term risks, short-term risks, and fertility. Dealing with these symptoms may prevent patients from meeting biosocial norms such as fertility, sexual functionality, economic productivity, and cosmetic attractiveness.² Failure to meet these societal expectations compound with the condition's tendency to lower serotonin production; this combination often manifests as psychological obstacles such as depression and feelings of low self-worth.²

Some clinicians and scientific organizations contend that the current “healthy” range of thyroid hormones used to diagnose hypothyroidism is too broad. If they are correct, currently undiagnosed patients may merit diagnosis and treatment. This possibility implies that these patients are currently grappling with the biopsychosocial consequences of hypothyroidism without the medical help they need. Patient coalitions stand with this opinion; they argue that the diagnostic threshold for hypothyroidism is too high since many of their members deal with these consequences without hope for receiving treatment.¹⁰

On another note, about 12.5% of Americans (41 million people) were inadequately insured in the first half of 2020.¹⁴ It is estimated that roughly 4% of Americans have hypothyroidism, though most cases are mild.² This statistic implies that a staggering 1.6 million people deal with the biopsychosocial consequences of hypothyroidism without treatment if they are not paying for it out of pocket.

Biological Consequences of Undertreatment

Since the thyroid affects the body systemically, the list of hypothyroidism's physiological consequences is long. Untreated patients' symptoms can be categorized into five classes: lethargy, pain, long-term risks, short-term risks, and fertility.²

As hypothyroidism slows the metabolism, the body's utilization (metabolization) of energy becomes suboptimal. This process manifests as symptoms of lethargy, like chronic fatigue and “brain fog.” Untreated patients describe feeling “out of energy” even after having slept and eaten adequately. Some describe needing to sleep for more than 12 hours to feel functional.⁹

Untreated patients often experience constipation due to the digestive system's slower rate of operation. This slow-down may prevent or discourage proper excretion of waste, leading to an uncomfortable “backup.” Severe bouts of constipation may become painful or dangerous. In some patients, the body does not produce stomach acid quickly enough to digest food properly. This lack of timely stomach acid production may cause bloating, gas, heartburn, and other painful digestive symptoms.²

Therapies like laxatives may provide temporary relief, but they can not serve as a long-term solution. After use, patients usually experience constipation again within a few days. Cycling anti-constipation medications like these can present problems; chronic use may lead to other health issues like dehydration and gut microbiome dysbiosis, and it may worsen patients' patterns of constipation over time. Plus, these medications can become expensive and are often

paid for out of pocket. Faced with these obstacles, many untreated patients live in a perpetual state of painful constipation.²

Hypothyroidism heightens patients' risks of developing other expensive and painful health conditions like obesity, diabetes, atherosclerosis, and myocardial infarction (heart attack). Untreated patients' slowed metabolisms make weight gain challenging to avoid and to combat; consistent weight gain may lead to obesity and other health issues over time. The condition may also lead to insulin resistance, slowed excretion of cholesterol, and increased blood levels of lipoproteins, which increases patients' risk of facing costly, dangerous, and painful conditions like diabetes and heart disease.²

Though the long-term risks are ominous, hypothyroidism's short-term risks may be even more threatening for those with severe cases. Bradycardia, the slowing of the heartbeat, is particularly problematic. Prolonged bradycardia can cause heart failure, fainting, or cardiac arrest, and even death. These risks are not common among most patients, however.²

Fertility complications are another consequence of the disease. Untreated men may experience poor semen quality, low sperm count, erectile dysfunction, and lowered libido, making conception challenging. Untreated women may experience irregular menstrual cycles and imbalanced sex hormone secretions, which can cause other health issues. Some untreated patients become infertile, and many experience miscarriage. According to the American Thyroid Association, higher than average levels of TSH (a thyroid hormone), which usually indicates hypothyroidism, significantly increases patients' risk of miscarriage. Patients with mild to moderate elevations of TSH concentration, 4.5 - 10 mU/L, are 1.8 times more likely to experience miscarriage than healthy women are. Those with severe cases of hypothyroidism, indicated by a TSH concentration of 10 or higher, are 3.95 times more likely to experience miscarriage than healthy women are.¹⁵ Because miscarriage is so strongly linked to hypothyroidism, physicians are required to test pregnant women's TSH levels upon conception.

Sociological Consequences of Undertreatment

Societal stigmatization of infertility, erectile dysfunction, unproductiveness, and perceived unattractiveness may create sociological pressure for untreated patients. Patients may turn to expensive "crutch" therapies to combat their symptoms and meet societal expectations, creating a financial burden that could be avoided if they were to receive hypothyroidism treatment.¹⁶

Patients' grapplings with fertility may create social consequences for patients.¹⁶ Female patients who experience frequent miscarriage or infertility may experience stigmatization. Male patients struggling with infertility due to low sperm count or erectile dysfunction may also grapple with stigma. Chronic fatigue and digestive symptoms may create challenges in the workplace in that constant constipation, sleepiness, and "brain fog" may lead to a lower level of productivity. Decreased productivity can lead to grapplings with societal stigmas of "laziness." Physiological symptoms like hair loss, swelling of the face, and weight gain may create cosmetic concerns for patients struggling with societal pressures to look aesthetically attractive.¹⁶

To combat their symptoms or meet societal standards, untreated or uninsured patients may turn to expensive “crutch” therapies. Patients may choose to use copious amounts of caffeine or stimulants to cope with fatigue. They may turn to expensive medications, laxatives, or other over-the-counter digestive aids for painful digestive symptoms. If they have one, their provider may recommend other expensive drugs or therapies in response to their weight gain and dyslipidemia. Bradycardia (slow heartbeat) may require expensive drugs too. To combat infertility, patients may see fertility specialists who may *also* recommend expensive drugs or therapies. Beyond that, if a patient wishes to combat other cosmetic concerns like hair loss, yet another expensive over-the-counter treatment becomes stacked on their list. Psychological therapies such as psychiatrist and therapist visits can create financial burdens as well. If untreated patients wish to combat their symptoms, a treadmill of financial consequences ensues.

Psychological Consequences of Undertreatment

The physiological difficulties patients experience daily may manifest as psychological challenges in and of themselves, but patients often experience depression for another reason: the condition may slow serotonin production.² Constipation and other digestive issues may amplify this issue; gut issues are correlated with mental health issues.¹⁷

Patients self-report that their physiological and psychological symptoms lower their quality of life. Taken with daily physical and mental obstacles, failure to meet biosocial expectations like fertility, sexual functionality, economic productivity, and cosmetic attractiveness causes many hypothyroidism patients to experience feelings of low self-worth. The condition is unfortunately associated with high rates of suicide and suicidal ideation.^{19, 20} According to the Journal of Psychiatric Practice, hypothyroidism may manifest as acute mania with psychotic features in severe cases.¹⁸ Ample evidence incontrovertibly demonstrates that hypothyroidism creates psychological obstacles for patients.²¹

The Untreated Patient: High Stakes

As patient coalitions repeatedly contend, dealing with these high biopsychosocial stakes without treatment can be challenging and dangerous for patients. If the current diagnostic threshold is too high, groups of patients may currently be experiencing these symptoms without the hope of receiving medical help, which patient coalitions maintain is true. It is critical to physicians’ credibility and patients’ well-being that medical standards do not leave patients to face these obstacles without treatment.

The Overtreated Patient

Some clinicians and scientific organizations contend that the current “healthy” ranges of certain thyroid hormones used to diagnose hypothyroidism are too narrow and that the condition is likely overdiagnosed in America. If they are correct, patients may currently be receiving diagnoses and treatments not physiologically appropriate for them. This possibility implies that these patients are currently grappling with the biopsychosocial consequences of overdiagnosis

and treatment, though the solution to these consequences is usually quite simple: stop or reduce the treatment. Since treatment usually consists of taking pills daily, it is easy to stop treatment. Hypothyroidism patient coalitions claim that patients do not commonly experience this.

Inappropriately diagnosed hypothyroidism patients face biological, psychological, and sociological obstacles, just as untreated patients do. Biological consequences of overtreatment usually include symptoms of *hyperthyroidism*, the opposite of hypothyroidism.²² Dealing with these symptoms may prevent patients from meeting biosocial societal norms such as sexual functionality, economic productivity, and cosmetic attractiveness. Failure to meet these societal expectations compound with overtreatment's tendency to cause anxiety; this combination may manifest as psychological issues. Biopsychosocial stakes are high for overtreated patients, but proper communication of their symptoms to providers is likely to solve these issues since the solution is simple: stop or lower treatment.

Biological Consequences of Overtreatment

If a patient is overtreated, he or she may experience symptoms of *hyperthyroidism*. Symptoms of hyperthyroidism include hyperactivity, insomnia, heat sensitivity, diarrhea, frequent urination, excessive thirst, heart palpitations, weight loss, low libido, and eye problems.²² Providers of hypothyroid medication are taught to look out for these symptoms once patients begin treatment. If the symptoms occur, providers will likely lower the patient's dose or stop treatment altogether. However, if patients do not communicate their symptoms to their provider, they may continue to experience these consequences of their treatment.

These patients' symptoms may be caused by something other than hypothyroidism. If they are treated for hypothyroidism improperly, perhaps the condition that is truly causing their symptoms is undiagnosed and untreated. Depending on what type of condition the provider is missing, patients could face dangerous consequences from misdiagnosis.

Sociological Consequences of Overtreatment

Receiving a hypothyroidism diagnosis may cause sociological consequences for patients. If those in the patients' community are aware of hypothyroidism's consequences, such as infertility or lowered productivity, patients could face stigmatization by community members.²² However, patient coalitions do not express that this is a common narrative since patients can choose to keep their diagnosis private.

Physiological symptoms incurred by overtreatment may prevent patients from meeting biosocial expectations such as sexual functionality, economic productivity, and cosmetic attractiveness.²² Overtreated patients may experience lowered libido, an issue for meeting societal expectations of sexual functionality. Hyperactivity and diarrhea may prevent patients from being productive in the workplace. Additionally, severely overtreated patients may experience thyroid eye disease, which causes eye irritation and a widening of the eyes at rest. This eye disease may be interpreted as cosmetically unattractive. If treatment is stopped, the eye condition will usually go away in time.



Thyroid eye disease caused by severe overtreatment²³

Psychological Stakes

Physiological symptoms of overtreatment may cause psychological obstacles.²² If patients feel that their symptoms prevent them from meeting biosocial expectations, this may cause them to experience feelings of low self-worth. Further, overtreatment may cause anxiety and hyperactivity - presenting another obstacle for overtreated patients.

The Overtreated Patient: High Stakes, Clear Solution

Overtreatment may be physiologically, sociologically, and psychologically difficult for patients. If the current diagnostic threshold is too low, groups of patients may experience these symptoms until their providers change their treatments. However, this narrative is uncommon. Patient coalitions do not express this to be a problem, and providers seem to respond quickly if patients begin to experience symptoms of overtreatment. It is essential to physicians' credibility and to patients' well-being that medical standards do not create these obstacles for patients, regardless of the clarity of the solution.

High Stakes for Patients

Prestigious organizations such as the AACC, studies by NHANES, groups of physicians, and patient coalitions contend that the diagnostic threshold for hypothyroidism may be incorrect, suggesting that the medical community may currently be applying incorrect medical standards to patients. As the Institute of Medicine and the American Medical Association emphasize, correct medical standards are critical to both patients' wellbeing and physicians' credibility. If the diagnostic standard for hypothyroidism is indeed incorrect, patients' biopsychosocial well-being may be in jeopardy. Further, if different standards are applied to different patients, some patients must be receiving the incorrect standard. This uneven application of standards would imply a shortcoming in healthcare equity.

The stakes of being undiagnosed or overdiagnosed are high for patients. Being left without treatment creates uncomfortable and painful physiological symptoms that manifest as psychosocial challenges, which, according to patients, significantly lower their perceived quality of life and self-worth. Overtreatment also causes uncomfortable and painful symptoms that may

create psychosocial obstacles, but this is usually easier to solve since stopping treatment prevents these issues.

Grounds for Controversy

Biological, psychological, and sociological aspects of hypothyroidism provide grounds for disagreement about diagnostic criteria. Some clinicians point to both biochemical and psychosocial characteristics of the condition to argue for a more liberal attitude toward diagnosis and treatment. Others are more cautious of doing so - these clinicians point to both biochemical and psychosocial characteristics of the condition to argue for a more conservative attitude toward diagnosis and treatment.

Psychosocial Grounds for Controversy

Patient coalitions, as noted earlier, present an unambiguous stance: they want treatment, citing both physiological and psychological improvements upon receiving medical attention. Sociological studies amplify this; they exhibit that hypothyroidism patients almost always desire diagnosis and treatment. The consistency of these sociological studies' results taken with the "blogosphere" implies that most hypothyroidism patients believe the pros of diagnosis and treatment outweigh the cons.

Liberal-leaning providers emphasize the positive psychological and sociological aspects of diagnosing and treating borderline cases, while conservative-leaning providers emphasize the negative aspects of diagnosing and treating borderline cases. The validity of both sides' points provides ample grounds for controversy.

Psychosocial Grounds for Liberal Diagnosis and Treatment

Psychosocial arguments for liberal-leaning diagnosis and treatment include potential improvement of patients' mental health, patients' potentially increased ability to meet biosocial norms, and patients' feelings of validation upon receiving diagnoses and treatments.

Treatment of "borderline" cases of hypothyroidism often improves these patients' symptoms. Patients report that this improvement in symptoms upgrades their quality of life for a few reasons. Firstly, they feel better - the lethargy and pain they experience usually subsides at least in part. Eliminating or reducing frustrating health struggles may improve patients' psychological well-being. Secondly, improvement of symptoms tied to biosocial norms may improve their feelings of self-worth. With treatment, fertility, sexual functionality, and productivity levels often improve. Treatment may also restore hair growth, regulate weight, and reduce facial swelling, which patients say helps alleviate cosmetic concerns. Beyond that, treatment of these borderline cases has been shown to help remedy depression.²⁴ As patient coalitions echo, these borderline-case patients desire treatment in hopes of alleviating the psychological and sociological implications of hypothyroidism.

Studies such as Winther et al.'s "Disease-Specific as Well as Generic Quality of Life Is Widely Impacted in Autoimmune Hypothyroidism and Improves during the First Six Months of

Levothyroxine Therapy” evidence patients’ improved quality of life upon treatment. It strongly suggests that receiving treatment benefits hypothyroidism patients psychologically.²⁴ The study examined hypothyroidism patients’ self-reported quality of life before and after treatment compared to a normal-thyroid control group. The majority of the patients’ quality of life scores improved by the first six weeks of starting the medication and continued to improve for the entirety of the study, which was six months long. The patients’ rates of depression decreased, and cosmetic concerns improved over the treatment period.

Besides alleviating symptoms that obstruct patients’ psychological health, another aspect of receiving diagnosis and treatment improves borderline patients’ mental health: validation. Jane Milliken and Herbert Northcott’s study titled “Seeking Validation: Hypothyroidism and the Chronic Illness Trajectory” emphasized the negative psychological and social impacts that *not* being diagnosed brings upon a patient.¹⁶ Patients explained that being denied a diagnosis makes them feel “crazy,” in that doctors implied their symptoms were psychosomatic (“in their head”) or not worthy of treatment. The study concluded that hypothyroidism “follows a U-shaped trajectory;” first, patients’ self-image is damaged because their symptoms are brushed off as psychosomatic by providers. When and if the patients receive diagnoses and treatments, their self-image improves, mainly because they feel validated. Having their symptoms validated by a doctor that “appreciates that symptoms are real and require treatment” is what seemed to be the driving factor of enhanced self-image.

Arguments for more liberal diagnosis and treatment emphasize the psychosocial benefits of giving borderline patients a diagnosis and treatment plan. Patients’ symptoms may improve, which may eliminate some psychological stress in and of itself. They may be able to meet biosocial expectations more efficiently, such as economic productivity and fertility. Cosmetic concerns may subside as well, and depression often improves. Most impactful, however, are patients’ feelings of validation upon receiving diagnosis and treatment. Because their provider’s diagnosis indicates that someone “appreciates that symptoms are real,” patients’ feelings of being deemed “crazy,” “lazy,” or “dramatic” subside, and self-image improves.

Psychosocial Grounds for Conservative Diagnosis and Treatment

Psychosocial arguments for conservative-leaning diagnosis and treatment practices include avoiding stigmatization that comes with diagnoses, biological risks of overtreatment that cause psychological stressors such as anxiety, and difficulties associated with acquiring medication.

Overtreatment may cause physiological symptoms that patients find psychologically challenging to deal with. If patients are significantly overtreated, they may begin to experience hyperthyroidism symptoms, though this is uncommon. These symptoms may prevent patients from meeting biosocial expectations such as fertility and productivity. Further, this overtreatment can cause anxiety, yet another psychological hurdle for overtreated patients. The solution to these overtreatment symptoms is relatively simple: stop treatment or lower the dose.

Receiving a diagnosis may cause psychological obstacles in and of itself. It may suggest to patients that something is “wrong” with them. This argument does not seem to apply to hypothyroidism, however, since most patients desire a diagnosis.

Linda Hunt’s “Changing Diagnostic and Treatment Criteria for Chronic Illness: A Critical Consideration of Their Impact on Low-Income Hispanic Patients” explores potential negative impacts of diagnoses for patients - in her case, low-income Hispanics with diabetes.²⁵ She explains, “it is important to consider whether these efforts” to improve low-income Hispanics’ health through diagnosis “may be promoting overdiagnosis and overtreatment, drawing them into an expensive chronic patient role with uncertain benefit.” Barriers to accessing health resources made reaching the goal number for the threshold difficult for these patients, which can, in turn, create other obstacles for the patients. Hunt’s sociological study shows how lowering the hypothyroidism diagnostic threshold could theoretically negatively impact patients. Prescriptions may be difficult for patients from marginalized communities to attain.

Though the solution to challenges created by overtreatment is relatively simple, the psychosocial consequences remain significant enough for some providers to avoid diagnosing and treating borderline cases. These conservative-leaning providers cite physiological risks of overtreatment’s potential to create psychological stressors such as anxiety, a lack of productivity, and low libido. Additionally, receiving any diagnosis in and of itself may create psychological obstacles for patients, such as believing there is something “wrong” with them and financial struggles. Though valid, these reasons contradict patient coalitions’ narratives.

Biological Grounds for Controversy

Physiological and biochemical aspects of the condition constitute most of the weight of the attention within the medical community. The following list of biological disagreements comprise aspects of the disease that seem to garner the most attention in the medical community. However, this list is not comprehensive.

Biological Disagreement #1: Establishing a Healthy TSH Range

Healthcare professionals disagree about several thyroid hormone ranges. Establishing a standard range for thyroid-*stimulating* hormone, TSH, is a hormone of particular focus. A basic understanding of TSH’s role in the body is key to grasping the controversy.

TSH, or thyroid-stimulating hormone, does as it is named: it stimulates the thyroid to produce thyroid hormones such as thyroxine (T4) and triiodide (T3), which control the body’s metabolic rate.² TSH can be thought of as a call for backup; when the body senses that there is not enough thyroid hormone in the body, it sends TSH to the thyroid to tell it to produce more thyroid hormones. High TSH levels usually indicate that the body needs more thyroid hormones - an inadequacy may be at play. Low TSH levels usually indicate that the body does not need more thyroid hormone, meaning the thyroid produces plenty of it.

Because hypothyroidism occurs when the body lacks thyroid hormones, high TSH levels usually indicate hypothyroidism. Therefore, TSH is the primary measurement used to diagnose

the condition.² Some argue that TSH alone is not enough to diagnose the condition - they say the level of thyroid hormones in the bloodstream should also be tested.

The “healthy” range of TSH - how much thyroid stimulation the body is calling for - is what healthcare professionals primarily disagree over. Some see certain TSH levels as “code red,” while others see them as “smooth sailing.” As mentioned previously, prominent organizations like the AACE, the AACC, and the IQEHC disagree on the subject.

Arguments for Contraction of the Healthy TSH Range

The primary biological argument for narrowing the healthy TSH range, which would lead to an increase in diagnoses - a liberal-leaning perspective - is that the TSH reference range distribution is abnormal.

The TSH reference range distribution is statistically irregular. The median TSH level, 1.5, falls far below the middle of the current reference range, 0.5 - 4.12.⁵ Medians of other conditions’ lab tests fall near the middle of reference ranges. Statisticians argue that this is an essential measure of a reference range’s accuracy. The AACC cites this abnormal data distribution as their primary argument for narrowing the TSH reference range.

An NHANES study introduced another data-based inconsistency.⁸ The study surveyed 14,000 Americans’ TSH and thyroid antibody levels. If present in significant amounts, thyroid antibodies indicate Hashimoto’s disease - an autoimmune disease that causes the patient’s body to attack his or her thyroid. This autoimmune attack often causes slowed or impaired production of thyroid hormones, leading to a lack of thyroid hormones in the body: hypothyroidism. NHANES’s study found that patients who fell within the current “healthy” TSH reference range often tested positive for antibodies. Over 20% of those at the high end of the current reference range (around 4 mU/L) had the antibodies.⁸ NHANES boldly concluded that although population studies cannot determine TSH reference ranges because “occult” thyroid dysfunction skews the upper limit (see “Subtypes of Hypothyroidism”), the “healthy” TSH reference range is likely inaccurate.

These studies indicate that patients who fall near the upper end of the reference range should not be deemed healthy. The data skew and NHANES’ antibody findings constitute many liberal-leaning practitioners’ arguments for narrowing the healthy TSH range. Narrowing it would lead to an increase in diagnoses.

Arguments for Preserving or Expanding the Current TSH Range

The primary argument against narrowing the current TSH range is that there is a lack of evidence for clinical benefits of lowering TSH. This argument stands in opposition to borderline patients’ testimonies that they feel better after receiving treatments. Some practitioners argue that treating a TSH value in and of itself is just medicalizing a biochemical finding - it will not necessarily lead to clinical benefits. Many practitioners respond to AACC’s argument with this counterpoint.

Biological Disagreement #2: Subtypes of Hypothyroidism

Hypothyroidism comes in many forms. Subtypes of the condition add another layer of complexity to the controversy and render diagnostic criteria complicated to standardize. A brief explanation of what the subtypes are is key to understanding disagreements over them.

Inadequacies of only *some* thyroid hormones characterize these other forms of hypothyroidism - some of the patients' hormones fall in the healthy reference ranges, but others do not. These patients often experience symptoms of hypothyroidism, but they are not considered to have overt hypothyroidism. Instead, these subtypes are called "subclinical hypothyroidism" and "occult thyroid disease."

Patients with "occult" thyroid disease lack the thyroid hormones T4 and T3 despite having normal TSH levels.⁵ These "normal" TSH levels indicate that the body does *not* signal the thyroid to produce more T4, even though the body lacks it. The mystery, hence its name, "occult," regards why TSH does not elevate in response to a lack of thyroid hormone. It may be due to damage to the gland that produces TSH, the pituitary gland. This condition is called central or secondary hypothyroidism.²⁶ Because occult thyroid disease patients' TSH levels fall within the current "healthy" reference range - even though their other thyroid hormones do not - they are not commonly diagnosed or treated unless their provider chooses to check their pituitary gland. Testing the pituitary gland can be expensive.

Some argue that because the body does not signal for more thyroid hormone when it "lacks" it, that lower T3 and T4 levels are appropriate for the individual at hand. Others note that perhaps their body cannot produce enough TSH - a malfunctioning signal. Alternatively, perhaps the current "healthy" range is wrong, and the patient's "normal" TSH *is* elevated, as NHANES suggested.⁸

Subclinical hypothyroidism is another version of abnormal thyroid function that is not consistently diagnosed or treated.⁷ In these cases, thyroid hormones T3 and T4 fall in healthy ranges, which are disputed too. These patients' TSH levels are elevated, however. Put simply, the body calls for more thyroid hormone, though according to current standards, it does not need it. These patients commonly experience hypothyroidism symptoms.

Arguments for Diagnosing and Treating Subclinical or Occult Hypothyroidism

Arguments for treating subclinical or occult hypothyroidism are primarily psychosocial in that these patients desire treatment and often feel better with it. Additionally, fertility is an important factor: females with TSH levels above 2.5 are treated if they want to become pregnant due to high TSH's correlation with miscarriage. This clinical standard for pregnancy is not debated, and therefore for the sake of simplicity, will not be discussed below. One other argument for treating subclinical hypothyroidism exists, though clinicians' opinions about it vary: higher TSH values are correlated with heart problems.

Higher but clinically normal TSH levels are strongly correlated with heart issues like atherosclerosis and cardiovascular disease.⁵ A meta-analysis of 10 longitudinal studies of "subclinical" hypothyroidism, which excluded patients with atherosclerotic cardiovascular

disease at baseline, showed hypothyroidism was associated with a relative risk of coronary heart disease of 1.2 when all studies were combined.²⁷ Another meta-analysis of 15 studies that included over 2500 participants with subclinical hypothyroidism showed elevated odds ratios for the incidence of atherosclerotic cardiovascular disease and cardiovascular all-cause mortality for those under 65 years, but not for those over 65 years.²⁸ Studies like these, of which there are several, demonstrate that heart issues are correlated to TSH levels falling within the current “healthy” range.

Arguments Against Diagnosing and Treating Subclinical or Occult Hypothyroidism

Those *against* narrowing the TSH range say symptom confusion is the culprit of the controversy. A study by the Institute for Quality and Efficiency in Health Care concluded that subclinical hypothyroidism is likely *not* the cause of the symptoms subclinical hypothyroidism patients complain about.⁷ Instead, they assert, their symptoms are probably due to other issues. The study does acknowledge that treatment should come down to personal preference; they claim that if levothyroxine treatment (the most common type of hypothyroidism drug) does not work for the patient - though studies have shown levothyroxine is not very effective - then “it is not the thyroid causing their problems.”

The study’s conclusion regarding levothyroxine is questionable because treatments other than levothyroxine exist. Perhaps their argument could be adapted to, “if no hypothyroidism medication works after trying types other than levothyroxine, then the patients’ symptoms are likely caused by something other than hypothyroidism.”

Clinicians who lean conservatively in their practice respond to the heart issue argument by explaining that no causation has been determined. Although high TSH levels are correlated to heart issues, there is no evidence that high TSH levels cause heart issues. Further, there is no evidence that treating TSH will fix their heart issues either.

Other Biological Disagreements

The debate is not limited to these two disagreements, though much of it is focused on them. For the sake of simplicity, we will briefly touch on a few other points of controversy. These include the age variable, testing other hormones, and treatment methods.

The Age Factor

Data asserts that TSH naturally rises with age, implying that reference ranges should be adapted to age as well. The median TSH level for people over 60 is drastically higher than it is for young adults. So, some argue, a TSH level on the higher end of the reference range may be appropriate for older patients - but not for younger patients. Younger patients whose TSH levels fall near the upper end of the reference range - near the median for someone over 60 - often do not receive treatment since they fall within the current reference range. According to some, this gradual rise of TSH with age constitutes grounds for adapting the reference range to account for age.⁸

Testing Other Hormones

Which thyroid hormones to measure is also a key question in the controversy. Some argue that TSH should not be the only measure used to make a diagnosis and that the hormones the thyroid produces, like T4, should be included in the measurement, too.⁴ They suppose that occult or subclinical hypothyroidism may be missed if TSH is the only hormone tested. In other words, if the signaling system (TSH) is malfunctioning - and only the signal is tested for - patients who truly lack thyroid hormone could be presumed healthy. Testing T3 and T4 as well would catch these cases. Some say other hormones in addition to T4 should be tested as well.⁹ Explanations of these hormones are excluded from this paper for the sake of simplicity.

Types of Treatment

Treating hypothyroidism is a profoundly political issue within the medical community. Levothyroxine, the most common pharmaceutical drug given to hypothyroidism patients, is a synthetic T4 replacement. T4 is just one type of thyroid hormone. Other drugs combine replacements of another thyroid hormone, T3, in addition to the replacement of T4. Some drugs are synthetic, while others are made from animals' hormones. Patient coalitions typically argue for the use of animal-derived treatments that combine T3 and T4, but there is contradictory evidence for this. The issue is polarizing and deeply political in that pharmaceutical companies have a significant financial stake in it.

Methods

The Survey

We created and distributed a redcap survey designed to garner clinicians' opinions on various facets of the hypothyroidism debate. For organizational purposes, we divided the survey into ten parts for analysis:

1. Experience With the Controversy
2. Evolution of Standards
3. Opinions on Organizations' Standards
4. Opinions on Arguments for Change
5. Which Hormones Do They Use?
6. Importance of Hormones Other Than TSH
7. Ranges of Hormones
8. Patient Cases
9. Psychosocial Factors
10. Conservative or Liberal Practices?

Though the answers leave room for several types of analysis, we focused on answering two questions: do the participants disagree, and if so, what are their conflicting arguments? Our quantitative results exhibited that the participants significantly disagreed about nearly every facet of the condition. Our qualitative results provided us with their grounds for disagreement.

Survey Distribution

We distributed the survey through emails. Participants' emails were collected by searching through public hospital, clinic, and university directories. We sent out 750 emails and received 48 responses. The emails were sent to practitioners from hospitals, clinics, and universities in every state in America.

The subject line of each email read: "Asking For Your Opinion: Vanderbilt Hypothyroidism Study." The body of the email read:

Hello (Dr. X),

My name is Lana Schwartz, and I am an undergraduate researcher from Vanderbilt University. Dr. Allison Leich-Hilbun and I are conducting an anonymous survey of healthcare professionals about opinions on hypothyroidism and thyroid hormone ranges. There are no correct answers in the survey. The goal is to discover which opinions on hypothyroidism are most common among healthcare professionals. We hope to learn about varying diagnosis and treatment practices throughout the field.

Your responses will be completely anonymous. All responses will be recorded in a password-protected file that only Dr. Allison Leich-Hilbun and Lana Schwartz will have access to. The survey will take about **7 minutes** - however, you may exit the survey at any time.

Thank you for your consideration - we appreciate that you are willing to share your opinion with us. The link to the survey is here: <https://redcap.vanderbilt.edu/surveys/?s=XAPT8LLA77>

If you have any colleagues that you believe would be willing to take the survey, please consider sending the link to them as well. Thanks!

Sincerely,

Lana Schwartz
Vanderbilt University
310-422-2189
Lana.r.schwartz@vanderbilt.edu

Dr. Allison Leich-Hilbun
Vanderbilt University
Allison.leich.hilbun@vanderbilt.edu

Before reviewing the results, we came up with hypotheses about how the clinicians would answer each question. We reviewed the responses using data interpretation tools on RedCap and in Excel. MatLab was used to create statistical inferences.

Hypotheses, Results, and Inferences

In each section in the Hypotheses, Results, and Inferences section, we present what we asked in the survey, why we asked it, our hypotheses, the results, and implications of the results. Afterward, we condense the information into statistical analyses that exhibit trends in the clinicians' answers.

Who Are Our Participants?

At the beginning of the survey, participants were asked a series of questions about their background. The answers to these questions were used to look for similarities in the background of participants who answered the questions similarly.

1: "What kind of healthcare professional are you?"

- a) MD, not an endocrinologist: 12.5%
- b) MD, an endocrinologist: 83.3%
- c) PA: 2.1%
- d) NP: 2.1%
- e) Pharmacists: 0%
- f) Other: 0%

The vast majority of our participants were endocrinologists.

2: "Which condition do you find most fulfilling to help patients with? (optional)"

We asked this question to spark positive thoughts for participants before they began answering the bulk of the survey.

3: "Which region of the country do you practice medicine in?"

- a) West coast: 25%
- b) Southwest: 8.3%
- c) Southeast: 37.5%
- d) Midwest: 25%
- e) East coast: 4.2%

We attempted to recruit participants from all regions of the country, but response rates from the east coast and southwest were low.

4: "Which type of area do you practice medicine in?"

- a) City with a population above 1 million: 50%
- b) City with a population between 100,000 and 1 million: 37.5%
- c) City with a population between 50,000 and 100,000: 8.3%
- d) City with a population between 10,000 and 50,000: 2.1%
- e) Town with a population under 10,000: 2.1%

We attempted to recruit participants from both urban and rural areas. Response rates from rural areas were low.

5: “How old are you?”

- a) 18-24: 2.1%
- b) 25-34: 6.4%
- c) 35-44: 23.4%
- d) 45-54: 36.2%
- e) 55-64: 12.8%
- f) 65-74: 17%
- g) 75+: 2.1%

We attempted to recruit participants from several age groups. The majority of our participants were in their forties.

Part One: Experience with the Controversy

Questions and Hypotheses

To gauge clinicians’ experience with the controversy in their own practices, we asked participants three questions:

1: “Have your patients received diagnoses from other healthcare professionals that you feel were inappropriate? If so, how often do you see this?”

- a) Always
- b) Usually
- c) Sometimes
- d) Not usually
- e) Never

2: “Do you feel that you and your peers commonly agree on hypothyroidism diagnosis?”

- a) Always
- b) Usually
- c) Sometimes
- d) Not usually
- e) Never

3: “Do you feel that you and your peers commonly agree on hypothyroidism treatment?”

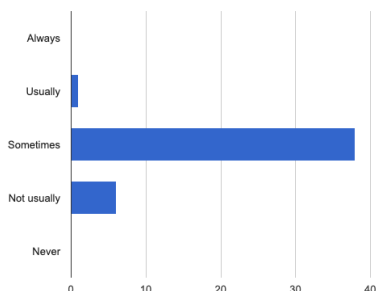
- a) Always
- b) Usually
- c) Sometimes
- d) Not usually
- e) Never

Answers to these questions imply whether 1) clinicians commonly disagree with clinicians from other practices - ones that have previously diagnosed or treated their new patients, and 2) whether clinicians commonly disagree with those in their professional circles, their “peers”. If so, did they disagree about diagnosis or about treatment? In light of the controversy’s breadth, we hypothesized that clinicians would have at least sometimes disagreed with both their peers and clinicians who formerly treated their patients.

Results

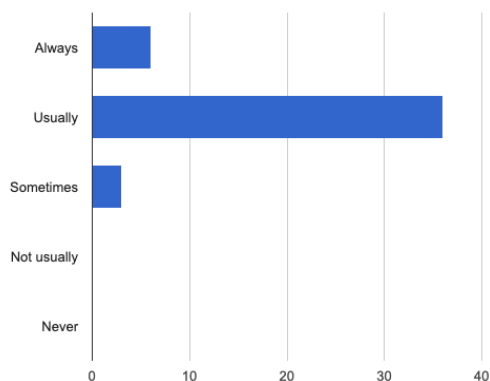
Question 1: “Have your patients received diagnoses from other healthcare professionals that you feel were inappropriate? If so, how often do you see this?”

Usually 2.2%, Sometimes 84.4%, Not usually 13.3%



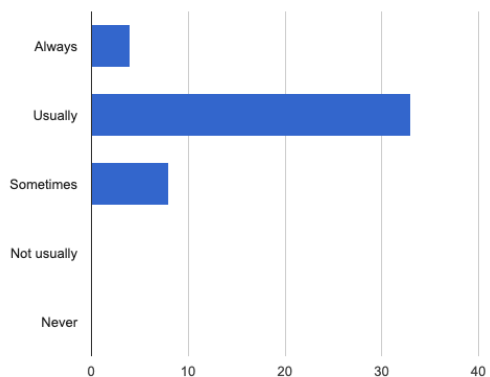
The majority of participants, 85% of them, sometimes disagree with providers that have formerly seen their new patients - providers from other practices. This statistic implies the existence of disagreements between clinics.

Question 2: “Do you feel that you and your peers commonly agree on hypothyroidism diagnosis?” *Always 13.3%, Usually 80%, Sometimes 6.7%*



The majority of participants, 80% of them, usually agree with those in their professional circles about diagnoses. This statistic implies that providers working in the same clinic usually agree with each other regarding diagnosis.

Question 3: “Do you feel that you and your peers commonly agree on hypothyroidism treatment?” *Always 8.9%, Usually 73.3%, Sometimes 17.8%*



The majority of participants, 73.3%, usually agree with those in their professional circles about treatment. This statistic implies that providers working in the same clinic usually agree with each other regarding treatment, but not as often as they do about diagnoses.

Inferences

These results imply that providers tend to agree with peers working in their same clinic but disagree with providers from other clinics. They agree with their peers about diagnosis more often than they agree about treatment, however. These answers directly indicate the existence of disagreement among practitioners regarding hypothyroidism, in that practitioners sometimes see the work of patients' previous providers as inappropriate.

Part Two: Evolution of Standards

Questions and Hypotheses

Conflicting scientific opinions exhibit that the science currently referenced to diagnose and treat patients is being challenged, at least by some. We wanted to gauge clinicians' opinions on the science that constitutes current diagnostic standards. To do so, we asked: "What degree of confidence do you have in modern research's ability to diagnose hypothyroidism accurately?"

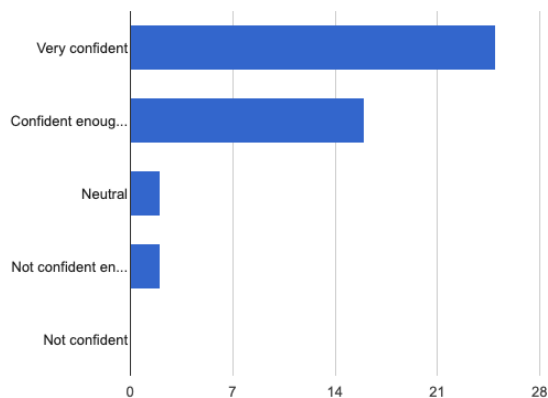
- a) Very confident
- b) Confident enough, but there is more to learn
- c) Neutral
- d) Not confident enough, there is more to learn
- e) Not confident

Answers to this question might imply whether clinicians feel that their current practices will evolve with new research. Do they regard the current standard as fact or as a robust theory? We presupposed that most participants would mark "confident enough, but there is more to learn." There is always more to learn in science, but they are confident enough to diagnose and treat patients. Perhaps those who argued that current standards should change would be unlikely to mark "very confident."

Results

"What degree of confidence do you have in modern research's ability to diagnose hypothyroidism accurately?"

Very confident: 55.6%, Confident enough but there is more to learn: 35.6%, Neutral: 4.4%, Not confident enough, there is more to learn: 4.4%



The majority of clinicians, 56%, feel very confident in the current scientific basis for hypothyroidism diagnosis and treatment, meaning they feel their practices rely on sturdy science. About a third feel confident but argue there is more to learn. About a tenth do not feel confident in modern research.

Inferences

These statistics imply that about half of providers regard current standards as factually sound and unlikely to change. Another third feels confident but argues there is more to learn; perhaps they are open-minded to the idea that standards will evolve in light of discoveries. The small group that answered “neutral” or “not confident enough” may feel that the basis of current standards is on shaky ground.

The rest of the survey indicated that those who answered “very confident” disagreed with each other. For example, some participants said they were “very likely” to diagnose and treat an example patient, while others said they were “very unlikely” to diagnose and treat that same patient (see “Cases”). This discrepancy implies that modern research is being interpreted and applied in contradictory ways. Therefore, the science that modern standards rely on must not be indisputable enough to provide unambiguous diagnostic standards. Therefore, the confidence these clinicians indicate they hold in modern research must regard confidence in their personal interpretation of it, rather than what the science means to other providers. Either that or the clinicians are not aware that modern research is being interpreted and applied in contradictory ways.

These findings directly indicate the existence of disagreement among practitioners regarding the stability of diagnostic criteria for hypothyroidism.

Part Three: Opinions on Organizations’ Standards

Questions and Hypotheses

To gauge clinicians’ opinions about organizations’ recommended TSH ranges, we asked three questions:

The first question asked for their opinion on AACE’s standard, though we did not indicate that the range came from AACE:

1. “In your opinion, would you say that 0.5 - 4.12 is an appropriate range for TSH?”

- a) Strongly agree
- b) Agree
- c) Neutral
- d) Disagree
- e) Strongly disagree

The second question asked if they believed the AACE's range should change, though we did not indicate that the range came from AACE:

2. "In your opinion, should this clinical range for TSH, 0.5 - 4.12, be expanded or contracted for the diagnosis of hypothyroidism?"

- a) Expanded
- b) Contracted
- c) Leave as is

The third question asked what clinicians thought of AACC's argument for a narrower TSH range:

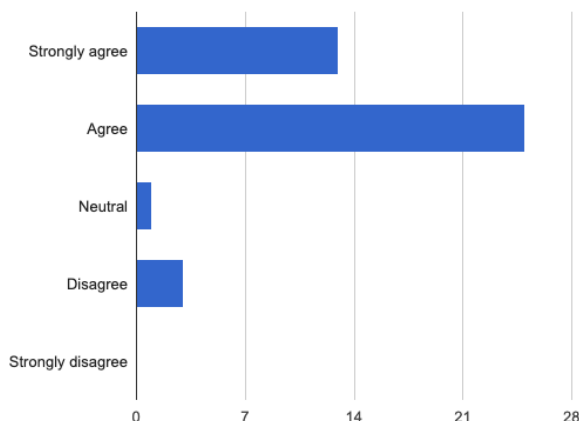
3. "The National Academy of Clinical Biochemists [now known as the American Academy of Clinical Chemistry] indicated that 95% of individuals without evidence of thyroid disease have TSH concentrations below 2.5. Therefore, they assert that the upper limit of the TSH reference range should be lowered to 2.5. Do you agree that the data skew warrants this reduction?"

- a) Strongly agree
- b) Agree
- c) Neutral
- d) Disagree
- e) Strongly disagree

Answers to these questions might imply whether most clinicians think AACE's range should contract, expand, or stay the same. It may also imply whether they see AACC's argument as valid. We hypothesized that clinicians' answers to these questions would vary significantly but that most would lean toward agreeing with the standard they were clinically taught (AACE's old standard, 0.5 - 4.5).

Quantitative Results:

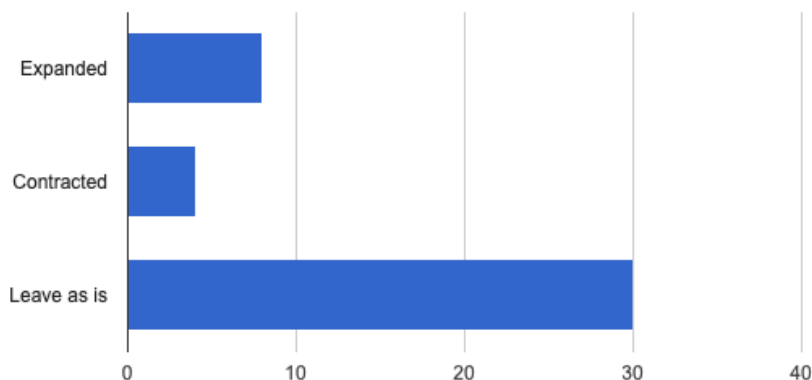
Question 1: "In your opinion, would you say that 0.5 - 4.12 is an appropriate range for TSH?"
31% Strongly Agree, 59.5% Agree, 2.4% Neutral, 7.1% Disagree



Less than 10% of participants disagreed with AACE's standards, implying that they see it as an appropriate standard. This result contradicts the following two questions' results.

Question 2: “In your opinion, should this clinical range for TSH, 0.5 - 4.12, be expanded or contracted for the diagnosis of hypothyroidism?”

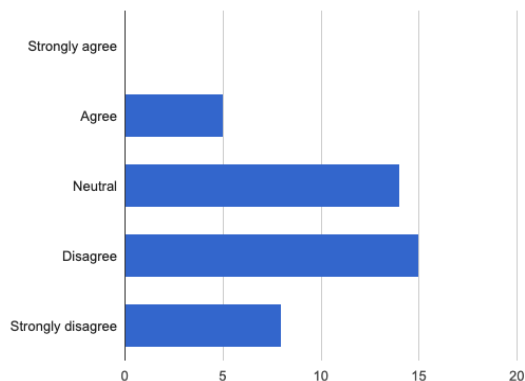
19% Expanded, 9.5% Contracted, 71.4% Leave as is



About a third of participants marked that AACE’s standard should change. More professionals indicated that it should be expanded rather than contracted. This result indicates that only 70% of participants think AACE’s range should remain as is, contradicting the previous question’s result, which indicated that roughly 90% think AACE’s range is appropriate.

Question 3: “The National Academy of Clinical Biochemists [now known as the American Academy of Clinical Chemistry] indicated that 95% of individuals without evidence of thyroid disease have TSH concentrations below 2.5. Therefore, they assert that the upper limit of the TSH reference range should be lowered to 2.5. Do you agree that the data skew warrants this reduction?”

Agree 11.9%, Neutral 33.3%, Disagree 35.7%, Strongly disagree 19%



Clinicians’ reactions to AACC’s argument vary widely. This result contradicts the results of the previous two questions as well. Nearly half of the participants were neutral to or agreed with the AACC’s argument for contraction of AACE’s range. This finding contradicts the results of the previous question, which showed that only 10% of participants believed AACE’s range should contract, as the AACC suggests it should.

Inferences from Quantitative Results

On the first question, only 10% of the participants indicated that AACE's range is inappropriate. Yet on the second question, roughly 30% indicated AACE's range should change. So, a fifth of the participants see AACE's range as appropriate but also argue it should change. Perhaps this discrepancy is due to varying interpretations of the word "appropriate." Alternatively, the participants could believe that the range is appropriate but that an ideal range would look different.

The first two questions' results indicate that at least 70% of the participants believe the range should be left as is. However, the third question presents yet another contradiction. Nearly half of participants were either neutral to or agreed with AACC's argument for contracting AACE's range. This finding contradicts the results of the previous questions, which showed that only 10% of participants indicated that AACE's range should contract. This discrepancy could be explained by participants who selected "neutral." 12% selected "agree," which is close to the 10% who said AACE's range should contract. Perhaps those who selected neutral do not practice in accordance with a strict range. Maybe they are open to an alteration in the range but follow AACE's clinical standards for now.

Regardless of their reasoning, the variety of responses to AACC's recommendations directly indicates disagreement among practitioners regarding hypothyroidism diagnosis.

Qualitative Results:

On question 3, participants had the option to leave an explanation for their reasoning. Question 3: "The National Academy of Clinical Biochemists [now known as the American Academy of Clinical Chemistry] indicated that 95% of individuals without evidence of thyroid disease have TSH concentrations below 2.5. Therefore, they assert that the upper limit of the TSH reference range should be lowered to 2.5. Do you agree that the data skew warrants this reduction?" *Optional: Please explain if you would like to.*

Under "strongly disagree" and "disagree," several participants asserted that there needs to be evidence for the benefit of lowering TSH, meaning the data skew alone does not merit narrowing the reference range. They wrote:

- *"Why medicalize a lab result without strong evidence for benefit"*
- *"I would also require that there be evidence that treatment was beneficial"*
- *"This will lead to treatment that has not been studied for therapeutic effect. We will likely give LT4 without knowing that it actually helps in any measurable way other than TSH numbers."*
- *"Before we call something abnormal it is important to show that it is associated with clinical abnormalities and that treatment results in benefit. Following their definition, we would be treating a lot more people with no clear evidence that they would benefit."*

One participant who selected "strongly disagree" answered: *"Biochemists do not treat patients."* It is unclear whether this is an emotional response - perhaps the participant means to indicate the importance of observing clinical symptoms. Regardless, the comment most definitely exhibits the polarity and animosity behind the controversy.

Under “disagree,” a participant brought up the importance of patients’ ages and other hormones for context. They wrote: [the AACC’s range is] *“likely appropriate for younger patients, but not necessarily for older patients. Again, T4 is relevant here as normal T4 would not need treatment.”*

Participants that selected “neutral” were interested to learn more - they wrote: *“they should conduct good population studies and then present the evidence to the scientific community for discussion,”* and *“not educated enough to weigh in.”*

A participant that selected “agree” explained their reasoning, citing the inadequacy of old cohorts used to define current standards: *“ranges of TSH and free T4 are both too broad, they are likely left over from older cohorts that participated in the lab testing, but in whom thyroid disease was not excluded.”*

Qualitative Inferences:

The qualitative data provided us with reasons behind clinicians’ opinions. First and most commonly, participants felt that the AACC’s argument relied too heavily on data skew; these clinicians explained that evidence for clinical benefits of lowering TSH was needed to make their claim. Another participant’s argument seemed to imply that the AACC’s argument is irrelevant since biochemists do not treat patients, though this argument seems to be an outlier.

Alternatively, some supported the AACC’s argument by asserting that the old cohorts used to set current diagnostic standards are obsolete or inaccurate, as NHANES’s study indicated. Lastly, the age argument came into play as well. This qualitative data further illustrates the breadth of disagreement among practitioners.

Part Four: Opinions on the Arguments for Change

Questions and Hypotheses

Beyond the discussion of numerical ranges for TSH, we looked to gauge what clinicians thought about three arguments commonly made against the current range: heart issues, age, and TSH’s diurnal fluctuation (TSH levels vary throughout the day).

The first question addressed the heart issue argument.

1: “To what extent do you agree with this statement: higher but clinically normal TSH levels are strongly associated with heart issues like atherosclerosis and cardiovascular disease - therefore, the TSH reference range should be lowered.”

- | | |
|-------------------|----------------------|
| a) Strongly agree | d) Disagree |
| b) Agree | e) Strongly disagree |
| c) Neutral | |

The second question addressed awareness of TSH’s diurnal pattern.

2: “Do you feel that the time of day that the patient’s blood was drawn should influence the interpretation of TSH results?”

- | | |
|------------|----------------|
| a) Always | d) Not usually |
| b) Usually | e) Never |

c) Sometimes

The second and third questions addressed how clinicians adapted TSH values to patients' age. The second question addressed a borderline TSH value (AACE's range is 0.5-4.12, 4.2 falls just outside it).

3: "In your opinion, a TSH of 4.2 is appropriate for which of the following age groups (you may select more than one)?"

- | | |
|------------|---|
| a) 9 - 13 | f) 45 - 54 |
| b) 14 - 17 | g) 55 - 64 |
| c) 18 - 24 | h) 65 - 74 |
| d) 25 - 34 | i) 75+ |
| e) 35 - 44 | j) It is usually inappropriate for all age groups |

The third question addressed the average TSH value for people over 65, 6.0. It falls outside AACE's range of 0.5-4.12.

4: "In your opinion, a TSH of 6.0 is appropriate for which of the following age groups (you may select more than one)?"

- | | |
|------------|---|
| a) 9 - 13 | f) 45 - 54 |
| b) 14 - 17 | g) 55 - 64 |
| c) 18 - 24 | h) 65 - 74 |
| d) 25 - 34 | i) 75+ |
| e) 35 - 44 | j) It is usually inappropriate for all age groups |

We asked the following two questions later on in the survey to bring out any inconsistencies between how they say they adapt TSH to age and how they apply patients' ages to TSH in practice:

5: "Do you feel that TSH ranges should be adapted to the age of the patient?"

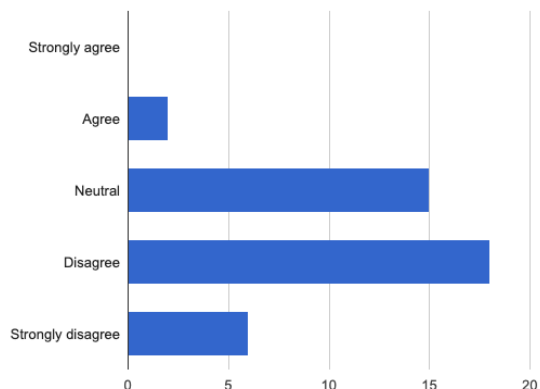
- | | |
|-------------------|----------------------|
| a) Strongly agree | d) Disagree |
| b) Agree | e) Strongly disagree |
| c) Neutral | |

Answers to these questions might imply whether the clinicians agree with the arguments cited for changing AACE's current range. They will indicate whether they think high TSH's association with heart issues merits lowering the range. Also, it will point out if clinicians agree about how to measure TSH - whether they see the time of day blood is drawn as relevant. They will also imply how they adapt borderline lab results' appropriateness to patients' age. We hypothesized that clinicians would assert that correlation with heart issues does not mean a higher TSH causes the heart issues. We also hypothesized that most clinicians would agree that TSH ranges should change with age. Perhaps those who wish to expand the TSH range for all ages would select that it is appropriate for everyone. And since it is not currently implemented in the standards, we hypothesized that most clinicians would not value what time of day of TSH is measured.

Quantitative Results:

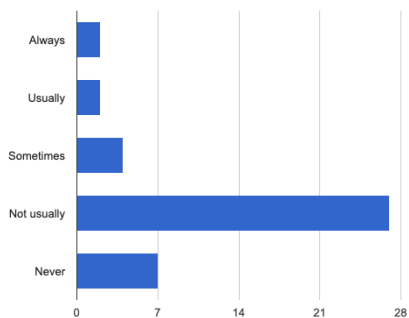
1: “To what extent do you agree with this statement: higher but clinically normal TSH levels are strongly associated with heart issues like atherosclerosis and cardiovascular disease - therefore, the TSH reference range should be lowered.”

Agree: 4.9%, Neutral: 36.6%, Disagree: 43.9%, Strongly Disagree: 14.6%



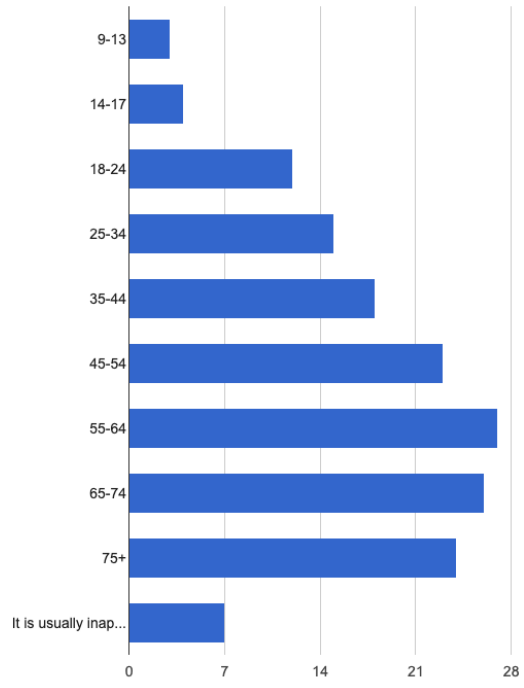
2: “Do you feel that the time of day that the patient’s blood was drawn should influence the interpretation of TSH results?”

Always: 4.8%, Usually: 4.8%, Sometimes: 9.5%, Not usually: 64.3%, Never: 16.7%



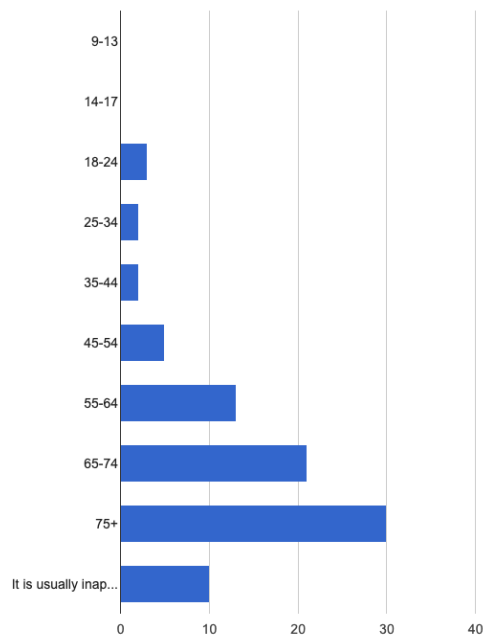
3: “In your opinion, a TSH of 4.2 is appropriate for which of the following age groups (you may select more than one)?”

It is usually inappropriate for all age groups: 16.7%



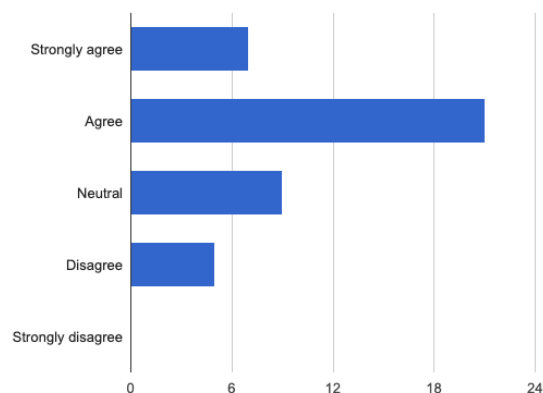
4: “In your opinion, a TSH of 6.0 is appropriate for which of the following age groups (you may select more than one)??”

It is usually inappropriate for all age groups: 23.8%



5: “Do you feel that TSH ranges should be adapted to the age of the patient?”

Strongly agree: 16.7%, Agree: 50%, Neutral: 21.4%, Disagree: 11.9%



Inferences from Quantitative Results

Answers to these questions imply that only some clinicians agree with the arguments usually cited for changing AACE's current range. Question one's answers imply that just over half of the participants do not think the association with heart issues merits lowering the range. Most of the rest of the participants are neutral to it. This result indicates that very few believe that this association should stand as a reason for changing the range. Most clinicians do not see the time of day that blood was drawn as a relevant factor. However, some do - some answered "always." Their responses to the age-related questions indicate that nearly all of them adapt their opinions of the healthiness of the range to patients' ages. It seems that the participants see borderline-high TSH results are more appropriate for older populations, though some think it is appropriate for everyone. Most see high TSH, 6.0, as much more appropriate for older folks. Though nearly all adapt their opinions to patients' ages, 12% disagree with the idea of adapting ranges to patients' ages. This data exhibits that practitioners significantly disagree regarding these biological points of contention.

Qualitative Results:

1: "To what extent do you agree with this statement: higher but clinically normal TSH levels are strongly associated with heart issues like atherosclerosis and cardiovascular disease - therefore, the TSH reference range should be lowered." *Optional: Please explain if you would like to.*

Participants who selected "strongly disagree" and "disagree" asserted that the correlation between higher TSH levels and heart issues does not indicate causation; amending TSH levels may not amend the heart issues. Participants wrote:

- "Again, no evidence that *TREATMENT* will correct cardiac issues,"
- "Need to recall that even if this association is true it would not necessarily follow that correcting that TSH would have any effect on the disease processes mentioned."
- "Need to show that lowering TSH with treatment reduces CVD. Associations do not indicate cause and effect."

The last participant also argued that the relative risk of treating these patients' thyroids rather than their hearts might be problematic:

- *“Also need to balance harm - thyroid replacement sometimes results in hyperthyroidism that can have adverse effects.”*

Another participant who selected “disagree” stated, *“there is no such clear evidence; and mild TSH elevations are not associated with significant dyslipidemia.”* Perhaps the participant has not seen these studies or disagrees with the methods used behind the studies. This response is also interesting because this statement is directly contradictory with the statements of two other participants who selected “neutral.” They mentioned the same data this participant denies exists. One simply wrote, *“some data to suggest this.”*

Participants who selected “neutral” also offered explanations. One provided the same primary argument that those who disagreed with the statement provided, explaining:

- *“There is data but association does not prove causation and there is data to suggest that in the setting of CVD high normal or high TSH is associated with better outcomes.”*

Another participant suggested interest, saying:

- *“Don’t know enough about it. Interesting though.”*

Inferences from Qualitative Results:

We can infer from this data one primary argument behind opposition to the heart issue argument: the correlation between higher TSH levels and heart issues does not indicate causation. Until there is evidence that treatment will help, some clinicians do not wish to treat their patients for that reason only.

Part Five: Which Hormones Do They Use?

Questions and Hypotheses

In the next section, we asked clinicians which hormones and antibodies they test to diagnose and treat patients. Six thyroid hormones and two thyroid antibodies were listed. Next to each hormone, the clinician was instructed to indicate whether they “always,” “sometimes,” or “never” use the hormone at hand to diagnose hypothyroidism. The six hormones included were TSH, Free T4, Total T4, Free T3, Total T3, and Reverse T3. The two antibodies listed were thyroid peroxidase antibodies and thyroglobulin antibodies.

We hypothesized that all of the participants would select “always” for TSH, that most would select “always” for Free T4, and that none would select “never” for the two thyroid antibodies. In other words, we assumed that these hormones and antibodies would be the most important to clinicians but that they would disagree about them significantly.

Quantitative Results

Participants were asked to adjust the slider in response to each hormone. Here is an example:

TSH

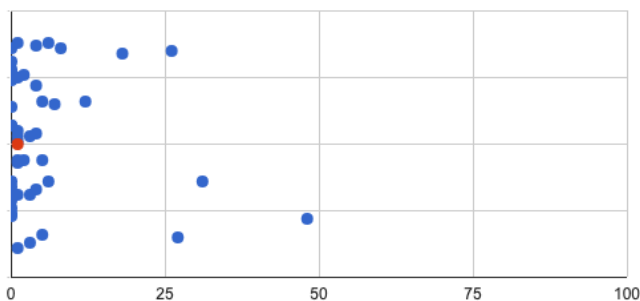
* must provide value

Always Sometimes Never

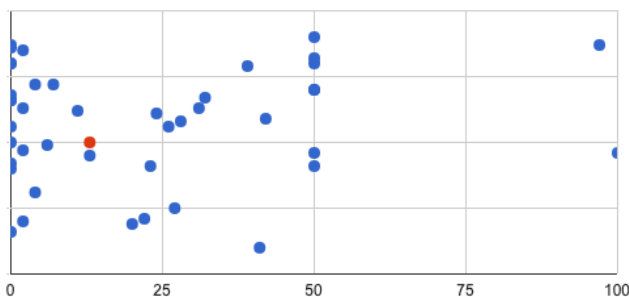
Change the slider above to set a response
reset

The following charts represent where participants moved the slider. On the Y-axis, 0 represents always, 50 represents sometimes, and 100 represents never. The red dot represents the median response.

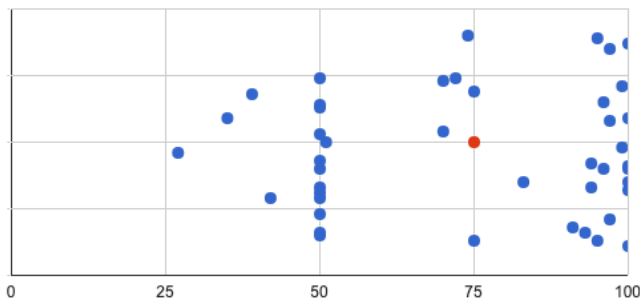
1. TSH: *Seems to be a consensus: "always." Some outliers only use it sometimes.*



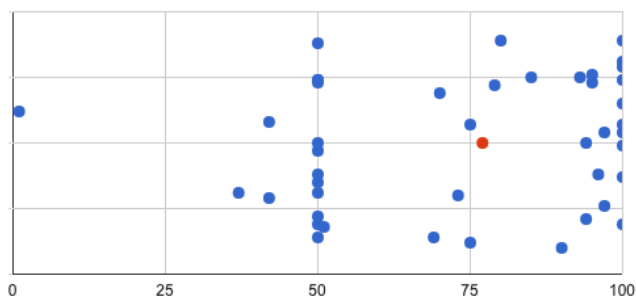
2. Free T4: *Almost all use it at least sometimes, or often. Two outliers do not use it.*



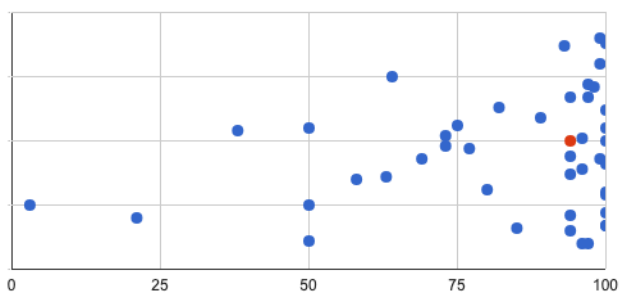
3. Total T4: *More disagreement here. Most tend not to use it, though some use it sometimes. A few outliers commonly use it.*



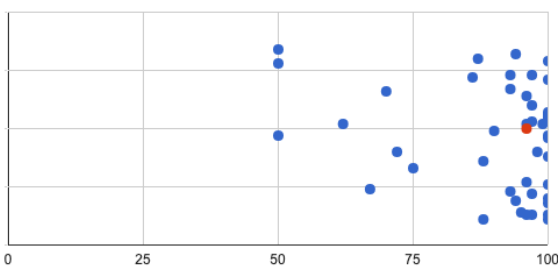
4. Free T3: *More disagreement here. This chart looks similar to Total T4. Most tend not to use it, though some use it sometimes. A few outliers commonly use it, and one outlier always uses it.*



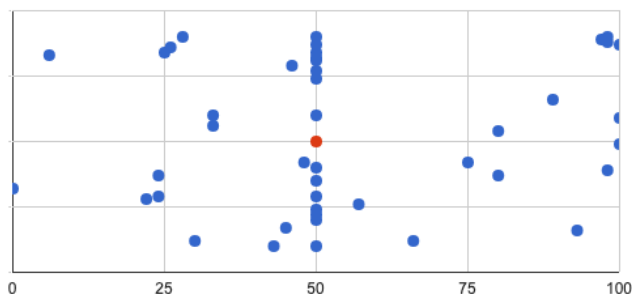
5: Total T3: *Most practitioners do not use it. Some use it sometimes, and a few outliers often or always use it.*



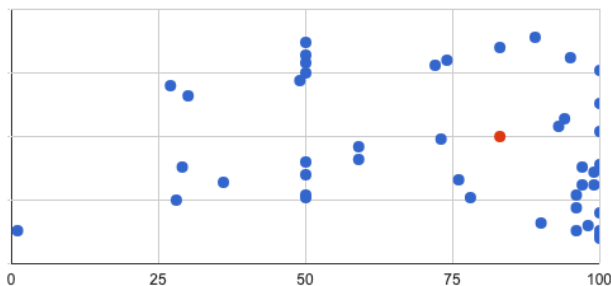
6: Reverse T3: *There is more agreement on this one. Most do not use it, but a few outliers use it sometimes.*



7: Thyroid Peroxidase Antibodies: *There is a wide spread of opinions on this. The median falls at sometimes, but several use it often, and several do not use it often or never use it.*



8: Thyroglobulin Antibodies: *There is also a wide spread of opinions on this. The median falls at not usually, though some use it sometimes, some outliers use it often, and one outlier always uses it.*



Inferences:

These statistics clearly and conclusively imply that clinicians disagree about which hormones to use. Clinicians especially disagree about the use of antibodies. Most agree about TSH, however.

Part 6 - Importance of Hormones Other Than TSH

Questions and Hypotheses

To determine clinicians' thoughts on the importance of other hormones, we asked whether TSH alone could be used to make a diagnosis:

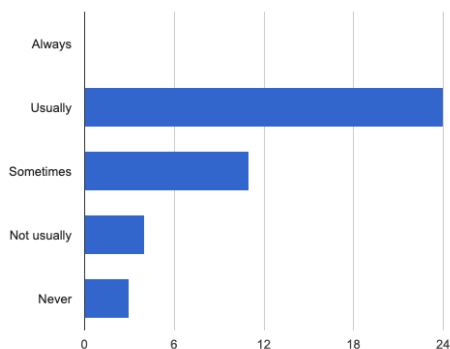
“In your opinion, can hypothyroidism be diagnosed based on TSH only?”

- a) Always
- b) Usually
- c) Sometimes
- d) Not usually
- e) Never

Answers to this question could imply how much importance clinicians place on other hormones. It could also imply the degree of importance AACE's TSH range plays for them; perhaps if they look to other hormones as well, AACE's range would not mean as much to them as it would to clinicians who look at TSH alone. We hypothesized that most clinicians would put sometimes and that none would put “always” or “never.”

Quantitative Results:

Always: 0%, Usually: 57.1%, Sometimes: 26.2%, Not usually: 9.5%, Never: 7.1%



Inferences from Quantitative Results:

Only about 16% think other hormones usually need to be used to make a diagnosis. This finding contradicts the results from the previous set of questions that indicated Free T4 is usually used. These answers also demonstrate a significant amount of disagreement between the practitioners.

Qualitative Results:

Participants were given the optional opportunity to provide explanations for their answers. Several participants who selected “usually” provided examples of when hormones other than TSH would be needed to make a diagnosis, such as when patients have pituitary problems, are sick or take medications that interact with thyroid lab assays. One explained that TSH “*can usually establish hypothyroidism but not the cause. Does not rule out pituitary insufficiency.*”

Some participants referred to subclinical hypothyroidism, though some indicated it needed treatment, while others said it did not. One participant who selected “usually” explained that:

- *“elevated TSH with normal T4,”* subclinical hypothyroidism, *“is not usually clinically relevant and does not necessarily indicate hypothyroidism.”*

Alternatively, a participant who selected “not usually” said:

- *“subclinical hypothyroidism exists. Not sure if that counts in this definition of hypothyroidism, but I get free T4 to look.”*

These participants’ answers are the opposites of each other.

Aside from the subclinical argument, some participants indicated that other hormones are relevant to making diagnoses:

- *“free T4 is helpful in the diagnosis for many people,”* for example.
- *“Need FT4 +/- FT3 to make the correct diagnosis. DDx in elevated TSH include primary hypothyroidism vs subclinical hypothyroidism vs TSHoma in the right clinical setting.”*

Inferences from Qualitative Results

These qualitative responses indicate that most clinicians agree there are cases when hormones other than TSH are needed to make diagnoses - but only some regularly order tests for them. This finding exhibits differences in diagnosis practices.

Part 7: Ranges of Hormones

In the following section, we asked practitioners for their opinions regarding specific ranges of thyroid hormones. We did so to get a direct quantitative measure of what ranges they believed were appropriate.

TSH

Questions and Hypotheses

The first hormone we asked for practitioners’ opinions on was TSH. We hypothesized that clinicians’ TSH would vary significantly. Practitioners were asked to indicate the appropriateness of TSH values as follows:

In your professional opinion, the TSH ranges below are always, sometimes, or never healthy?

23) 0.1 to 0.5
* must provide value

Always Sometimes Never

Change the slider above to set a response

reset

24) 0.5 - 1.7
* must provide value

Always Sometimes Never

Change the slider above to set a response

reset

25) 1.8 - 2.5
* must provide value

Always Sometimes Never

Change the slider above to set a response

reset

26) 2.6 - 4.12
* must provide value

Always Sometimes Never

Change the slider above to set a response

reset

27) 4.13 - 5.0
* must provide value

Always Sometimes Never

Change the slider above to set a response

reset

28) 5.0 - 10.0
* must provide value

Always Sometimes Never

Change the slider above to set a response

reset

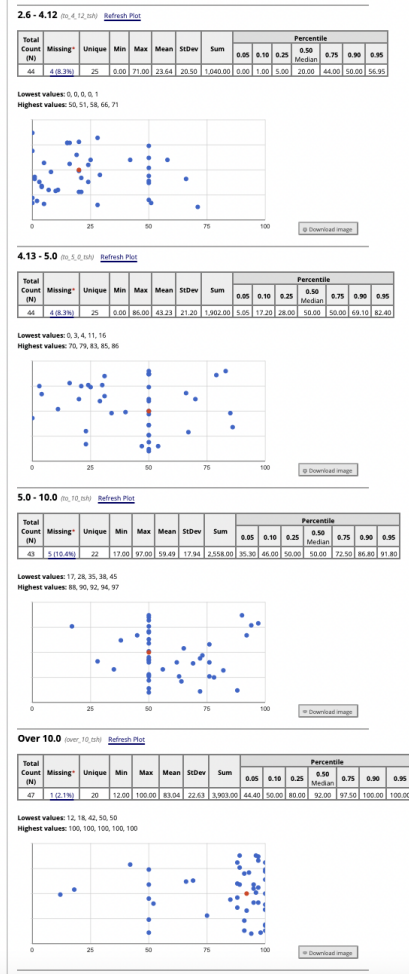
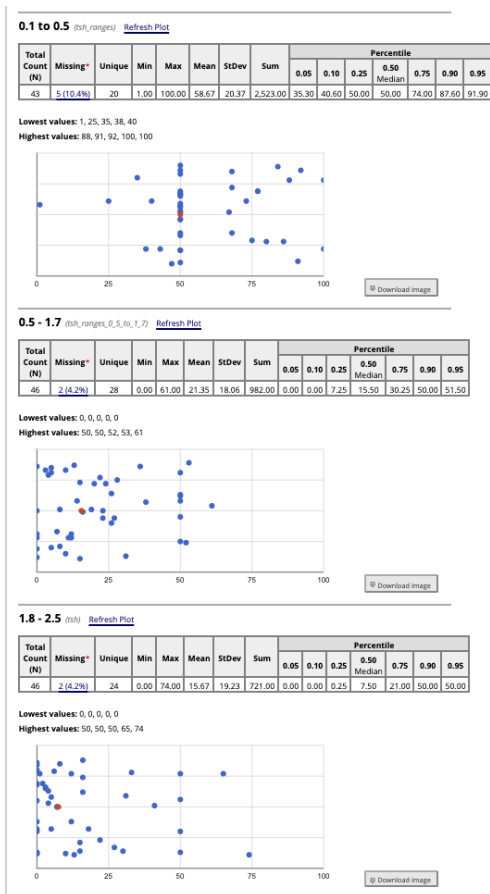
29) Over 10.0
* must provide value

Always Sometimes Never

Change the slider above to set a response

reset

Results



As indicated by the scatter plots, certain subranges of TSH proved more controversial than others. Most practitioners agreed about TSH values within all organizations' recommended ranges, like 1.8-2.5. Others, like 4.12-5.0 and 5.0-10.0 were more controversial than the universally recommended values.

Inferences

Practitioners seemed to agree on the subranges of TSH that organizations unanimously accept. Ranges that fell on the borderline of organizations' recommended ranges proved to be more controversial.

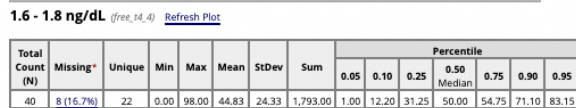
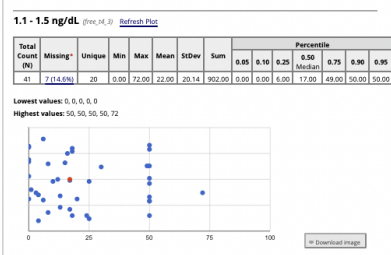
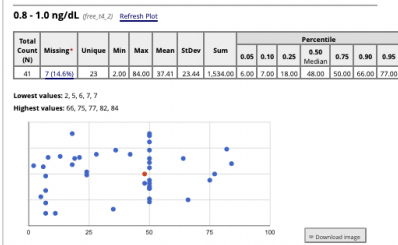
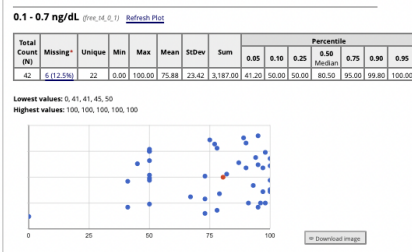
Free T4

Questions and Hypotheses

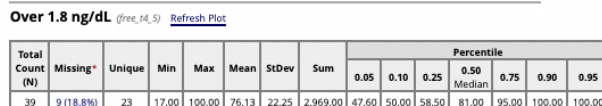
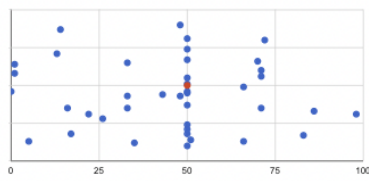
The next hormone we asked for practitioners' opinions on was Free T4. We hypothesized that clinicians' responses would vary significantly. Practitioners were asked to indicate the appropriateness of specific Free T4 values.

Results

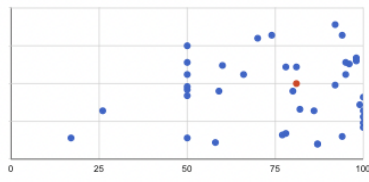
As indicated by the scatter plots, certain subranges of Free T4 proved more controversial than others. Borderline values like 1.6-1.8 and 0.8-1.0 indicated more disagreement than values clearly outside the range.



Lowest values: 0, 1, 1, 5, 13
Highest values: 71, 72, 83, 86, 98



Lowest values: 17, 26, 50, 50, 50
Highest values: 100, 100, 100, 100, 100



Inferences

Practitioners seemed to agree on the subranges of Free T4 that organizations unanimously accept. Ranges that fell on the borderline of organizations' recommended ranges proved to be more controversial.

Free T3

Questions and Hypotheses

The next hormone we asked for practitioners' opinions on was Free T3. We hypothesized that clinicians' Free T3 would vary significantly. Practitioners were asked to indicate the appropriateness of specific Free T3 values.

Results

As indicated by the scatter plots, certain subranges of Free T3 proved controversial across the board. Borderline values like 1.6-1.8 and 0.8-1.0 indicated more disagreement than values clearly outside the range.



Inferences

Practitioners seemed to disagree about most of the subranges of Free T3. Ranges that fell on the borderline of organizations' recommended ranges proved to be more controversial.

Reverse T3 Questions and Hypotheses

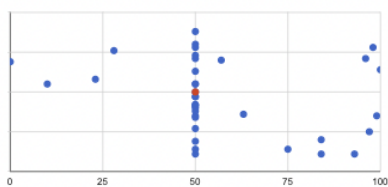
The next hormone we asked for practitioners' opinions on was Reverse T3. We hypothesized that clinicians' responses would vary significantly. Practitioners were asked to indicate the appropriateness of specific Reverse T3 values.

Results

1 - 10 ng/dL (r13_1) [Refresh Plot](#)

Total Count (N)	Missing*	Unique	Min	Max	Mean	StDev	Sum	Percentile						
								0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
37	11 (22.9%)	15	0.00	100.00	56.95	23.61	2,107.00	20.40	41.20	50.00	50.00	63.00	96.40	98.20

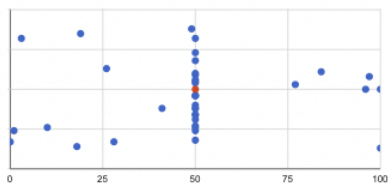
Lowest values: 0, 10, 23, 28, 50
Highest values: 96, 97, 98, 99, 100



11 - 18 ng/dL (r13_2) [Refresh Plot](#)

Total Count (N)	Missing*	Unique	Min	Max	Mean	StDev	Sum	Percentile						
								0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
37	11 (22.9%)	16	0.00	100.00	48.62	25.26	1,799.00	2.60	14.80	49.00	50.00	50.00	88.80	97.60

Lowest values: 0, 1, 3, 10, 18
Highest values: 84, 96, 97, 100, 100

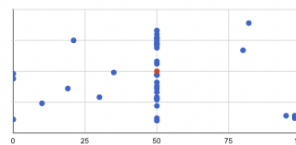


18 - 21 ng/dL (r13_3) [Refresh Plot](#)

18 - 21 ng/dL (r13_3) [Refresh Plot](#)

Total Count (N)	Missing*	Unique	Min	Max	Mean	StDev	Sum	Percentile						
								0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
37	11 (22.9%)	12	0.00	100.00	49.14	25.03	1,818.00	0.00	15.40	50.00	50.00	50.00	87.20	98.00

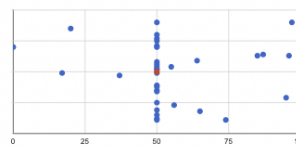
Lowest values: 0, 0, 0, 10, 19
Highest values: 82, 95, 98, 98, 100



22 - 27 ng/dL (r13_4) [Refresh Plot](#)

Total Count (N)	Missing*	Unique	Min	Max	Mean	StDev	Sum	Percentile						
								0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
37	11 (22.9%)	16	0.00	100.00	56.70	22.36	2,098.00	19.40	44.80	50.00	50.00	64.00	95.40	97.60

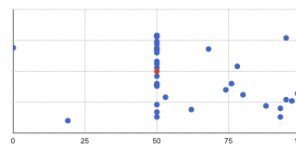
Lowest values: 0, 17, 20, 37, 50
Highest values: 95, 96, 97, 100, 100



Over 27 ng/dL (r13_5) [Refresh Plot](#)

Total Count (N)	Missing*	Unique	Min	Max	Mean	StDev	Sum	Percentile						
								0.05	0.10	0.25	0.50 Median	0.75	0.90	0.95
37	11 (22.9%)	16	0.00	100.00	62.70	23.40	2,320.00	43.80	50.00	50.00	50.00	80.00	95.80	99.20

Lowest values: 0, 19, 50, 50, 50
Highest values: 95, 97, 99, 100, 100



As indicated by the scatter plots, certain subranges of Reverse T3 proved controversial across the board, but most wrote “sometimes” for each of the subranges. There does not seem to be much consistency among those who did not select “sometimes.”

Inferences

Practitioners seemed to disagree about most of the subranges of Reverse T3 without much pattern. Most practitioners selected “sometimes” for each range, implying that Reverse T3 ranges may be ambiguous or less critical to diagnosing and treating the condition.

TPO Antibodies Questions and Hypotheses

Next, we asked for practitioners' opinions on a thyroid antibody. We hypothesized that clinicians' ideas of TPO antibody ranges would vary significantly. Practitioners were asked to indicate the appropriateness of specific TPO antibody values.

Results



As indicated by the scatter plots, certain subranges of TPO antibodies proved more controversial than others. Borderline values like 10-35 indicated more disagreement than values clearly outside the range.

Inferences

Practitioners seemed to agree on the subranges of TPO antibodies that organizations unanimously accept. Ranges that fell on the borderline of organizations' recommended ranges proved to be more controversial.

Part 7 Conclusion

Asking practitioners for their opinions regarding specific ranges of thyroid hormones provided direct, quantitative measures of which ranges they believed were appropriate. Through their responses, disagreements regarding appropriate levels were represented quantitatively.

These findings represent how significantly diagnostic criteria vary from practitioner to practitioner.

Part 8: Fictional Patient Cases

To directly survey whether practitioners implement different diagnostic and treatment criteria, we presented the participants with nine fictional patient cases. Each patient case we presented included the patient's age, BMI, hormone levels, and symptoms. Following the presentation of a patient case, we asked the participants to indicate whether they were "very likely," "likely," "moderately," "unlikely," or "very unlikely" to diagnose the hypothetical patient. We then asked how likely they would be to treat the hypothetical patient.

We kept the gender the same in all of the patients, female, to see if participants would note the importance of miscarriage rates. We changed as few factors as possible from patient case to patient case. Other than the control, we used just two hypothetical patients. The first was a 71-year-old female with a BMI of 24, and the second was a 20-year-old female with a BMI of 24. Every patient case experienced symptoms of hypothyroidism. Each case included differing thyroid hormone levels.

The set of cases was designed to provide clinicians with cases we believed they were likely to agree on and ones they were likely to disagree on. Before viewing the results, we ranked the perceived "difficulty" of each case on a scale of 1 to 5. More "difficult" cases, which were signified by higher ratings, were more likely to demonstrate disagreements between the practitioners. More "easy" cases, which were signified by lower ratings, were more likely to demonstrate agreement between the practitioners.

Each case was designed to survey how practitioners would diagnose and treat certain types of hypothyroidism. We designed cases for occult thyroid disease in both young and old patients, subclinical hypothyroidism with antibodies in both young and old patients, subclinical hypothyroidism without antibodies in both young and old patients, and borderline but classic hypothyroidism in both young and old patients. We also included a control.

Upon coming to the cases section, practitioners were reminded that there is no correct answer and that we are simply looking for their opinions:

Beyond these questions, we are looking to see how healthcare professionals would diagnose and treat certain hypothyroidism case studies. There is no right answer - our goal is to uncover which opinions on the subject are most common among healthcare professionals. We appreciate that you are willing to share yours with us.

Case 1: Control

Questions and Hypotheses

The first case was a patient who experienced symptoms but had hormone levels within all organizations' perceptions of healthy thyroid hormone ranges (including patient coalitions' recommendations). This case was intended to be a control.

Case 1**Age 20, female, BMI of 27****TSH: 1.8, free T4 of 1.6 ng/dL, free T3 of 5.1 pmol/L, RT3 of 18 ng/dL, antibodies < 2 IU/mL****Symptoms: depression, chronic fatigue, constipation, weight gain, irregular menstruation****70) How likely would you be to consider diagnosing the patient with hypothyroidism?**
 Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

71) How likely is it that you would consider treating the patient for hypothyroidism?
 Very likely Likely Moderately
 Unlikely Very unlikely

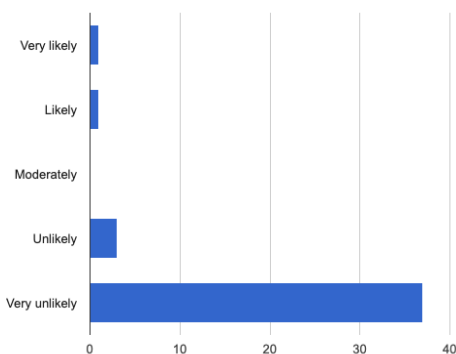
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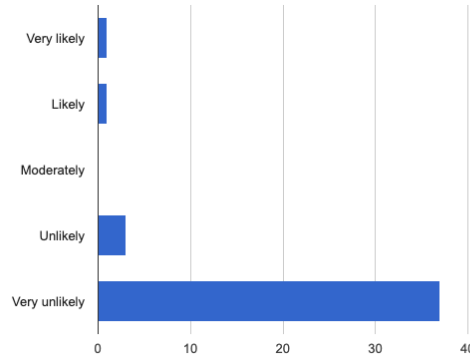
We hypothesized that practitioners would unanimously agree that the patient does not have hypothyroidism since their hormones are considered to be healthy according to all groups. Her symptoms would probably be resulting from something other than hypothyroidism. We, therefore, gave the case a hypothesized difficulty rating of 1.

Quantitative Results

Diagnosing:



Treating



*Very likely: 2.4%, Likely: 2.4%,
Unlikely: 7.1%, Very unlikely: 88.1%*

Same responses as diagnosing

Quantitative Inferences

The vast majority of participants, 95.2%, would not diagnose or treat this patient. Two participants would do so, however. Clinicians who want to diagnose and treat this patient for hypothyroidism seem not to follow any recommended standard range in practice - they follow their own scientific opinions. Except for these outliers, this case demonstrates minimal disagreement.

Qualitative Results

None of the two participants who answered “very likely” or “likely” indicated why they chose to diagnose and treat this patient. Other participants provided reasoning as to why they would not diagnose or treat this patient, pointing to the likelihood of the patient having another condition: *“important to evaluate for other causes of her symptoms, rather than treating*

hypothyroidism which is unlikely to be the culprit,” and “this is most likely PCOS in context of overweight.” These results echo a common conservative-leaning argument - that patients who experience symptoms of hypothyroidism but have hormones within the healthy range are likely dealing with a different condition.

Cases 2 and 3: Potential Occult Thyroid Disease

Questions and Hypotheses

The second and third cases provided clinicians with an old patient and a young patient whose hormones fell on the borderline of occult thyroid disease. Occult thyroid disease occurs when patients lack thyroid hormones T4 and T3 despite having normal TSH levels. These patients in these two cases also have low levels of antibodies. That could signal to some clinicians that Hashimoto’s thyroiditis is beginning to progress. These patients also experience symptoms of hypothyroidism. The only difference between the two is their age.

Answers to these cases are intended to indicate participants’ opinions regarding occult thyroid disease. We presumed that clinicians would disagree on these cases since there are not standards for diagnosing or treating occult thyroid disease. Since lower T3 and T4 are arguably more appropriate for older patients than they are for younger patients, we gave case two a difficulty rating of 5 and case four a difficulty rating of 4.

Case 2

Age 71, female, BMI of 24

TSH: 2.5, free T4 0.5 ng/dL, free T3 0.9 pmol/L, RT3 28 ng/dL, TPO antibodies 46, TG antibodies 40

Symptoms: chronic fatigue, constipation, hair loss, high cholesterol

73) How likely is it that you would consider diagnosing the patient with hypothyroidism?

* must provide value

Very likely Likely Moderately Unlikely Very unlikely

reset

74) How likely would you be to consider treating the patient for hypothyroidism?

* must provide value

Very likely Likely Moderately Unlikely Very unlikely

reset

Case 3

Age 20, female, BMI of 24

TSH: 2.5, free T4 0.5 ng/dL, free T3 0.9 pmol/L, RT3 28 ng/dL, TPO antibodies 46, TG antibodies 40

Symptoms: chronic fatigue, constipation, hair loss, high cholesterol, irregular menstruation

76) How likely is it that you would consider diagnosing the patient with hypothyroidism?

Very likely Likely Moderately Unlikely Very unlikely

reset

77) How likely is it that you would consider treating the patient for hypothyroidism?

* must provide value

Very likely Likely Moderately Unlikely Very unlikely

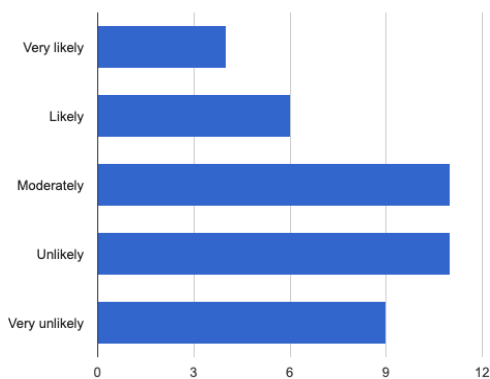
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Quantitative Results

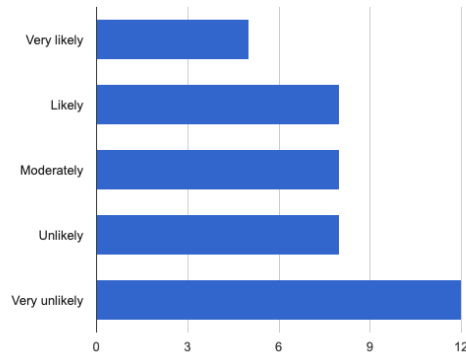
Case 2 (Age 71)

Diagnosing:

Treating:



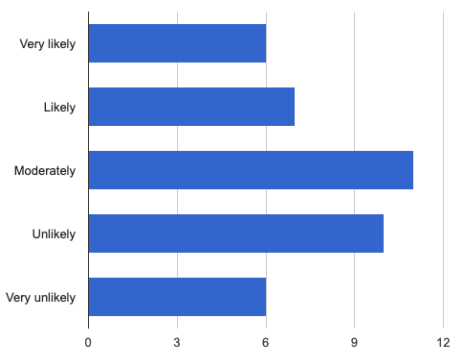
Very Likely: 9.8%
Likely: 14.6%
Moderately: 26.8%
Unlikely: 26.8%
Very Unlikely: 22%



Very Likely: 12.2%
Likely: 19.5%
Moderately: 19.5%
Unlikely: 19.5%
Very Unlikely: 29.3%

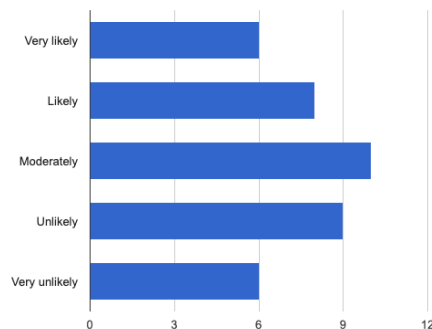
Case 3 (Age 20)

Diagnosing:



Very Likely: 15%
Likely: 17.5%
Moderately: 27.5%
Unlikely: 25%
Very Unlikely: 15%

Treating:



Very Likely: 15.4%
Likely: 20.5%
Moderately: 25.6%
Unlikely: 23.1%
Very Unlikely: 15.4%

Quantitative Inferences

As we predicted, the participants were more likely to diagnose and treat the younger patient than the older patient. The participants disagreed widely on these cases. To illustrate just how vast the differences in responses are here, look to case 3's "treating" responses. They nearly represent a bell curve. Nearly the same number of participants were likely to treat this patient as the number of participants that were unlikely to.

Qualitative Results

Case 2 (Age 71)

Several of the participants who selected “very likely,” “likely,” or “moderately” indicated that they wanted to investigate further. One “unlikely” participant also indicated they would test for central hypothyroidism. They explained:

- *“needs more investigation”*
- *“she needs an MRI”*
- *“need further information. Patient may have secondary hypothyroidism due to a pituitary process”*

Other participants argued that they are unlikely to treat a patient in the case of a normal TSH value. A participant who selected “very unlikely” explained that they would be:

- *“very unlikely to treat anyone with a normal TSH, particularly and elderly patient.”*

Case 3 (Age 20)

Participants provided similar explanations here. Some copy-pasted their explanations from case 2.

Qualitative Inferences

These qualitative responses present two reasons behind participants’ answers: they need more information to make a diagnosis, or they are not likely to see normal TSH values as indicative of hypothyroidism.

Cases 4 and 5: Potential Subclinical Hypothyroidism With Antibodies

Questions and Hypotheses

The fourth and fifth cases provided clinicians with an old patient and a young patient whose hormones typically classify them with subclinical hypothyroidism, which is when thyroid hormones T3 and T4 fall in the healthy range, but TSH levels are elevated. Put simply, the body calls for more thyroid hormone, though according to current standards, it does not need it. The patient has low levels of antibodies, but they do exist in their bodies - so that could signal to some clinicians that Hashimoto’s thyroiditis is beginning to progress as well. These patients experience symptoms of hypothyroidism. The only difference between the two is their age.

Answers to these cases are intended to indicate participants’ opinions regarding subclinical hypothyroidism that presents with antibodies. We presumed that clinicians would disagree on these cases since there are not standards for diagnosing or treating subclinical hypothyroidism.

For case 4, the older patient, we hypothesized that clinicians would primarily agree that the patient does not need diagnosis or treatment and that something else is causing her symptoms. She is a case of only slightly elevated TSH, which is pretty average for her age. For these reasons, we gave case 4 a difficulty rating of 4.

For case 5, we hypothesized that clinicians’ opinions would vary widely. Elevated TSH is not as appropriate for younger patients. Clinicians who believe subclinical hypothyroidism merits diagnosis and treatment will probably diagnose and treat this patient. All other

participants most likely will not unless they see low levels of antibodies as problematic. For these reasons, we gave case 5 a difficulty rating of 5.

Case 4

Age 71, female, BMI of 24

TSH: 4.6, free T4 1.6 ng/dL, free T3 5.1 pmol/L, RT3 28 ng/dL, TPO antibodies 46, TG antibodies 40

Symptoms: chronic fatigue, constipation, hair loss, high cholesterol

79) How likely is it that you would consider diagnosing the patient with hypothyroidism?

Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

80) How likely is it that you would consider treating the patient with hypothyroidism?

Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

Case 5

Age 20, female, BMI of 24

TSH: 4.6, free T4 1.6 ng/dL, free T3 5.1 pmol/L, RT3 28 ng/dL, TPO antibodies 46, TG antibodies 40

Symptoms: chronic fatigue, constipation, hair loss, high cholesterol, irregular menstruation

82) How likely is it that you would consider diagnosing the patient with hypothyroidism?

Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

83) How likely is it that you would consider treating the patient with hypothyroidism?

Very likely Likely Moderately
 Unlikely Very unlikely

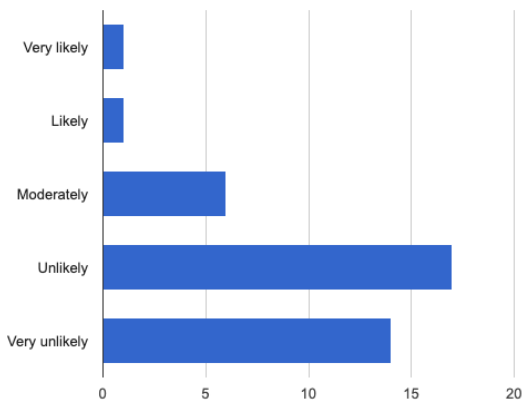
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Quantitative Results

Case 4

Diagnosing



Very likely: 2.6%

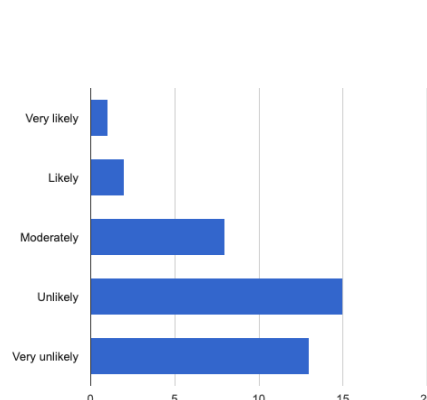
Likely: 2.6%

Moderately: 15.4%

Unlikely: 43.6%

Very Unlikely: 35.9%

Treating



Very likely: 2.6%

Likely: 5.1%

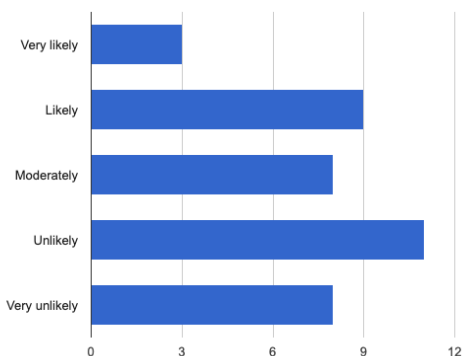
Moderately: 20.5%

Unlikely: 38.5%

Very Unlikely: 33.3%

Case 5

Diagnosing



Very likely: 7.7%

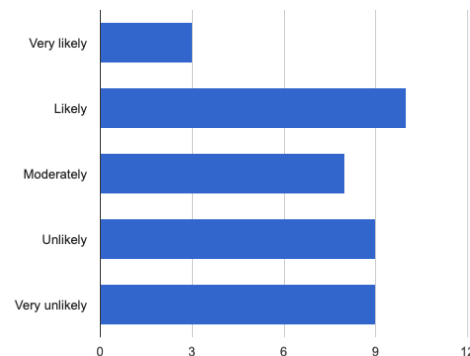
Likely: 23.1%

Moderately: 20.5%

Unlikely: 28.2%

Very Unlikely: 20.5%

Treating



Very likely: 7.7%

Likely: 25.6%

Moderately: 20.5%

Unlikely: 23.1%

Very Unlikely: 23.1%

Quantitative Inferences

Disagreement is rampant in these cases as well, though participants disagreed much more about case 5, the younger patient. Participants were mainly unlikely to treat the older patient, but answers were all over the board for the younger patient.

Qualitative Results and Inferences

Not many participants provided explanations for their responses on case 4, the older patient. Only those who selected very unlikely or unlikely provided reasoning. One echoed a response we have heard before: *“look for other causes of symptoms, other autoimmune diseases.”*

Another participant cited the reason that many participants used to argue that the AACC’s claim is invalid: there is not enough evidence for clinical benefits of lowering TSH. A participant wrote: *“despite high normal TSH, little to no data of benefit of thyroid treatment here.”*

The qualitative responses present two reasons behind participants’ answers: something else is causing the patient’s symptoms, and lowering her TSH value will not necessarily provide a clinical benefit.

For case 5, on the other hand, several practitioners provided explanations, citing a reason we have not seen on the survey until now: fertility. Practitioners who selected “likely” or “moderately” wrote:

- *“her childbearing potential is important here”*
- *“would be more likely to treat if she were considering pregnancy, but otherwise would not likely treat.”*

Even one who selected “unlikely” wrote that they:

- “*would treat if patient trying to get pregnant and history of miscarriage.*”

A practitioner who selected very likely brought up a new point as well:

- “*minimal downside to cautious replacement.*”

They note that conservative treatment does not pose many risks. So, they would treat the patient.

The qualitative responses for case 5 present two new reasons for treating subclinical patients: patients’ childbearing potential and the minimal risks of conservative treatments.

Cases 6 and 7: Potential Subclinical Hypothyroidism

Questions and Hypotheses

The sixth and seventh cases provided clinicians with an old patient and a young patient whose hormones typically classify them with subclinical hypothyroidism, which is when thyroid hormones T3 and T4 fall in the healthy range, but TSH levels are elevated. These patients do not have antibodies. The only difference between the two is their age.

Answers to these cases are intended to indicate participants’ opinions regarding subclinical hypothyroidism that does not present with antibodies. We presumed that clinicians would disagree on these cases since there are not standards for diagnosing or treating subclinical hypothyroidism.

For case 6, the older patient, our hypothesis was similar to that of case 4: that clinicians will primarily agree that the patient does not need diagnosis or treatment and that something else is causing her symptoms. She is a case of only slightly elevated TSH, which is pretty average for her age. Plus, she does not have antibodies. For these reasons, we gave case 6 a difficulty rating of 2.

For case 7, we hypothesized that clinicians’ opinions would vary widely. Elevated TSH is not as appropriate for younger patients. Clinicians who answered previously in the survey that subclinical hypothyroidism merits diagnosis and treatment (question x) will probably diagnose and treat this patient unless they think a TSH of 4.6 is not elevated enough. All other participants most likely will not diagnose or treat this patient. For these reasons, we gave case 7 a difficulty rating of 5.

Case 6

Age 71, female, BMI of 24

TSH: 4.6, TPO antibodies <2, TG antibodies <2, free T4 1.6 ng/DL, free T3 5.1 pmol/L, RT3 28 ng/dL

Symptoms: chronic fatigue, constipation, hair loss, high cholesterol

85) How likely is it that you would consider diagnosing the patient with hypothyroidism?

- Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

86) How likely is it that you would consider treating the patient with hypothyroidism?

- Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

Case 7

Age 20, female, BMI of 24

TSH: 4.6, TPO antibodies <2, TG antibodies <2, free T4 1.6 ng/dL, free T3 5.1 pmol/L, RT3 28 ng/dL

Symptoms: chronic fatigue, constipation, hair loss, high cholesterol

88) How likely is it that you would consider diagnosing the patient with hypothyroidism?
 Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

89) How likely is it that you would consider treating the patient for hypothyroidism?
 Very likely Likely Moderately
 Unlikely Very unlikely

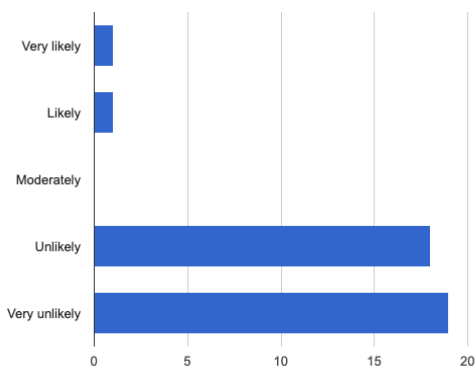
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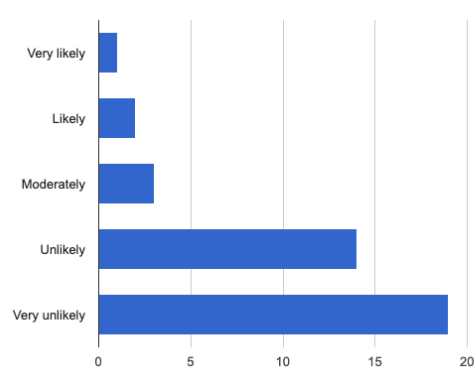
Quantitative Results

Case 6

Diagnosing

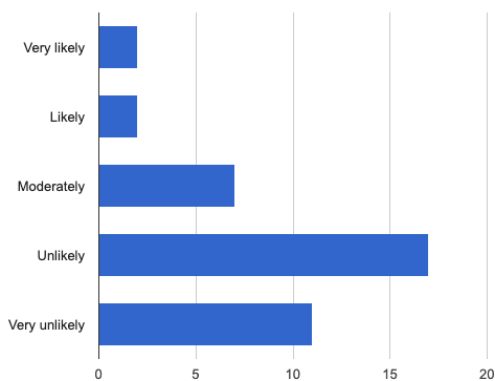
*Very likely: 2.6%**Likely: 2.6%**Moderately: 0%**Unlikely: 46.2%**Very Unlikely: 48.7%*

Treating

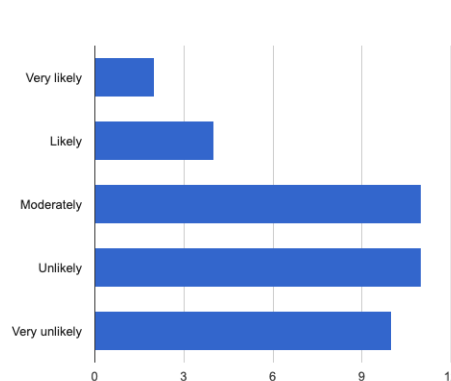
*Very likely: 2.6%**Likely: 5.1%**Moderately: 7.7%**Unlikely: 35.9%**Very Unlikely: 48.7%*

Case 7

Diagnosing

*Very likely: 5.1%*

Treating

*Very likely: 5.3%*

Likely: 5.1%
Moderately: 17.9%
Unlikely: 43.6%
Very Unlikely: 28.2%

Likely: 10.5%
Moderately: 28.9%
Unlikely: 28.9%
Very Unlikely: 26.3%

Quantitative Inferences

Case 7 directly indicates rampant disagreement among practitioners. Like we hypothesized, more practitioners agreed about case 6 than they did case 7. Case 7, the younger patient, brought out rampant disagreement. Participants were mainly unlikely to treat the older patient, but answers were all over the board for the younger patient.

Qualitative Results and Inferences

In case 6, only one participant left an explanation. They selected “unlikely” and wrote: “*I will be worried about a fib,*” meaning they are worried that treatment could cause the patient to experience symptoms of hyperthyroidism. This response echoes a common argument for conservative treatment practices: overtreatment may cause problems for patients.

Qualitative responses for case 7 were similar to those from case 5. They presented two reasons for treating subclinical patients: childbearing potential and minimal risks of conservative treatments. Some copy-pasted their answers from case 5.

Those who argued for fertility wrote:

- *“her childbearing potential is important here”*
- *“would treat if patient trying to get pregnant and history of miscarriage”*

A practitioner who selected “very likely” brought up the minimal risks of conservative treatments argument:

- *“safe to conservatively replace”*

They note that conservative treatment does not pose many risks. So, they would treat the patient.

Cases 8 and 9: “Borderline” Hypothyroidism Cases

Questions and Hypotheses

The eighth and ninth cases presented clinicians with an old patient and a young patient whose hormones would be at the upper level of AACE’s healthy range but out of range according to the AACC. These patients experience symptoms of hypothyroidism. The only difference between the two is their age.

Answers to these cases are intended to indicate participants’ opinions regarding “borderline” hypothyroidism. We presumed that clinicians would disagree on these cases since different organizations would theoretically disagree on these cases.

For case 8, the younger patient, we hypothesized that clinicians’ opinions would vary widely. Clinicians who side with the AACC will likely diagnose and treat this patient. Clinicians who side with AACE may not diagnose and treat this patient, but perhaps because the patient is young, some who stand with AACE but believe TSH should be lower in younger patients may diagnose and treat the patient. For these reasons, we gave case 8 a difficulty rating of 3.

For case 9, we hypothesized that clinicians' opinions would vary widely. Clinicians who side with the AACC will likely diagnose and treat this patient, but perhaps some will argue that they do not need treatment because the patient is 71. Clinicians who side with AACE may not diagnose and treat this patient. For these reasons, we gave case 8 a difficulty rating of 2.

Case 8

Age 20, female, BMI of 24

TSH: 3.8, TPO antibodies <2, TG antibodies <2, free T4 0.8 ng/dL, free T3 1.9 pmol/L, RT3 28 ng/dL

Symptoms: chronic fatigue, constipation, hair loss, high cholesterol

91) How likely is it that you would consider diagnosing the patient with hypothyroidism?

Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

92) How likely is it that you would consider treating the patient for hypothyroidism?

Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

Case 9

Age 71, female, BMI of 24

TSH: 3.8, TPO antibodies <2, TG antibodies <2, free T4 0.8 ng/dL, free T3 1.9 pmol/L, RT3 28 ng/dL

Symptoms: chronic fatigue, constipation, hair loss, high cholesterol

94) How likely is it that you would consider diagnosing the patient with hypothyroidism?

Very likely Likely Moderately
 Unlikely Very unlikely

* must provide value

reset

95) How likely is it that you would consider treating the patient for hypothyroidism?

Very likely Likely Moderately
 Unlikely Very unlikely

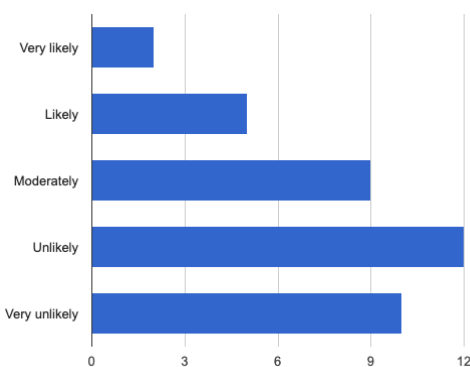
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Quantitative Results

Case 8

Diagnosing



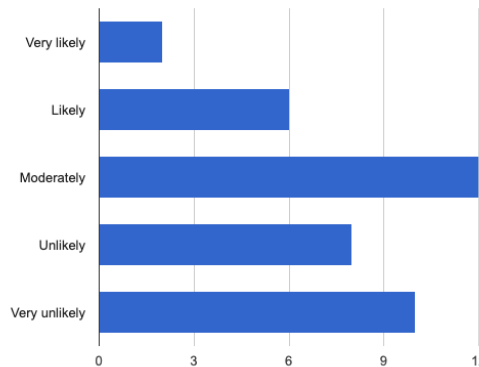
Very likely: 5.3%

Likely: 13.2%

Moderately: 23.7%

Unlikely: 31.6%

Treating



Very likely: 5.3%

Likely: 15.8%

Moderately: 31.6%

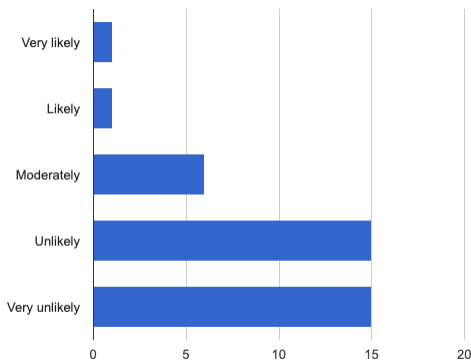
Unlikely: 21.1%

Very Unlikely: 26.3%

Very Unlikely: 26.3%

Case 9

Diagnosing



Very likely: 2.6%

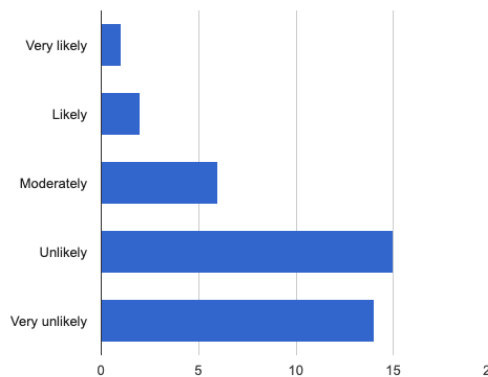
Likely: 2.6%

Moderately: 15.8%

Unlikely: 39.5%

Very Unlikely: 39.5%

Treating



Very likely: 2.6%

Likely: 5.3%

Moderately: 15.8%

Unlikely: 39.5%

Very Unlikely: 36.8%

Quantitative Inferences

Case 8 directly indicates rampant disagreement among practitioners. Like we hypothesized, more practitioners agreed about case 9 than they did case 8. Results from case 8, the younger patient, exhibited rampant disagreement. Participants were mainly unlikely to treat the older patient, but answers were all over the board for the younger patient.

Qualitative Results and Inferences

Qualitative responses for case 8 presented two arguments we saw previously in the survey: needing more information and fertility. Those who indicated they needed additional information wrote that they:

- *“would do pituitary work up”*
- *“assess for secondary hypothyroidism”*

One pointed to the fertility argument, explaining that *“her childbearing potential is important here.”*

Only one participant responded to case 9. They also indicated that they needed additional information, writing *“would do pituitary work up.”*

Part 9: Opinions on Psychosocial Stakes

Self-Image

Questions and Hypotheses

To gauge clinicians' thoughts on how hypothyroidism affects patients' self-image, we asked two questions:

1: “In your opinion, does diagnosing a patient with hypothyroidism affect their self-image?”

- a) Always
- b) Usually
- c) Sometimes
- d) Not usually
- e) Never

2: “In your opinion, does treating a patient with hypothyroidism affect their self-image?”

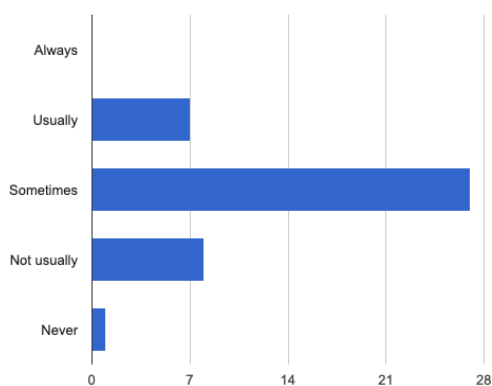
- a) Always
- b) Usually
- c) Sometimes
- d) Sometimes
- e) Not usually
- f) Never

Answers to these questions might imply whether clinicians think the diagnosis and treatment of patients who merit it affects their self-image. We hypothesized that clinicians would select sometimes or usually; no clinicians will select “not usually” or “never.”

Quantitative Results:

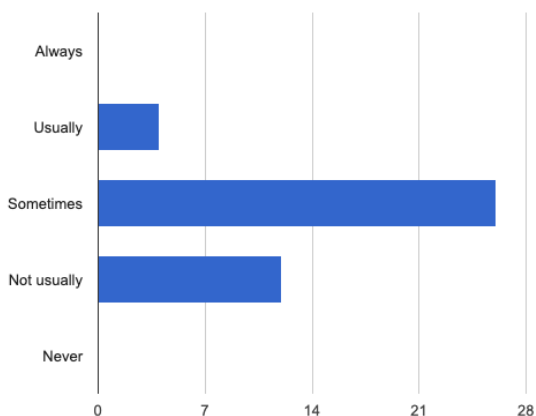
Question 1: “In your opinion, does diagnosing a patient with hypothyroidism affect their self-image?”

Always: 0%, Usually: 16.3%, Sometimes: 62.8%, Not usually: 18.6%, Never: 2.3%



Question 2: “In your opinion, does treating a patient with hypothyroidism affect their self-image?”

Always: 0%, Usually: 9.5%, Sometimes: 61.9%, Not usually: 28.6%, Never: 0%



Inferences

This result indicates a moderate amount of disagreement, shown through the groups of participants that selected “usually” and “not usually.” Most clinicians think the diagnosis and treatment of hypothyroidism sometimes affect patients’ self-image, however.

Quality of Life

Questions and Hypotheses

To gauge clinicians’ thoughts on how hypothyroidism affects patients’ quality of life, we asked four questions:

The first question was intended to gauge clinicians’ thoughts on how hypothyroidism diagnosis affects patients with definite cases’ quality of life.

1: “In your opinion, does diagnosing a patient with undeniably out-of-range hormones with hypothyroidism affect their quality of life?”

- | | |
|--------------|----------------|
| a) Always | d) Sometimes |
| b) Usually | e) Not usually |
| c) Sometimes | f) Never |

The second question was intended to gauge clinicians’ thoughts on how hypothyroidism diagnosis affects “borderline” patients’ quality of life.

2: “In your opinion, does diagnosing a patient with subclinical-level hormones with hypothyroidism affect their quality of life?”

- | | |
|--------------|----------------|
| a) Always | d) Sometimes |
| b) Usually | e) Not usually |
| c) Sometimes | f) Never |

The third question was intended to gauge clinicians’ thoughts on how hypothyroidism *treatment* affects patients’ quality of life.

3: “In your opinion, does treating a patient with hypothyroidism affect their quality of life?”

- | | |
|--------------|----------------|
| a) Always | d) Sometimes |
| b) Usually | e) Not usually |
| c) Sometimes | f) Never |

The last question was designed to discover whether practitioners thought treatment positively or negatively affected patients psychosocially.

4: “In your opinion, does treating a patient with hypothyroidism positively or negatively affect their self-image and quality of life?”

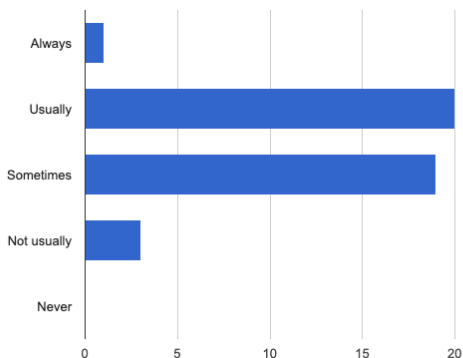
- | | |
|-------------|---------------------------|
| a) Positive | c) Negative |
| b) Neutral | d) Depends on the patient |

Answers to these questions might imply whether clinicians think diagnosing and treating patients who merit it affects their quality of life. We hypothesized that clinicians may disagree slightly but that most will agree that patients’ quality of life improves with diagnoses and treatments.

Quantitative Results

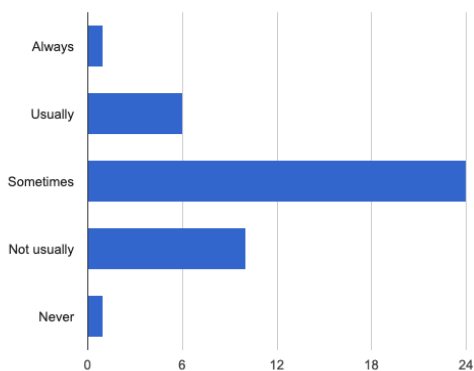
1: “In your opinion, does diagnosing a patient with undeniably out-of-range hormones with hypothyroidism affect their quality of life?”

Always: 2.3%, Usually 46.5%, Sometimes: 44.2%, Not usually: 7%, Never: 0%



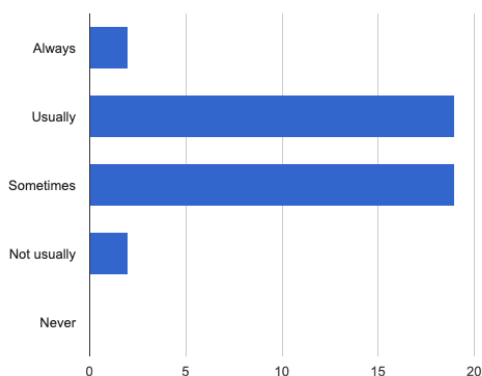
2: “In your opinion, does diagnosing a patient with subclinical-level hormones with hypothyroidism affect their quality of life?”

Always: 2.4%, Usually 14.3%, Sometimes: 57.1%, Not usually: 23.8%, Never: 2.4%



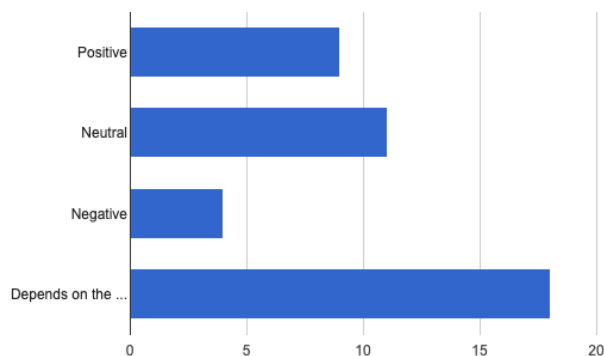
3: “In your opinion, does treating a patient with hypothyroidism affect their quality of life?”

Always: 4.8%, Usually 45.2%, Sometimes: 45.2%, Not usually: 4.8%, Never: 0%



4: “In your opinion, does treating a patient with hypothyroidism positively or negatively affect their self-image and quality of life?”

Positive: 21.4%, Neutral: 26.2%, Negative: 9.5%, Depends on the patient: 42.9%



Quantitative Inferences

This result indicates a moderate amount of disagreement. Most clinicians think diagnosis and treatment of definite hypothyroidism affect patients' quality of life more often than it does subclinical hypothyroidism.

Part 10: Perceptions of Hypothyroidism

Conservative or Liberal in Practice

Questions and Hypotheses

We wanted to ask the clinicians point-blank whether they feel that it is better to diagnose and treat debatable or "borderline" cases or that it is better to avoid doing so. We asked:

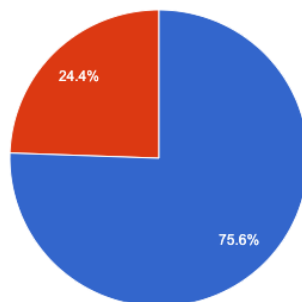
1: "Would you say that you are more conservative or more liberal with your diagnosis of hypothyroidism?"

- a) Conservative b) Liberal

We left out a "moderate" option for a reason: we wanted to force the participants to indicate whether they think it is a better bet to diagnose and treat a mild case or not to do so. We hypothesized that those who indicated they were more "conservative" about hypothyroidism diagnosis and treatment would argue that hormone ranges should stay the same or expand. We hypothesized that those who indicated they were more "liberal" about hypothyroidism diagnosis and treatment would argue that hormone ranges should stay the same or contract.

Quantitative Results:

24.4% Liberal, 75.6% Conservative



Quantitative Inferences

These quantitative results may indicate that most professionals believe that it's a better bet not to diagnose and treat a debatable case. Qualitative responses were abundant - they provide reasonings behind this result.

Qualitative Results and Inferences

Qualitative answers from participants who answered "conservative" presented four main arguments: perhaps patients' symptoms are caused by something else, there is no clear benefit of treating borderline patients, lab results should be double-checked, and committing patients to a lifetime of medication can be undesirable.

One participant who argued that perhaps patients' symptoms are caused by something else was particularly strongly worded in their response - they wrote:

- *"You should not over diagnose thyroid disease and tell someone his or her symptoms are from hypothyroidism when TSH is normal. You are missing something else. It's really malpractice."*

This comment about malpractice characterizes the polarizing nature of the controversy. Another who argued for this position simply explained that:

- *"symptoms of hypothyroidism are very non specific and may be related to many other conditions."*

One practitioner noted one of these conditions: vitamin deficiencies. Vitamin deficiencies can cause low-grade hypothyroidism. They wrote:

- *"the effects of biotin and iodine deficiency are under-appreciated."*

Qualitative answers from participants who answered "liberal" presented three main arguments: "borderline" cases often progress over time, how the patient feels is most important, and there are limited risks to trying low doses of medication out to see if it helps.

One participant noted that since "borderline" cases often progress over time, treating the patient before it progresses is valid:

- *"It is sometimes helpful to treat patients with borderline hypothyroidism as then the recheck will not be missed. If the patient is not on replacement they may not have their test rechecked and could show up years later with a TSH of 20. Refills are a safety net of sort."*

Another participant noted the importance of how patients feel, explaining that:

- “I care more about how the patient feels. As long as the labs are safe, I don't mind increasing to see if quality of life improves.”

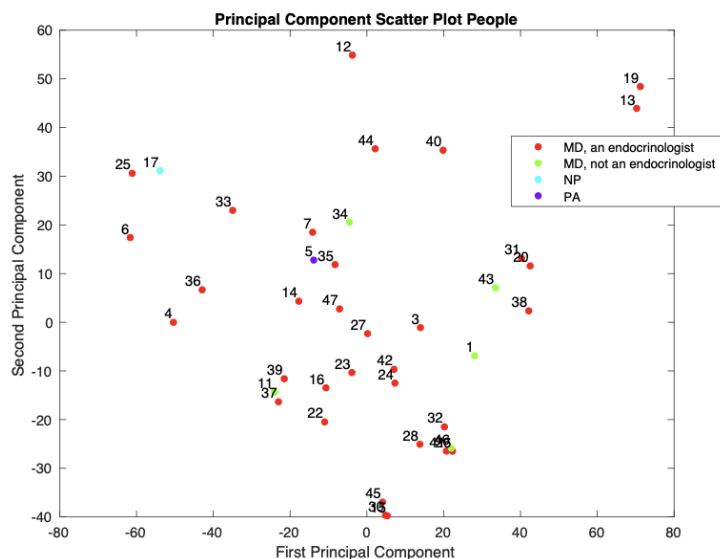
On this note of providing or increasing treatment, other participants explained that there are usually limited risks to trying low doses of medication. They wrote:

- “In younger patients with slightly high TSH and symptoms, I often just repeat the TSH and then try T4 Rx for a period of time to see how they feel,”
- “If people have TSH on the higher end of normal, and have symptoms, I will often do a time-limited trial of treatment.”

Statistical Inferences

Model 1: Opinions on Thyroid Hormone Ranges Do Not Correlate With Profession

In the Principal Component Analysis plot below, practitioners’ opinions on appropriate thyroid hormone ranges were compared with their professions. The data spread indicates that participants’ opinions do not seem to correlate with their particular degree. However, most participants were endocrinologists - perhaps the data would look different if more participants of other professions were included.



Model 2: Perception of Psychosocial Factors Changes Ideas of Appropriate Hormone Ranges

Table 1: Quality of Life and Self Image versus Recommended Hormone Ranges

The following is a Repeated Measures ANOVA model. This model compares multiple dependent variables with a few independent variables. The dependent variables it uses are practitioners’ answers to appropriate ranges for thyroid hormones (collected from Part 7). The independent variables it incorporates are practitioners’ answers to questions about patients’ quality of life and self-image.

MATLAB syntax:

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t2 =





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	SumSq	DF	MeanSq	F	pValue	pValueGG	pValueHF
(Intercept):Biomarkers	64276	5	12855	34.509	7.9963e-24	1.927e-20	1.5815e-23
SelfImage:Biomarkers	7238	10	723.8	1.943	0.04303	0.05512	0.043966
QualityofLife:Biomarkers	9872.8	15	658.19	1.7668	0.043637	0.05634	0.044616
Error(Biomarkers)	59604	160	372.52				

The central p-value column shows p-values below 0.05 for Self-Image and Quality of Life. This finding means that practitioners' perceptions of patients' self-image and quality of life significantly change their perceptions of appropriate thyroid hormone levels.

Table 2: Quality of Life and Recommended Hormone Ranges

QualityofLife_1	QualityofLife_2	Difference	StdErr	pValue	Lower	Upper
Always	Not usually	-15.595	8.9509	0.31934	-39.846	8.6563
Always	Sometimes	-24.455	6.7304	0.0050966	-42.69	-6.2194
Always	Usually	-13.859	6.6339	0.17833	-31.833	4.1143
Not usually	Always	15.595	8.9509	0.31934	-8.6563	39.846
Not usually	Sometimes	-8.8596	6.6055	0.5443	-26.756	9.0372
Not usually	Usually	1.7356	6.6703	0.9937	-16.337	19.808
Sometimes	Always	24.455	6.7304	0.0050966	6.2194	42.69
Sometimes	Not usually	8.8596	6.6055	0.5443	-9.0372	26.756
Sometimes	Usually	10.595	3.1215	0.0095171	2.1378	19.053
Usually	Always	13.859	6.6339	0.17833	-4.1143	31.833
Usually	Not usually	-1.7356	6.6703	0.9937	-19.808	16.337
Usually	Sometimes	-10.595	3.1215	0.0095171	-19.053	-2.1378

From Table 2, we can see that practitioners who said hypothyroidism diagnosis and treatment “always” affects patients’ quality of life were significantly different in the means of their thyroid hormone ranges from those who said “sometimes.” Practitioners who said “sometimes” were also significantly different from those who said “usually.” Practitioners who believe that patients’ quality of life and self-image is always or usually affected by diagnosis and treatment may tend to take more of a holistic approach to diagnostics than practitioners who say sometimes, as evidenced by lower mean scores for confidence in use of TSH, Free T4, Free T3, Total T3, Total T4, and Reverse T3.

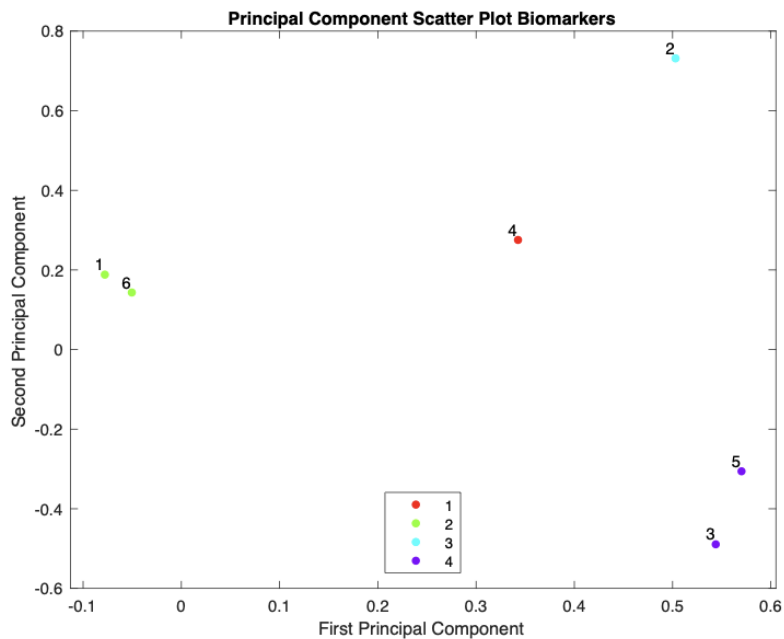
Table 3: Self Image and Recommended Hormone Ranges

<u>SelfImage_1</u>	<u>SelfImage_2</u>	<u>Difference</u>	<u>StdErr</u>	<u>pValue</u>	<u>Lower</u>	<u>Upper</u>
Not usually	Sometimes	-2.3568	3.4383	0.7736	-10.806	6.0923
Not usually	Usually	0.77646	5.3867	0.98861	-12.461	14.014
Sometimes	Not usually	2.3568	3.4383	0.7736	-6.0923	10.806
Sometimes	Usually	3.1332	4.818	0.79353	-8.7065	14.973
Usually	Not usually	-0.77646	5.3867	0.98861	-14.014	12.461
Usually	Sometimes	-3.1332	4.818	0.79353	-14.973	8.7065

From table 3, we can see that practitioners who said “not usually,” “sometimes,” or “usually” did not differ in their *mean* thyroid hormone range. However, the first table indicated that self-image did indicate a significant change between the practitioners. The first table showed that self-image affected the slope of practitioners’ thyroid hormone ranges. In other words, participants who said “sometimes” were different from those who said “usually” in their changes between the dependent variables (thyroid hormone ranges).

Model 3: Patterns in Opinions on Hormone Ranges

In the following Principal Component Analysis plot, practitioners’ opinions on TSH, Total T4, Total T3, Reverse T3, Free T3, and Free T4 were compared. In the plot, number 1 is TSH, number 2 is Free T4, number 3 is Total T4, number 4 is T3, number 5 is total T3, and number 6 is Reverse T3.



The plot indicates that practitioners' responses to TSH ranges were similar to their responses to Reverse T3. Additionally, their responses to Total T3 and Total T4 were similar. However, responses to Free T3 and Free T4 did not seem to correlate to one another.

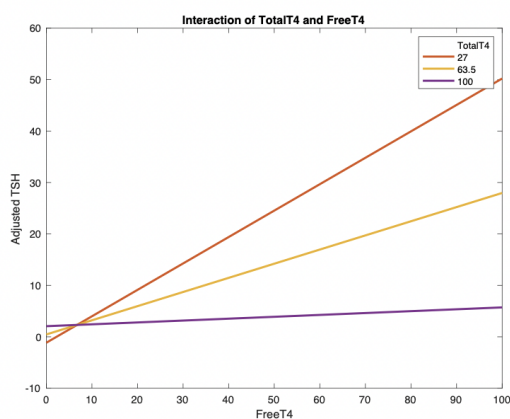
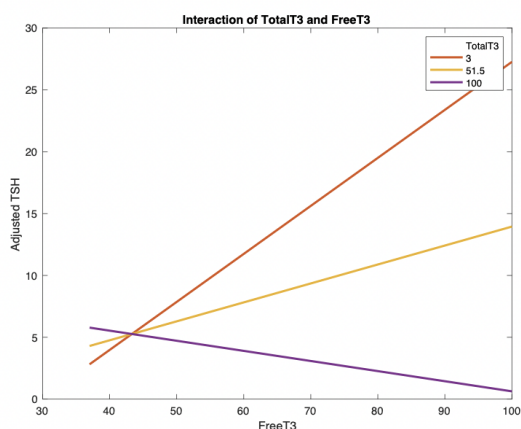
Model 4

Next, we used a linear regression model that predicted practitioners' responses to TSH based on their responses to Free T4, Free T3, and Total T3.

Linear regression model:
 $TSH \sim 1 + FreeT4*TotalT4 + FreeT3*TotalT3$

Estimated Coefficients:

	Estimate	SE	tStat	pValue
(Intercept)	-19.461	14.474	-1.3446	0.18767
FreeT4	0.69006	0.22023	3.1333	0.0035479
TotalT4	0.044	0.080071	0.54951	0.58625
FreeT3	0.40265	0.18313	2.1987	0.034801
TotalT3	0.2098	0.16726	1.2543	0.21828
FreeT4:TotalT4	-0.0065353	0.0025087	-2.605	0.01353
FreeT3:TotalT3	-0.0048442	0.0021824	-2.2196	0.033217



These show that as a practitioner moves from a low level of Free T3 to a high level of Free T3, their perception of TSH changes. This indicates that among the practitioners who indicated that they commonly use total T3 and total T4, if they also indicated that they commonly use free T3 and free T4, their marked use of TSH greatly increases in comparison to those who did not commonly use total T3 and T4.

Limitations

There are several limitations to this study's results, including its scale, relatively homogeneous group of participants, recruitment, wording and length of the survey, and issues with reference ranges.

The scale of the study is not large enough to illustrate American practitioners' clinical tendencies - there were only 48 participants. For that reason, we did not look to make claims about how most practitioners in America practice. Instead, we simply looked for disagreement. The sample is large enough to indicate that current diagnostic thresholds are not conclusive enough to provide unchanging, unambiguous standards for equitable and consistent application throughout the country.

The participants in the study were not diverse, either. Most were of the same age group and profession, endocrinologist, though other practitioners like NPs, PAs, and other types of MDs diagnose and treat hypothyroidism regularly. Additionally, most participants were from cities. Response rates from rural practitioners were low.

Participants were recruited through emails. Participants' emails were collected by searching through public hospital, clinic, and university directories. Many hospitals, clinics, and universities do not publicize their practitioners' emails, so perhaps responses could be skewed in that participants were connected through organizations that publicized their contact information.

The survey's wording and length could be deemed a limitation; several participants did not provide answers for every question or did not complete it. Additionally, using words like "appropriate," as in "is 0.5-4.12 an *appropriate* range" may be interpreted differently from participant to participant.

The most notable limitation is that a reference range was not provided for the participants. One participant explained in a comment section that they were "*not answering because I do not have the normal ranges (when it turns red) memorized, therefore do not want to answer the case. I use the references provided by our lab for free T4.*" We also received two emails from participants that said they did not feel comfortable participating in the survey because they did not have the reference ranges other than TSH memorized. This aspect is essential to consider when interpreting Part 7 on clinicians' opinions on hormone ranges. Perhaps an exciting proposition for future research would be to investigate how labs' reference ranges vary throughout the country.

Conclusion

In conclusion, practitioners disagree over several facets of appropriate diagnostic and treatment criteria. As emphasized in fictional patient cases 3, 5, and 8, their consistent, significant levels of disagreement imply that standards are being applied inconsistently throughout the country. This disagreement indicates that some patient populations must be receiving the wrong one. The condition's high biopsychosocial stakes make this inconsistency a pressing issue for patients' health. Consistent application of a diagnostic standard unambiguous enough to lead to the near-unanimous agreement among practitioners is critical to patients' health and practitioners' credibility. Further research should be conducted with a larger sample size to replicate these results. Public health interventions should be implemented to remedy this inconsistent application of medical standards.

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