The current controversy over recommendations for thyroid screening during pregnancy has its origins in the 1999 publication of an observational study based on thyroid function analysis of stored second-trimester serum samples. In this study, 62 children of mothers identified with thyroid-stimulating hormone (TSH) levels greater than the 98th percentile were compared with 124 children of euthyroid-matched controls. Neurodevelopmental testing at 7–9 years of age revealed that children born to women with untreated thyroid dysfunction had lower mean IQ scores. Women included in this study had low mean serum-free thyroxine (T\textsubscript{4}) levels, and many would be considered to have had overt hypothyroidism. Despite that, this and other studies linking increases in preterm birth, placental abruption, and fetal death to subclinical thyroid dysfunction have been cited by professional organizations as the impetus for recommendations of routine prenatal screening for and treatment of subclinical hypothyroidism. In contrast, the American College of Obstetricians and Gynecologists has consistently recommended against universal screening and supported a risk-based approach until there is evidence of treatment benefit in women with subclinical hypothyroidism or their offspring. Importantly, women with subclinical hypothyroidism represent the majority of those who would be identified through routine TSH screening. Of note, the recently completed international multicenter Controlled Antenatal Thyroid Screening study did not demonstrate improvement in cognitive function of 3-year-old children born to women screened and treated for subclinical thyroid dysfunction during pregnancy.

In contrast to subclinical thyroid dysfunction, it is well-established that untreated overt hypothyroidism during pregnancy is associated with adverse outcomes for both the mother and her fetus and that treatment mitigates many of these risks. Overt hypothyroidism is defined by an elevated TSH level and decreased free T\textsubscript{4} level according to thresholds that vary by gestational age and population studied.

If one were to set aside the debate surrounding routine identification and treatment of pregnant women with subclinical thyroid dysfunction, the remaining question is whether detecting and treating women with undiagnosed overt hypothyroidism provides sufficient rationale for universal screening during pregnancy. It has been suggested that targeted thyroid testing during pregnancy may miss approximately 30% of women with elevated TSH due to overt or subclinical hypothyroidism. However, a recent cost-effectiveness analysis suggests that a policy of universal screening to detect overt hypothyroidism during pregnancy falls below recommended U.S. cost-effectiveness thresholds.

This month in Obstetrics & Gynecology, Granfors and colleagues (see page 10) assess the practice of targeted thyroid testing in a retrospective cohort of women whose blood was drawn at the time of routine ultrasound screening at 17–19 weeks of gestation and stored for later study.
The authors estimate that only 50% of women who could have had their blood drawn and stored during the 3-year study period actually did. Prenatal and medical records were reviewed for evidence of TSH testing or treatment with levothyroxine. Women with a personal history of thyroid disease, family history of thyroid dysfunction, goiter, type I diabetes, or other autoimmune diseases were targeted for testing. Targeted testing was performed in 1,054 (20%) of the 5,254 women who delivered during the study period. Of these, 163 women were identified as taking levothyroxine at conception and thus considered to have overt hypothyroidism. Of the 4,200 samples from women not targeted for testing, 1,006 were randomly selected and analyzed for TSH and free T4 levels. Trimester-specific thresholds for TSH were used (2.5 or 3.0 milliunits/L), and the threshold for a low free T4 was 9.7 pmol/L (0.75 ng/dL).

In their analysis, the prevalence of elevated TSH in the study cohort was approximately 12% and equal between those targeted and those untested. This is much higher than has been reported previously and, as the authors suggest, is probably related to use of trimester-specific thresholds that are too low. Nevertheless, the authors propose that a remarkable 82% of women with elevated TSH levels would not have been detected through targeted screening. They conclude, based largely on the 86% of women identified with subclinical hypothyroidism, that targeted thyroid testing is unsatisfactory in their clinical practice. Moreover, they suggest that, if evidence to support treatment of women with subclinical hypothyroidism becomes available, a universal thyroid testing approach would be favored. Until such evidence is available, however, it is hard to disagree with current recommendations by the American College of Obstetricians and Gynecologists for screening based on risk factors.

What if we were to analyze those women identified with overt hypothyroidism in this retrospective cohort study? Targeted screening yielded seven new cases of overt hypothyroidism. If we were to extrapolate findings from samples analyzed from the untested group, an additional 29 cases of overt hypothyroidism theoretically could have been identified. Again, this may be an overestimation, given that the TSH thresholds were likely too low. Regardless, one might conclude that universal screening is superior to a targeted approach. However, Granfors et al also identified 163 women treated with levothyroxine at conception. Although the exact proportion with overt hypothyroidism is unknown, all these women potentially would have been identified to have overt hypothyroidism. Taken together, as many as 170 women in their cohort had overt disease identified without universal screening. Assuming an additional 29 women could have been identified through universal screening, one might argue that the clinical practice of targeted thyroid screening in this cohort would have identified more than 85% of pregnant women with overt hypothyroidism.

It is anticipated that the controversy regarding routine screening and treatment of pregnant women with subclinical hypothyroidism eventually will be settled as new evidence emerges from ongoing treatment trials. As Granfors et al suggest, if there is evidence of benefit to mothers or their children, routine screening during pregnancy seems assured. However, if ongoing treatment trials yield negative results, the screening debate would seem to hinge on the additional women with overt hypothyroidism who would be identified through routine pregnancy screening. Based on Granfors et al’s data and the inevitable cost associated with universal screening, targeted screening seems to be the best approach.

REFERENCES