Results
After screening 648 articles, only 14 published between 1987 and 2010 were considered suitable for inclusion in the review. These studies included 20,723 patients in the single-nodule group and 23,565 in the multinodular group. In a meta-analysis of these studies, the risk of thyroid cancer was significantly lower in the multinodular group than in the single-nodule group (odds ratio [OR], 0.8; 95% CI, 0.67 to 0.96) with some inconsistency among the studies. The four studies in the United States did not support this conclusion; the odds of thyroid cancer in multiple versus single nodules did not differ (OR, 1.00, 95% CI, 0.79 to 1.26). Based on whether a region was considered iodine-deficient, there was an association between iodine deficiency and the finding of lower risk in multinodular goiter.

Conclusions
Thyroid cancer may be less frequent in multinodular goiter as compared with single nodules, particularly outside the United States.

SUMMARY

Background
Many years ago the dogma was that multinodular goiter was usually a benign condition and, in contrast, a single “dominant” nodule was much more likely to be malignant than the nodules in a multinodular goiter. However, various studies have contradicted this belief and convinced endocrinologists to evaluate nodules in multinodular goiter for the possibility of malignancy. This study is a systematic review of the prevalence of malignancy in the nodules of multinodular goiter versus that in single nodules.

Methods
The authors reviewed MEDLINE and other databases to find studies of adults with diagnoses of multinodular goiter or single thyroid nodules by ultrasound who underwent FNA of a nodule or surgery. FNA results indicating malignancy required pathological diagnosis on the resected specimen. “Hot” nodules were excluded from the study.

Weak Evidence Suggests That Multinodular Goiter Is Less Likely to Harbor a Malignancy than a Solitary Nodule
Jerome M. Hershman

ANALYSIS AND COMMENTARY

I used to believe that multinodular goiter was nearly always a benign condition, but my belief was shattered by the 1992 report of Belfiore et al. from Italy, who reported that the frequency of thyroid cancer in patients with a solitary nodule was not different from the frequency in patients with multiple nodules—about 5% (1). This conclusion about frequency (prevalence) was confirmed by the study of Frates et al. in Boston, who reported the same prevalence of cancer in multinodular goiter and in single nodules (about 15%), although the single nodule was twice as likely to be malignant as a nodule in a multinodular goiter; biopsy of each nodule >1 cm in a multinodular goiter increased the prevalence so that it became the same in multinodular goiter as that in the single nodule (2).
Weak Evidence Suggests That Multinodular Goiter Is Less Likely to Harbor a Malignancy than a Solitary Nodule

The results of this review are highly influenced by one study, by Rago et al. in Pisa. They reported that papillary thyroid cancer (901 cases) was more frequent in solitary nodules (446 of 13,549 [3.3%]) than in multinodular goiter (411 of 19,923 [2%], P<0.0001) (3). None of the other studies showed a significant difference in odds ratios, but the meta-analysis that included this study supported the conclusion noted above.

References