

A Survey Finds Thousands of Patient Counterexamples Disputing the Enforced Proscription of All Triiodothyronine Containing Therapies

Eric K. Pritchard, MSc¹

¹Metis Research, Inc., 340 Pritchard Lane, Berkeley Springs, WV 25411

Abstract Background: *Although treated per the current standard of care, millions are suffering from the symptoms of hypothyroidism in spite of contrary medical science.*

Objectives: *This study advocates a proper care of patients suffering with the continuing symptoms of hypothyroidism (for months, years, even decades) by demonstrating the excessive breadth and unscientific support of the blanket proscriptions in enforced, effectively mandatory, hypothyroidism practice guidelines and policy statements against triiodothyronine-containing therapies.*

Design: *The documentation of patient counterexamples and personal experiences has inspired the finding of many more patient counterexamples. Patient counterexamples refer to people who have successfully treated their continuing symptoms of hypothyroidism with triiodothyronine-containing therapies. The existence of patient counterexamples is caused by medical practice ignoring medical evidence.*

Setting: *This study was done via an internet-based survey, which was advertised on thyroid-related forums. The participants had complete knowledge of their participation when they opted to participate.*

Main Outcome Measures: *The survey consisted of four questions about the participants thyroid-related counterexample experiences. Since counterexamples to a scientific concept only need to exist, no statistical design beyond totaling the responses was necessary.*

Results: *This study survey found 2,080 unique patient counterexamples, that is, individuals who answered the survey positively.*

Conclusion: *Patients with the continuing symptoms of hypothyroidism may benefit from a triiodothyronine-containing therapy. Consequently, the scope of the proscription against all triiodothyronine-containing therapies is overly broad and improperly extends beyond the endocrine system.*

Introduction

Study Question: Do patient counterexamples to the blanket proscription or effective ban of all triiodothyronine (T3)-containing therapies exist? A positive answer will bring pressure to recognize the thyroid-related post-thyroid functions in the peripheral tissue and related diagnostics so that patients with the continuing symptoms of hypothyroidism may be properly diagnosed and treated.

Background Knowledge

Counterexample patients by the thousands, both past and present, have regained their active, attractive lives from the debilitating continuing symptoms of hypothyroidism when treated with T3, a therapy contrary to hypothyroidism practice guidelines and policy statements. Ipso facto, these counterexamples disprove or limit the scope of endocrinology's proscriptions of all types of T3 therapy. By extension, their experi-

ences also disprove the effective bans against all related tissue diagnostics of functionally post-thyroid physiology.

Indeed, 9% to 14% of those treated for hypothyroidism are not satisfied medically.¹ Thus, Saravanan predicts generally unacceptable p-values of 0.09 to 0.14 for hypothyroidism care.¹ (These percentages times the tens of millions of patients treated suggest millions of suffering patients.)

Symptoms of hypothyroidism can appear without thyroid gland deficiencies in euthyroid hypometabolism.² Although this disease may adversely affect 6% of the population, the medical community denies its existence, particularly in guidelines, policy statements, and proscriptions. By extrapolation, millions in the United States, and many more millions worldwide are needlessly suffering from these proscriptions or bans.

Theoretical Companion Study

This study is the patient experience companion to the author's theoretical advocacy³ to reduce the scope of the hypothyroidism guidelines and policy statements.⁴⁻¹² This advocacy is based upon the following generally ignored medical science facts:

1. Circa 1947, thyroxine (levothyroxine, T4) does not reduce or eliminate symptoms of hypothyroidism in some patients.¹³ This was confirmed in 1954.¹⁴
2. Euthyroid hypometabolism presents the symptoms of hypothyroidism. It exists. It is treated with T3. This 1960 study produced 32 patient counterexamples.²
3. Post-thyroid physiology and functions exist.¹⁵⁻¹⁸
4. Post-thyroid physiology has hundreds of references beginning in the 1950's. There are approximately 400 references to the mitochondria¹⁹ and more than a thousand to triiodothyronine.²⁰
5. Connecting post-thyroid functions with hypothalamus, pituitary, and thyroid glands shows that the thyroid stimulating hormone (TSH) is four functions, and T4 is three functions away from the production of symptoms. Thus, the standard thyroid function for TSH and T4 tests only partially indicate the causes

of the symptoms of hypothyroidism.^{3,15-18}

6. Patients, who present the continuing symptoms of hypothyroidism in spite of T4-only therapy, can be properly diagnosed, and treated with desiccated thyroid.²¹ This 2001 study produced 40 patient counterexamples.

7. A mathematical analysis of T3 therapy half-life for its alleged danger shows its therapeutic variation can readily lie within the T3 reference range and can be as low as the circadian variation.³

8. The meta-analyses²⁻²⁴ of combination T3 plus T4 therapy versus T4-only therapy do not support the blanket T3 proscription because (a) the subjects suffered predominately from thyroid dysfunctions, (b) the combination therapy generally had lower therapeutic value than the T4-only therapy, (c) the analyses used minimized low-occurrence rate phenomenon, and (d) since the conclusions were not completely supported, they were and are overly broad.³ Once again, "the initial design of a medical survey largely influences the usefulness of the results."²⁵

9. The meta-analyses²²⁻²⁴ found the T3-containing therapy ineffective. However, since T3 is the most active thyroid hormone, it is effective in general.²⁶ Consequently, these meta-analyses and their cited papers must have studied subjects with no T3-related deficiencies,^{3,15-18} a special case.

10. An egregious fault of the meta-analyses is the summary dismissal of medical science that was not based on randomized clinical trials as illustrated by Fig. 1 of Grozinsky-Glasberg.²² This bias, advocated by evidence-based medicine, is epitomized by the maxim: "If the study wasn't randomized, we'd suggest that you stop reading it and go on to the next article in your search. Only if you can't find any randomized trials should you go back to it."²⁷ Consequently and unscientifically, there was no reconciliation with prior medical science findings. (Supposedly, randomized clinical trials defeat author/investigator bias, but it does nothing against biased or errant study design, subjects, methods, analysis, and conclusion.)

11. If the definition for "hypothyroidism" were specified in either proper or popular ways and logical consistency were maintained, then the consequentially improved diagnosis

and treatment would significantly reduce the suffering from the continuing symptoms of hypothyroidism.^{3,28}

12. Synthetic T3 has been found safe and effective by the US Food and Drug Administration.²⁹ Desiccated thyroid meets United States Pharmacopeia (USP) requirements.

Scientific Misconduct by Definition

“Although the ultimate decisions concerning scientific misconduct are made by personal conscience, medical authorities, and the justice system, the definitions of scientific misconduct are quite clear and applicable. The summary dismissal and ‘omission of conflicting data’ in the above items^{1-4,6,10-12} constitute scientific misconduct.³⁰ The suppression of evidence is one of the most widely and successfully used strategies. These ‘errors of omission’ allow people to create false impressions and mislead others without actually lying overtly.”³¹ Similarly, the “improper manipulation of experiments to obtain biased results, deceptive statistical or analytical manipulations, or improper reporting of results”³⁰ in above items 8 and 9 also fall under the category of scientific misconduct.

The phrase “fabrication, falsification, plagiarism” is far more commonly used by scientific and medical societies and in law to define misconduct:³²

“Misconduct or Misconduct in Science means fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting, or reporting research. It does not include honest error or honest differences in interpretations or judgments of data.”

Unfortunately, “current research misconduct policy, by neither preventing nor effectively discouraging fabrication and falsification, serves to enable such conduct.”³³ The omission of literature from literature searches can lead to false conclusions.³⁴ The omissions by the meta-analyses²³⁻²⁵ include the connection of thyroid gland secretions to cellular functions¹⁵⁻²⁰ via T3 and successful uses of T3.^{2,21} This is unhealthy^{1,2,21} and potentially dangerous.³⁴

Dangers Associated With Triiodothyronine (T3)

Triiodothyronine has three danger issues, too little, too infrequent, and as in all medications, too much. T3 helps. It increases mitochondrial production of energy,¹⁷ which powers various cellular functions.¹⁸ “T3 regulates the expression of many cardiac genes and acts on the system vasculature by relaxing the vascular smooth muscle.”³⁵ T3 controls cardiac contraction, cardiac relaxation, and systemic vascular resistance.³⁶ Low T3 circulating levels have been studied in patients with acute myocardial infarction and heart failure. In fact, those with free T3 > 3.1 pmol/L had a 95% survival rate after one year, whereas those with free T3 < 3.1 pmol/L had a survival rate of less than 78%.³⁷ Near surgeries, low T3 syndrome is highly prevalent in patients undergoing brain tumor surgery and is independently associated with unfavorable clinical results.³⁸

T3 is allegedly dangerous³⁹ but this allegation cannot be ethically supported by clinical trials.⁴⁰ The old belief of only dosing T3 once a day may have contributed to this alleged danger, even though taking T3 once a day works for some. Nonetheless, the choice for the patient with the continuing symptoms of hypothyroidism is potential danger versus certain life-long suffering.

Counterexamples

The black swan is the iconic counterexample. In 1697 the Dutch explorer Willem de Vlamingh discovered black swans in Australia, which countered the European dogma that all swans were white. Later, this discovery seemed obvious because other animals had varying colors, so swans should have been expected to have different colors too.⁴¹

Similarly, since allopathic medicine is centered on bodily abnormalities, abnormalities in the post-thyroid tissue physiology¹⁵⁻¹⁸ should be expected as well. However, cellular operations are not part of any bodily system.⁴² But, they are assumed by hypothyroidism practice guidelines and policy statements⁴⁻¹² to function perfectly.^{39,43}

The key to avoiding a black swan counterexample is in the proper language description of our observations: "All swans observed so far have been white." The phrase, "observed so far" is key to inductive logic, the generalization based upon observations.⁴⁴⁻⁴⁶ So far, medical black swans have not shattered endocrinology's blanket proscriptions against T3,^{4-12,22-24} but they should have.^{2,3,21}

Sir Karl Popper's Influence

The great philosopher on science, Sir Karl Popper noted:

"Logically, no number of positive outcomes at the level of experimental testing can confirm a scientific theory, but a *single* counterexample is logically decisive: it shows the theory, from which the implication is derived, to be false (*italics added*)."⁴⁷

Sir Karl Popper stated a scientific concept must have two qualities: It must be both testable and have no counterexamples. Confirming studies, which are preferred by medicine, are inadequate because welcomed positive outcomes are not derived from unwelcome counterexample situations.⁴⁸ The cited meta-analyses are examples of such positive outcome studies.²²⁻²⁴ However, as detailed above, thousands of counterexamples exist, proving that the guideline proscriptions are not true as stated, but may be true in some reduced form.³

An example and its counterexamples must be logically opposite. In some medical settings, however, such a situation is not always conclusive because there may be unknown factors affecting the patient. Consequently, medical counterexamples are often not deemed to be "black swans". Evidence-based medicine⁴⁹ institutionalized the summary dismissal of counterexamples, in spite of their logical supremacy.⁴⁷ In the present context, all the evidence that counters endocrinology's claims regarding the virtual ban on T3 has been eliminated. This also eliminates any reconciliation with medical science. What has not been eliminated, however, is the suffering of many patients.^{1,2,13,14,21}

"Counterexamples compel changes to the formulation of general statements, so

that they should not claim more than they are entitled to, or else the theory supported by them becomes invalid, because it contradicts the truth asserted by the counterexample (p.28)."⁴⁶

As Macrina asserted in his text, *Scientific Integrity*: "Results may support or refute a hypothesis, but a hypothesis cannot be proved. Indeed, it can only be disproved."⁵⁰

Statistics and p-values

Counterexamples to studies make the study statistics and p-values meaningless because the statistics and p-values are based upon only the study data. This is quite obvious because the study data do not include counterexample data or enough counterexample data so that it is not drowned in the averaging processes. See Figure 1 in the corresponding reference here.⁵¹

Excuses for Failure

Endocrinology has provided physicians excuses for failure to mitigate the symptoms of hypothyroidism. It has offered and still offers "nonspecific symptoms" and "functional somatoform disorders,"^{39,43} which may be augmented by "you're just getting old." These excuses help physicians caught between their duty to patient health and avoiding enforcement actions by their board of medicine or medical council.

However, there is a compelling chain of evidence that begins with the 1895 discovery of thyroid hormones controlling metabolism rates that argues against these excuses. The late Dr. E. Chester Ridgway amplified this by noting the action is T3 in the cell and not T4 in the blood:

"T3 is the active ingredient, and it's the thing that accounts for the thyroid hormone action. As I've been reminded many times, there are no intracellular events that we know that can be described by T4 at the level of the nucleus. Only T3. T4 is not the active compound. Likewise, the site of action is in the nucleus."⁵²

Indeed, T3 has been linked to the upward regulation of the cellular respiratory cycle:¹⁷ "Triiodothyronine (T3) is considered a major regulator of mitochondrial activity." The

mitochondria produces energy in the form of adenosine triphosphate (ATP) to power virtually all of the cells' functions.¹⁸ Thus, microbiology shows that a substantial variety of seemingly disconnected "nonspecific" symptoms may occur.¹⁸ Medical ethics and the differential diagnostic protocol demand that these functions must be tested. Also, since the symptoms are physical, they must be eliminated instead of or prior to blaming the patients for their ills with untestable functional somatoform disorder beliefs.^{39,43}

Differential diagnostic protocol

Differential diagnostic protocol is a process of elimination applied to clinical problems. Physicians are required to make a list, at least mentally, of all the potential causes of the patient's symptoms and then test each of the potential causes: Differential Diagnosis "...is a systematic method used to identify unknowns. This method, essentially a process of elimination, is used...by physicians and other qualified professionals to diagnose the specific disease in a patient."⁵³

Obviously, the process of elimination is only successful if all of the potential unknown causes are considered by testing. The completeness of the list of unknown causes depends upon the state of medical science.⁵⁴ Equally as obvious, the state of medical science^{2,3,15-21} is beyond the state of the hypothyroidism guidelines and policy statements.⁴⁻¹² Consequently, the differential diagnostic protocol is generally not being followed in diagnosing patients with the continuing symptoms of hypothyroidism.

Physicians' Dilemma

Physicians owe their patients a fiducial responsibility for two reasons. First, there is an implied contract created by initiating diagnosis and treatment. Second, the relationship is asymmetrical with the physicians having superior information and prescription powers. On the other hand physicians must comply with medical guidelines, policies, and customs or face potential adverse actions by the board of medicine or general medical council. This potential enforcement makes

the guidelines, policies, and customs mandatory and not voluntary per US Supreme and Federal courts.^{55,56} All of this functions to the patients' benefits if the guidelines, policies, and customs are correct. However, if they are not correct, then the physicians are faced with a conflict of interest, which they are supposed to avoid.⁵⁷ So when a physician encounters a patient with the continuing symptoms of hypothyroidism, he/she is faced with four poor choices. He/she can:

1. Obey the guidelines, policies, and/or customs and not treat the patient with any form of T3 and violate his/her fiduciary duty and medical ethics.
2. Treat the patient with T3 and become liable to the board of medicine or general medical council.
3. Contrary to medical ethics, bully the patient into submission.
4. Not care for anyone with the continuing symptoms of hypothyroidism by referral to another physician or proper notification of termination of medical care.

The health of patients and the health of the physician-patient relationships demand correction of errant medical practice guidelines, policies, and customs.

Physicians' Dilemma Should Be Medicine's

"According to the model theory of deduction, people make inferences according to the semantic principle that a conclusion is valid if there are no counterexamples to it, that is, if there are no situations in which the premises are true but the conclusion is false." (Johnson-Laird & Byrne, 1991, page 350).⁵⁸ See also Sir Karl Popper.^{47,48}

But physicians find counterexamples are not readily available. There are no recognized medical counterexamples because medicine consistently dismisses them as mere anecdotes. Additionally, there are no endocrinology counterexamples because endocrinologists are seemingly not fully educated in the physiology of the peripheral tissue in spite of warnings of levothyroxine failures.^{13,14,21}

U.S. Supreme and Federal courts have

recognized human nature in their rulings that enforcement of practice policies and guidelines make them effectively mandatory.^{55,56} Thus, enforcement effectively precluding counterexample consideration. Counterexamples are also avoided with policies that excuse failures to mitigate the symptoms of hypothyroidism,^{39,43} and do not comply with differential diagnostic protocol.^{53,54} Further, if ranked at all, evidence-based medicine ranks counterexamples quite low along with other observations.⁴⁹ Consequently, in spite of medical science,^{2,13-17,19-21} many patients suffer with the continuing symptoms of hypothyroidism¹ and euthyroid hypometabolism.²

Further by the same metabolism deficiency and inadequate cellular energy production,¹⁵⁻²⁰ those suffering from the continuing symptoms of hypothyroidism face the dangers of untreated hypothyroidism: heart problems, high cholesterol, mental health issues, peripheral neuropathy, myxedema, infertility, birth defects,^{59,69} etc.¹⁹

Methods

Sir Karl Popper's arguments for counterexample supremacy,^{47,48} the overwhelming valuation of direct medical evidence, Dr. Ridgway's declaration that the action is in the cell,⁵² the author's prior study,³ and the author's personal knowledge inspired the use of the internet-based Survey Monkey to question members of numerous thyroid-oriented internet forum members about their hypothyroidism symptom related counterexample experiences, diagnoses and therapies. The surveying of patient experiences has gained greater credibility recently.⁶¹

This survey asked the following four questions: Question 1: "If T4 only (eg. Levothyroxine/Synthroid/Eltroxine) failed to relieve or eliminate your symptoms of hypothyroidism did you later have success with a T3 thyroid hormone replacement that did relieve or eliminate your symptoms (eg. Liothyronine/Cytomel/or natural thyroid extract)."

Question 2: "If your doctor, for any reason, stopped prescribing your synthetic or natural form of T3 therapy and replaced it with T4

only therapy did this result in a return of your hypothyroidism symptoms?"

Question 3: "If you were denied a diagnosis because your thyroid and pituitary gland function tests showed "normal, within range" result, but you had continuing symptoms of hypothyroidism, were these symptoms relieved or eliminated by you taking some form of a T3 containing replacement?"

Question 4: "If you answered yes to either questions 1, 2 or 3, would you be willing to testify to your experiences?"

Survey Analysis

The analysis is simple because the existence of the counterexamples provides decisive proof. Consequently, the only analysis needed was counting the number of "yes" responses.

Results

This survey produced 2,080 unique positive entries:

| | |
|-------------|------------|
| Question 1: | yes: 2,041 |
| Question 2: | yes: 635 |
| Question 3: | yes: 1,041 |
| Question 4: | yes: 1,437 |

Discussion

The total number of counterexamples (2,080) is greater than all of the subjects (1,398) in all of the studies cited by three anti T3 meta-analyses.²²⁻²⁴ When the numbers of counterexamples in medical history^{2,21} are added, the total is at least 2,152.

Sir Karl Popper's widely accepted philosophy asserts only one counterexample is necessary to disprove a theory or conjecture.⁴⁷ However, medicine, using evidence-based medicine, has veritably institutionalized the rejection of counterexamples.⁴⁹ The overwhelming number of patient counterexamples renders endocrinology's proscriptions to be not only wrong but also likely grounds to investigate for scientific misconduct. These counterexamples, the theoretical proof,³ and the linguistic demands for the stipulation of definitions²⁹ demand the reduction of the scope of the hypothyroidism policy statements and practice guidelines and an end to the blanket proscription of T3.

Relation to Other Evidence

Question 1: This response by 2,041 participants is a verification of Drs. Kirk and Kvorning, and Dr. Means 60-year-old warnings that thyroxine did not work for all patients.^{13,14} It also corroborated the long-term study, by Drs. Baisier, Hertoghe, and Eeckhaut.²¹ These doctors also provided greater insights to their patients' clinical presentations and diagnostics as well as producing 40 patient counterexamples in a follow-up study.

Question 2: This response by 635 participants suggests a variation on the challenge, re-challenge, de-challenge (CDR) test usually used for the low response rate of adverse drug reactions.⁶² However, in this case it produces positive instead of negative results: Some people are helped by T3 containing therapies, which is quite contrary to the conclusions of the aforementioned meta-analyses.²²⁻²⁴

Question 3: This response validates Dr. Goldberg's euthyroid hypometabolism,² which endocrinology dismissed more than 50 years ago. Indeed, some euthyroid patients with the symptoms of hypothyroidism need a T3 therapy as the study's production of 32 patient counterexamples showed.

Questions 1, 2, and 3 were answered "yes" by 327 respondents. This result suggests these respondents were substantially abused by endocrinology's dictates. Endocrinology forced them to return to misery and then regain their active, attractive lives a second time.

Question 4: Sixty-nine percent of the positive responses volunteered to testify. This shows just how serious this issue is to patients who have had the continuing symptoms of hypothyroidism.

Brief Review of Study Points

1. The inherent potential for counterexamples and their importance to all sciences.⁴⁴⁻⁴⁸
2. Patient counterexamples exist in medical science history.^{2,21}
3. Overwhelming number of patient counterexamples in the present survey,
4. Since medicine is abnormality oriented, patient counterexamples^{2,21} should have been expected.
5. P-values are not applicable in the presence of counterexamples.

6. No reconciliation of meta-analyses²²⁻²⁴ with counterexamples and medical science.^{2,15-21,25}

Additionally, this list also includes the important theoretical points listed under "Theoretical Companion Study," above by reference.

These points argue that endocrinology should be judged by its own measure: "Clinical investigators who fail to meet basic standards in ethical conduct or scientific integrity must also be excluded from the community of experts."⁸ Ethical standards include placing patient welfare first and foremost, knowing applicable medical science, and being honest in all professional relationships.

Conclusion

Thousands of patient counterexamples, confirmed by many studies, the author's prior study, and this study's results, demonstrate that many patients with continuing symptoms of hypothyroidism can be treated successfully and beneficially with safe and effective T3 therapies. At a minimum, these truly evidence-based medicine results call for a reduction in scope of endocrinology's proscription against all triiodothyronine (T3) containing therapies. That change can potentially alleviate the suffering of millions.

Unethically and unscientifically, the endocrinology establishment, via state enforced proscriptions on physicians, continually restrains patients with the continuing symptoms of hypothyroidism from realizing active and attractive lives.

The medical science and these counterexample results suggest diagnosis by trial treatment with a T3-containing therapy to mitigate the symptoms of hypothyroidism, to be healthier, and to improve their chances of surviving life's great killers.

The health of patients and the health of the physician-patient relationships demand correction of errant medical practice guidelines, policies, and customs.

Acknowledgments

A special appreciation goes to Sheila Turner for making Pritchard's survey concept a reality, to thyroid-related web sites for advertising the survey, to the many volun-

teers who took the survey, to Mariam Wilson for reducing and tabulating survey data, and to Linda Pritchard and Brian Pritchard for numerous edits.

Competing Interests

The author declares that he has no competing interests.

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