

COMMENTARY: Subclinical Thyroid Dysfunction: A Joint Statement on Management from the American Association of Clinical Endocrinologists, the American Thyroid Association, and The Endocrine Society

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I was the Chairman of the panel (“consensus panel”), appointed by the American Association of Clinical Endocrinologists, the American Thyroid Association, and The Endocrine Society, that was charged with developing evidence-based practice guidelines for the diagnosis and management of subclinical thyroid disease (1). I appreciate the opportunity to review, before publication, and to comment on the paper by Gharib *et al.* (2) in this issue of *JCEM*. This paper is a joint statement from the above societies/associations that presents opinions that are different from several recommendations in the evidence-based report (1). In this note, I will comment on the most important differences between the opinions expressed by Gharib *et al.* (2) and the recommendations published in the “Scientific Review” and “Clinical Applications” papers (1, 3).

Clinical Applications

The Scientific Review (1) repeatedly states that its evidence-based medicine recommendations are for populations and that doctors should use their best clinical judgment, in the context of the recommendations, for management of individual patients. The Clinical Applications paper, solicited by the editors of the *Journal of the American Medical Association*, provides practical examples for how the recommendations can be applied to patients by doctors, using their best judgment and considering the patients’ preferences.

Scientific Review

Routine levothyroxine treatment

Most patients with raised serum TSH have levels between 4.5 and 10 mIU/liter. Gharib *et al.* (2) recommend levothyroxine treatment for most of them. They cite as support a published opinion survey of thyroid specialists (4) and previously published recommendations of one of the authors (5). One could reasonably argue that opinion surveys should not be considered in development of practice guidelines and Gharib *et al.* (2) failed to cite the Clinical Perspective paper

(6) that followed the one of McDermott and Ridgway (5), which came to opposite conclusions.

Based on the evidence available at this time, the consensus panel recommended against routine treatment of patients with minimally raised serum TSH (4.5 to 10 mIU/liter). Despite many published reports, the endocrinologists on the panel as well as the panel’s nonendocrine experts could not find even fair data indicating adverse health outcomes in untreated patients in this group except for a higher rate of development of overt hypothyroidism [2.6% per year in the absence of antithyroperoxidase antibodies; 4.3% per year in their presence (7)]. Similarly, little to no benefit of treatment has been reported in this group other than averting development of overt disease, and the panel did recommend follow-up at appropriate intervals to detect disease progression.

We all acknowledge that approximately 20% of levothyroxine-treated patients in the community have decreased serum TSH (8), indicating overtreatment, and adverse health outcomes have been reported in such patients. Gharib *et al.* (2) suggest that physician education can improve this situation and state that these data should not argue against levothyroxine treatment. Because health care providers who are not endocrinologists care for most patients with hypothyroidism, I am not optimistic that their practice pattern will be rapidly improved by education. There are many examples of inertia in attempting to change practice patterns by education. In evaluation of thyroid disease, the continued use and misinterpretation of the T₃-resin uptake, despite nearly a generation of attempts at education (9), is a good example. Because levothyroxine treatment provides little to no demonstrable benefit in this group and overtreatment with reported adverse health outcomes occurs in approximately 20% of levothyroxine-treated patients, it seems prudent *not* to recommend routine levothyroxine treatment when serum TSH is minimally raised.

Routine screening

Gharib *et al.* (2) recommend routine serum TSH determination but fail to cite the Institute of Medicine analysis of this issue, which recommended that Medicare not pay for routine TSH measurement (<http://books.nap.edu/catalog/10682>).

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html). The data that argue against routine TSH screening have been presented both in the Institute of Medicine report and in the consensus report (1). Additionally, most individuals who have increased serum TSH are older than 60 yr of age, have minimally raised serum TSH concentrations (4.5 to 10 mIU/liter), and take other, often many other, medications. If one accepts the recommendation of Gharib *et al.* (2) for treatment of most patients with minimally raised TSH, typically detected by screening, levothyroxine would be added to their other medications. Polypharmacy contributes to medication errors and might increase the frequency of over-treatment with its attendant consequences.

Screening pregnant women

Both the American College of Obstetrics and Gynecology (10) and the consensus panel found insufficient evidence to recommend routine screening of pregnant women or women who plan to become pregnant. The high frequency of thyroid hormone and TSH determinations that are out of the normal range, but normal for pregnancy, is the major adverse effect of screening pregnant women by health care providers other than endocrinologists. These values are often misinterpreted by nonendocrine providers and result in unnecessary referral and anxiety for the pregnant woman. It is interesting to note that neither The Endocrine Society nor the American Thyroid Association has endorsed universal screening in pregnancy or in women desiring pregnancy (11).

Conclusion

The evidence-based medicine approach to guideline development identifies benefits and adverse consequences of clinical diagnostic or therapeutic actions. The benefits/risk ratio should always be considered in making recommendations to clinicians. Gharib *et al.* (2) state that “lack of definitive evidence for a benefit does not equate to evidence for lack of benefit.” I believe, and I think that the panel would concur, that until there is unequivocal evidence of benefit, the pru-

dent physician “will do no harm,” rather than institute treatment or screening that could have adverse consequences that outweigh any potential benefit, be they physical, psychological, or financial.

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