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## CLINICAL MANAGEMENT OF PRIMARY HYPERPARATHYROIDISM AND THRESHOLDS FOR SURGICAL REFERRAL: A NATIONAL STUDY EXAMINING CONCORDANCE BETWEEN PRACTICE PATTERNS AND CONSENSUS PANEL RECOMMENDATIONS

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### ABSTRACT

**Objective:** To determine whether 1990 guidelines established by the National Institutes of Health (NIH) for the optimal management (surgical versus nonsurgical) of patients with asymptomatic primary hyperparathyroidism (PHPT) are known and followed by endocrinologists.

**Methods:** We surveyed endocrinologists in the United States who were randomly selected in 1998 from two endocrine societies. Endocrinologists were asked about management of asymptomatic patients with PHPT, awareness of NIH recommendations, practice demographics, and annual PHPT case volume. We classified endocrinologists into either low-volume (<12 cases of PHPT per year) or high-volume (≥12 cases per year) physicians.

**Results:** Of 374 eligible physicians, 146 (39%) responded to our survey. In comparison with nonrespondents, respondents were of similar age, sex, years in practice, and geographic location profiles; this finding suggested minimal nonresponse bias. More high-volume physicians than low-volume physicians were aware of the NIH guidelines (75% versus 50%;  $P < 0.01$ ). Management of asymptomatic patients was similar between volume groups; overall, 39% of patients were referred for surgical treatment. Nevertheless, considerable variation in management existed; 7% of all physicians referred ≥90% of their asymptomatic patients for surgical treatment, whereas 31% referred ≤10%. Adherence to monitoring guidelines for nonsurgically managed patients ranged widely,

depending on the specific recommendation (from 6% of physicians obtaining creatinine clearance assessments every 6 months to 78% of physicians ordering serum calcium measurements every 6 months). Surgical referral practices also varied substantially, with 25% of all physicians referring a 40-year-old patient with PHPT when hypercalcemia was mild ( $\leq 1$  mg/dL above normal), 39% when hypercalcemia was moderate, and 31% when hypercalcemia was severe ( $> 1.5$  mg/dL above normal). Of the responding physicians, 4% reported that hypercalcemia alone was not sufficient justification to refer a patient for surgical intervention. Higher PHPT case volume was not associated with differences in surgical referral.

**Conclusion:** Suboptimal awareness of the 1990 NIH panel recommendations and the substantial variation in clinical management of PHPT indicate that newer NIH guidelines developed in 2002 must be more widely disseminated and strongly recommended if practice patterns are to be influenced and clinical outcomes improved. (*Endocr Pract.* 2003;9:494-503)

### Abbreviations:

MEN = multiple endocrine neoplasia; NIH = National Institutes of Health; PHPT = primary hyperparathyroidism; PTH = parathyroid hormone

### INTRODUCTION

Before the advent of “routine” biochemical blood testing, most patients with primary hyperparathyroidism (PHPT) presented with signs or symptoms of the disease or its complications—notably, nephrolithiasis, skeletal disease, or other manifestations of hypercalcemia (1-3). Currently, most patients with PHPT present asymptotically, usually diagnosed on the basis of a high serum calcium level discovered on untargeted biochemical screening (4,5). Surgical management is the preferred strategy for symptomatic PHPT because it is potentially curative and frequently reverses symptoms (6). For asymptomatic disease, however, the optimal management strategy (surgical treatment versus only observation versus medical therapy) is less clear (7,8). Controversy stems partially from an incomplete understanding of the natural history of PHPT.

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In an effort to provide guidance, a 1990 National Institutes of Health (NIH) consensus development conference panel established recommendations (which were published in 1991) on selection of patients with asymptomatic PHPT for surgical versus nonsurgical management (9). Characteristics of patients who can be safely managed nonsurgically included age greater than 50 years; absence of symptomatic manifestations (such as nephrolithiasis, fractures, and hypercalcemia-related symptoms); and absence of highly abnormal or worsening test results (for example, 30% decrease in creatinine clearance, serum calcium concentration  $>1.0$  mg/dL above normal, 24-hour urine calcium excretion  $>400$  mg, and bone mineral density more than 2 standard deviations below the age- and sex-corrected normal). Whether these published recommendations are followed, however, is unclear.

To gain an understanding of the general clinical management of PHPT and the degree to which it is concordant with the 1990 NIH guidelines, we surveyed the practice patterns of general endocrinologists and bone and mineral specialists in the United States pertaining to the usual evaluation and management of PHPT. Because a previously conducted survey of endocrine surgeons showed improved surgical outcomes in settings with higher case volumes (10), we hypothesized that physicians with more experience in managing patients with PHPT (high PHPT case volume) would be more aware of and would practice in concordance with the 1990 NIH consensus panel recommendations.

## METHODS

### Study Design and Participants

We performed a cross-sectional study of general endocrinologists and specialists in the management of PHPT (that is, bone and mineral specialists). For potential participation in the study, we randomly selected a sample of physicians from two endocrine societies, the American Association of Clinical Endocrinologists and the Endocrine Society. To gather information from highly experienced physicians who might be responsible for managing large numbers of patients with PHPT, we oversampled bone and mineral specialists, with a ratio of 1 bone and mineral specialist for every 2 general endocrinologists. Initially, the survey was faxed to physicians on two separate occasions. Subsequently, the survey was faxed a third time to nonrespondents, and up to three follow-up telephone calls were performed in an attempt to improve the response rate. The survey was conducted between May and August 1998.

### Questionnaire Development and Content

A multidisciplinary team that included representatives from the fields of endocrinology, endocrine surgery, and general internal medicine designed and conducted the survey. The Joint Committee on Clinical Investigation (institutional review board) at Johns Hopkins University approved the study protocol.

We assessed physician characteristics, which included personal demographics, training and practice status such as board certification, and annual PHPT case volume. We classified responding physicians into one of two volume categories, low volume ( $<12$  PHPT cases per year) or high volume ( $\geq 12$  PHPT cases per year).

Respondents were asked about the tests and procedures they would order for suspected cases of PHPT. For patients with established PHPT, we inquired about the initial management (surgical versus medical versus observation) for patients with asymptomatic, minimally symptomatic, and frankly symptomatic PHPT. For those patients who were treated medically, we surveyed the most frequent medications used for men and premenopausal and postmenopausal women.

To measure awareness of the consensus guidelines, we asked physicians whether they knew of PHPT guidelines originating from the American Association of Clinical Endocrinologists, the American Society of Bone and Mineral Research, the Endocrine Society, the NIH, or the Paget Foundation. Those respondents who acknowledged the existence of the 1990 NIH consensus guidelines were considered aware. Because the NIH guidelines are the only widely disseminated published PHPT guidelines, we classified physicians who selected only the NIH guidelines as being highly aware.

For measurement of adherence to guideline recommendations, we compared the physician self-reported practice patterns with the explicit guideline recommendations. The NIH consensus panel made explicit recommendations about three issues: the frequency of monitoring nonsurgically managed patients; the biochemical and symptomatic abnormalities that should prompt surgical referral (threshold values); and the use of preoperative localization studies (9).

To ascertain monitoring frequency, we asked, "In patients with PHPT not referred for surgical treatment, how often do you routinely obtain the following tests?" (see Table 4). Respondents were given choices of "3 months," "6 months," "9 months," "12 months," "24 months," or "only if clinically indicated" for each test. We considered the respondents' practice as concordant with the NIH guidelines if their monitoring schedule was the same as or more frequent than the recommended schedule.

To determine thresholds for surgical referral, we asked the following question: "In a 40-year-old person with PHPT (elevated intact parathyroid hormone [PTH] and serum calcium) and no significant comorbid conditions, which of the following abnormalities alone is sufficient for you to refer the patient to a surgeon?" Respondents were presented a list of abnormalities (Table 1) that were categorized into a low, middle, and high level of derangement and asked to choose the level that would prompt a referral for surgical treatment. If respondents did not specify a level for a particular indication for surgical referral, they were classified as having a "not sufficient alone" threshold for that indication. Respondents whose thresholds were concordant with those of the NIH guidelines were considered adherent.

**Table 1**  
**Definitions of Thresholds for Surgical Referral**  
**of Patients With Primary Hyperparathyroidism, Shown by Indication\***

Indication for surgical referral	Threshold†		
	Low	Middle	High
Test abnormalities			
Intact PTH level (normal, 10-65) (pg/mL)	66-75	76-95	>95
Serum calcium level (normal, 8.5-10.5) (mg/dL)	10.6-11.5	<b>11.6-12.0</b>	>12.0
Urine calcium level (normal <250) (mg/24 h)	251-300	301-400	<b>&gt;400</b>
Decrease in creatinine clearance below age-matched control subjects (%)	1-10	11-30	<b>&gt;30</b>
Z-score, SD below age-matched control subjects	<1	1-2	<b>&gt;2</b>
Nonspecific symptoms			
Psychiatric symptoms	Anxiety	Lack of energy	Depression
Neuromuscular weakness	Present	...	...
GI symptoms or PUD	Weekly dyspepsia	Daily dyspepsia	Nonbleeding ulcer
PHPT-associated symptoms			
Pancreatitis	...	<b>Asymptomatic</b>	Symptomatic
Fracture	...	<b>Vertebral</b>	Long bone
Nephrolithiasis	...	<b>1 episode</b>	Multiple episodes

\*GI = gastrointestinal; PHPT = primary hyperparathyroidism; PTH = parathyroid hormone; PUD = peptic ulcer disease; SD = standard deviation.

†Boldface definitions are thresholds recommended by National Institutes of Health consensus panel.

The NIH recommendations emphasized that younger patients (age <50 years) with PHPT should be treated surgically because of the longer anticipated time for disease progression and that those older than 50 years can be more conservatively managed. To determine whether patient age influences surgical referral, we also asked the aforementioned referral question for a hypothetical 65-year-old patient with PHPT. For patients referred for surgical treatment, we inquired about the use and rationale for ordering localization studies.

### Statistical Analysis

For analysis of associations between physician characteristics and adherence to NIH recommendations, we used the chi-square or Fisher exact test for categorical variables and the Student *t* test or Mann-Whitney *U* test for continuous variables. We performed multivariate regression analyses to find independent predictors for adherence to NIH guideline recommendations.

To evaluate whether PHPT case volume was independently associated with adherence to NIH guidelines, we adjusted for potential confounders such as physician age, sex, years in practice, proportion of time spent in clinical activities, board certification status, geographic region, practice type (academic versus private practice versus other), managed care penetration, self-identification as a

bone and mineral specialist, and awareness of NIH consensus panel recommendations. We also analyzed PHPT case volume as a log-transformed continuous variable. Because this analysis did not change our results, we report only the findings from the dichotomous grouping.

### RESULTS

Of 500 sampled endocrine society members, 374 fulfilled study eligibility. Reasons for exclusion from the study were the death or retirement of the member (*N* = 20), our inability to contact the person (*N* = 35), or the finding that the member was not a physician or was a physician from a different specialty (*N* = 71). Of the 374 eligible physicians, 146 (39%) responded to our survey. In comparison with nonrespondents, respondents were of similar age, sex, society membership status, postgraduate year, and geographic location; these similarities suggested no obvious nonresponse bias. Among respondents, however, 39% were bone and mineral specialists, and 61% were endocrinologists. Among nonrespondents, 22% were bone and mineral specialists, and 78% were endocrinologists. Therefore, bone and mineral specialists were significantly (*P* < 0.001) more likely to respond to the survey than were general endocrinologists.

### Physician and Practice Characteristics

The mean age of the respondents was 52 years, and 77% were men. Most respondents finished residency training in 1974, and they came from geographically diverse areas (Table 2). Nearly all (95%) had completed an endocrine fellowship and were board certified in endocrinology (85%). A third of the respondents were employed in academia, and more than half (51%) worked in a private practice setting. The median proportion of time spent in clinical practice was 83%, and the median proportion of clinical practice that was endocrine was 95%. Among all endocrine patients encountered by respondents, diabetes was the most common disorder (39%), followed by thyroid disease (26%), parathyroid or bone disorders (16%), pituitary or adrenal conditions (6%), lipid abnormalities (6%), gonadal disease (4%), and obesity (3%). The median number of annualized PHPT cases was 12 for all physicians (7 PHPT cases for low-volume physicians and 20 cases for high-volume physicians).

### Awareness of the NIH Guidelines

Seventy percent of respondents were aware of the NIH guidelines for management of PHPT; however, only 41% were highly aware (identified only the NIH and not the other indicated sponsors). More high-volume physicians than low-volume physicians were aware of the NIH guidelines (75% versus 50%, respectively;  $P < 0.01$ ) (Fig. 1). A greater proportion of high-volume physicians than of low-volume physicians were highly aware of the NIH guidelines (50% versus 26%, respectively;  $P < 0.01$ ).

### Assessment and Initial Management of Patients With PHPT

For the initial assessment of patients with suspected PHPT, almost all physicians ordered tests for intact PTH assay and serum calcium (Table 3). The frequency of ordering other tests ranged from as low as 8% for an abdominal ultrasound study to as high as 94% for blood urea nitrogen and creatinine. In comparison with low-volume physicians, high-volume physicians more frequently ordered 24-hour urine collections (95% of high-volume versus 75% of low-volume physicians;  $P < 0.001$ ) and abdominal radiography (28% of high-volume versus 13% of low-volume physicians;  $P < 0.05$ ).

Physicians reported that 77% of their patients with PHPT were asymptomatic, 18% were minimally symptomatic, and 5% were frankly symptomatic. Overall, physicians referred a mean of 39% of their asymptomatic patients for surgical treatment (Table 3). Nevertheless, a wide variation existed in referral practice—7% of physicians referred 90% or more of their asymptomatic patients for surgical treatment, whereas 31% of physicians referred 10% or less of their asymptomatic patients for such intervention. Among minimally symptomatic patients with PHPT, the percentage of patients referred for surgical management increased to 64%. Approximately 35% of physicians referred 90% or more of these patients for surgical treatment, and 22% of physicians referred 10% or

less of minimally symptomatic patients for surgical intervention. Almost all (96%) frankly symptomatic patients with PHPT were referred for surgical management; more than 93% of physicians referred 90% or more of frankly symptomatic patients for surgical treatment. No significant differences were found in surgical referral by physicians with low- and high-volume PHPT cases (data not shown).

For postmenopausal women with PHPT, estrogen therapy (46%) was the most commonly prescribed first-line treatment, followed by no therapy (30%), bisphosphonate therapy (11%), combination therapy (10%), calcitonin (2%), and phosphate therapy (1%). The most frequent combination therapy was hormonal and bisphosphonate therapy. Most commonly, no medical therapy was recommended for premenopausal women (74%) and men (77%), followed by bisphosphonate therapy (15% and 13%, respectively). Phosphate, calcitonin, or combination therapies accounted for only a small portion (1 to 6%) of first-line treatments in these patients.

### Adherence to Monitoring Recommendations

Adherence to any one of the five NIH consensus panel monitoring recommendations ranged widely, from 6% for measuring creatinine clearance every 6 months to 78% for measuring serum calcium every 6 months (Table 4). For each of the five recommendations, a greater proportion of high-volume physicians than low-volume physicians were adherent; however, a statistically significant difference was found only for the bone densitometry recommendation (88% adherence for high-volume versus 67% for low-volume physicians;  $P < 0.01$ ). With use of a summary scale (0 to 5) for adherence to NIH monitoring recommendations, high-volume physicians performed an average of 2.3 of the 5 recommendations versus 2.0 for low-volume physicians ( $P < 0.05$ ). Higher PHPT case volume was the only factor independently associated with greater adherence to the NIH monitoring recommendations in a multiple linear regression model, which was adjusted for age, sex, geographic location, managed care penetration, clinical time, and awareness of the NIH guidelines.

### Thresholds for Surgical Referral

In contrast to the situation with adherence to monitoring recommendations, higher PHPT case volume was not associated with differences in surgical referral. Therefore, we report overall referral findings. For a 40-year-old patient with PHPT and no major comorbid conditions, 25% of responding physicians would recommend surgical referral on the basis of low-level hypercalcemia, 39% for middle-level hypercalcemia, and 31% for high-level hypercalcemia (Table 5). Only 4% of physicians reported that hypercalcemia alone was not a sufficient reason for surgical referral. Physicians had higher thresholds for surgical referral if the only abnormality was an increased intact PTH concentration (19% low-level, 6% middle-level, and 6% high-level abnormality and 70% indicated



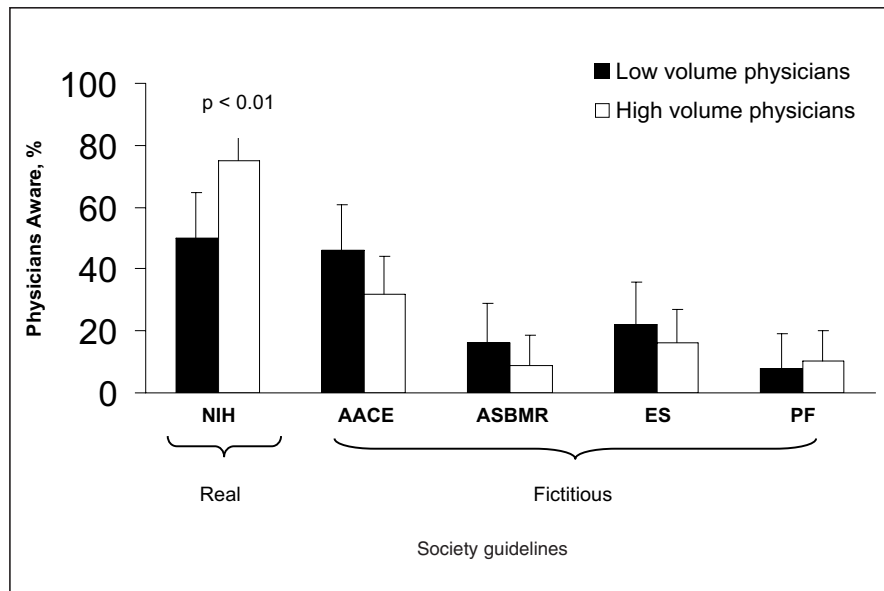
**Table 2**  
**Demographic Characteristics of All Surveyed Physicians,**  
**Low-Volume Physicians (<12 PHPT Cases Annually),**  
**and High-Volume Physicians (≥12 PHPT Cases Annually)\***

Characteristic	All physicians (N = 146)†	Low-volume physicians (N = 60)	High-volume physicians (N = 80)	P value for volume groups
Mean age‡ (yr ± SD)	52 ± 11	53 ± 12	50 ± 9	0.08
Sex‡ (% male patients)	77	73	78	0.57
Finished residency training‡ (median year)	1974	1972	1976	0.07
Geographic region‡ (%)				0.53
Northeast	31	32	29	
Southeast	23	27	22	
Midwest	19	18	22	
Southwest	11	7	15	
West	15	17	13	
Proportion of work time in clinical practice (median %)	83	85	80	0.56
Proportion of clinical practice that is endocrinology (median %)	95	90	99.5	0.06
Endocrine subspecialty (% bone and mineral specialists)	39	23	53	<0.001
Proportion of endocrine patients who have PTH or bone disorder (median %)	5	5	10	<0.01
Annual PHPT case volume (median no.)	12	7	20	<0.001
Practice setting (%)				0.62
Private practice (solo or group)	51	55	51	
University hospital or medical setting	33	29	37	
Other (community hospital, MCO, or government)	16	16	13	
Managed care penetration (%)				0.66
≤30	41	41	44	
31-50	35	40	33	
≥50	24	18	23	
Proportion of managed care patients who have fee-for-service arrangement (median %)	100	90	100	0.51
Completed endocrine fellowship (%)	95	92	96	0.38
Board certified in endocrinology (%)	85	81	86	0.46

\*MCO = managed care organization; PHPT = primary hyperparathyroidism; PTH = parathyroid hormone; SD = standard deviation.

†Six physicians did not report their annualized case volume and were excluded from PHPT case volume analysis.

‡Characteristics obtained from American Medical Association master file.



**Fig. 1.** Awareness of guidelines established by various organizations for management of primary hyperparathyroidism, as reported by physicians with a low volume (<12) or high volume ( $\geq 12$ ) of cases. AACE = American Association of Clinical Endocrinologists; ASBMR = American Society of Bone and Mineral Research; ES = Endocrine Society; NIH = National Institutes of Health; PF = Paget Foundation.

not sufficient alone) in comparison with hypercalcemia. Physicians had lower referral thresholds for a symptom strongly suggestive of PHPT such as nephrolithiasis (67% middle level, 24% high level, and 9% not sufficient alone) than for a nonspecific finding such as psychiatric symptoms (19% low level, 15% middle level, 15% high level, and 51% not sufficient alone).

Thresholds for surgical referral for a 65-year-old patient with PHPT followed a similar trend, with lower thresholds for conventional symptoms and derangements than for nonspecific symptoms (Table 5). Overall, physicians tended to have lower thresholds for referring a 40-year-old patient than a 65-year-old patient for parathyroid surgical treatment, a finding consistent with NIH consensus recommendations. For any given abnormality, however, most respondents (62 to 86%) had the same threshold for both 40- and 65-year-old patients (Table 5); thus, age alone did not seem to be a highly influential variable for determining surgical referral.

#### Use of Preoperative Glandular Localization Studies

Although the NIH consensus panel recommended against ordering preoperative localization studies, 53% of physicians reported ordering localization studies for some of their patients who were referred for surgical treatment, and 19% ordered localization studies for all their surgical referrals. Of those who ordered localization studies, 61% used sestamibi imaging, 17% sestamibi with single-photon emission computed tomography, 16% ultrasonography, 6% a technetium-thallium subtraction technique, and 1% computed tomography. When asked how the result of preoperative localization studies affected management, 53% indicated that it helped guide the surgeon, 35% said that it

was a requirement for surgical intervention, 11% stated that it influenced the decision for surgical referral, and 1% indicated that it influenced management during the post-operative period. Reported pathologic conditions were parathyroid adenoma in 86%, non-multiple endocrine neoplasia (MEN) glandular hyperplasia in 10%, MEN 1 or 2 in 3%, cancer in 1%, and unknown in 1%.

#### DISCUSSION

One rationale for the development of clinical practice guidelines is to reduce variability in patient care so that better quality evidence-based medicine is practiced (11). In light of the controversy surrounding the optimal management of asymptomatic PHPT, the NIH established a consensus panel in an effort to formulate recommendations that would improve patient care.

In this study, we found that management of PHPT is highly variable among endocrinologists in the United States. Some physicians refer almost all their patients with asymptomatic PHPT for surgical treatment, whereas others refer only a minority of patients. Although individual patient characteristics may account for some of the variability we found, the diverse thresholds for surgical referral suggest a lack of agreement about clinical management. Because the time between publication of the NIH panel recommendations and distribution of our questionnaire was sufficient to determine whether the recommendations had influenced practice patterns, we believe that the goal of the consensus panel recommendations has not been achieved.

Periodic monitoring for some potential signs of PHPT progression, such as renal dysfunction or development of

**Table 3**  
**Evaluation and Management of Primary Hyperparathyroidism**  
**by All Surveyed Physicians, Low-Volume Physicians, and High-Volume Physicians\***

<b>Evaluation and management strategy</b>	<b>All physicians (N = 146)†</b>	<b>Low-volume physicians (N = 60)</b>	<b>High-volume physicians (N = 80)</b>	<b>P value for volume groups</b>
Initial test ordering for evaluation of suspected PHPT (%)				
Intact parathyroid hormone	100	100	100	1.0
Repeated serum calcium	99	97	100	0.10
Ionized calcium	33	33	31	0.79
Serum chemistry panel	77	83	73	0.15
Blood urea nitrogen and creatinine	94	92	96	0.25
24-hour urine collection	87	75	95	<0.001
Creatinine clearance	42	38	44	0.53
Abdominal ultrasonography	8	8	9	0.90
Abdominal radiography	21	13	28	<0.05
Bone densitometry	77	72	81	0.21
Serum markers of bone turnover	13	13	12	0.75
Urine markers of bone turnover	16	17	14	0.71
Management of asymptomatic patients with PHPT (mean %)				0.31
Proportion referred for surgical treatment	39	41	38	
Proportion under observation	37	40	34	
Proportion treated medically	24	19	28	
Management of minimally symptomatic patients with PHPT (mean %)				0.99
Proportion referred for surgical treatment	64	63	64	
Proportion under observation	15	15	15	
Proportion treated medically	21	22	21	
Management of frankly symptomatic patients with PHPT (mean %)				0.56
Proportion referred for surgical treatment	96	97	95	
Proportion under observation	1	0	1	
Proportion treated medically	3	3	4	

\*PHPT = primary hyperparathyroidism.

†Six physicians did not report their annualized case volume and were excluded from PHPT case volume analysis.

nephrolithiasis, was uncommon even among highly experienced physicians. Among our responding physicians, 10 to 20% reported that overt symptoms of PHPT, such as fractures, nephrolithiasis, or pancreatitis, were not sufficient for surgical referral in an elderly patient. Very few physicians considered general or nonspecific symptoms, such as dyspepsia, weakness, or psychiatric illnesses, to be sufficient justification for surgical referral. This finding is

not surprising, inasmuch as the management of cases of PHPT with predominantly nonclassic symptoms is controversial and challenging (12).

More high-volume physicians, who are likely to be most experienced in managing PHPT, were aware of the NIH guidelines than low-volume physicians. In addition, high-volume physicians performed more of the monitoring recommendations than did low-volume physicians.



**Table 4**  
**Concordance Between National Institutes of Health Recommendations**  
**for Frequency of Monitoring Tests for Nonsurgically Managed Patients**  
**With Primary Hyperparathyroidism and Practice Patterns Overall and by Volume Group**

<b>Guideline recommendation</b>	<b>All physicians (N = 146)*</b>	<b>Low- volume physicians (N = 60)</b>	<b>High- volume physicians (N = 80)</b>	<b>P value for volume groups</b>
Serum calcium every 6 months (% concordant)	78	77	80	0.63
Bone densitometry annually or biennially (% concordant)	77	67	88	<0.01
Serum creatinine every 6 months (% concordant)	46	45	46	0.88
Abdominal radiography annually (% concordant)	7	3	10	0.19
Creatinine clearance every 6 months (% concordant)	6	3	8	0.47
Summary scale of aforementioned 5 items (0-5) (average score)	2.1	2.0	2.3	<0.05

\*Six physicians did not report their annualized case volume and were excluded from primary hyperparathyroidism case volume analysis.

Nevertheless, variability among high-volume physicians for surgical referral was as great as among low-volume physicians. This finding suggests that factors other than physician experience are important determinants in decision making regarding surgical referral.

A previous analysis of physician nonadherence to guideline recommendations (11) identified several important determinants of guideline adherence, including awareness of existing guidelines, familiarity with the contents, agreement with the recommendations, belief in the efficacy of following the guidelines, and feasibility of implementation. In our study, the responding physicians had some awareness of the NIH guidelines, but lack of familiarity and disagreement with specific recommendations could be substantial. Furthermore, feasibility of implementation of the NIH consensus panel recommendations may be a barrier to adherence.

For example, adherence to monitoring recommendations varied substantially, depending on the specific recommendation. Adherence for periodic monitoring of 24-hour urine tests was lower than adherence with serum-based tests. Patients often have difficulty completing 24-hour urine collections because of disruption in their daily lives (13). Poor adherence by patients attributable to difficulty in implementation has sometimes been cited as the rationale for physicians' deviation from guideline recommendations. Although our study did not directly address the reasons for poor physician (or patient) adherence, the consistently lower adherence on tests that were more difficult to obtain suggests that implementation barriers may account for some of the practice variability. Implementation of guidelines may be enhanced by inclu-

sion of alternative clinical strategies—such as timed or spot urine collections rather than 24-hour collections (14)—to improve feasibility and adherence.

Our study had several limitations. First, the results were based on self-reporting; therefore, a potential exists for reporting bias. Respondents were assured of the confidentiality of their responses to minimize this concern. Second, although we surveyed the group of physicians most interested in PHPT, many did not respond. Nonresponse or selection bias could limit the generalizability of our results. Our analysis of demographic characteristics between responders and nonresponders, however, showed no evidence of substantial nonresponse bias. Finally, clinical practice patterns could change with introduction of new technologies and techniques, such as minimally invasive parathyroidectomy (15,16).

In April 2002, an NIH-sponsored workshop was convened to review recent progress in the management and natural history of asymptomatic PHPT (17,18). International experts representing the specialties of medicine, pediatrics, and surgery attended this meeting and issued new recommendations for evaluation and management of asymptomatic PHPT. These revised recommendations will offer updated guidance to physicians. Our study provides a benchmark for evaluation of the success of the new guidelines. Whether awareness of or adherence to the newly revised guidelines will be greater than with the original guidelines developed by the 1990 NIH consensus panel remains to be determined. Similar studies of physician behaviors in the management of other conditions such as *Helicobacter pylori*-related disease, prostate cancer, high levels of serum cholesterol, and cesarean delivery

**Table 5**  
**Distribution of Respondents' Surgical Referral Thresholds**  
**for 40-Year-Old and 65-Year-Old Patients With PHPT**  
**and Percentage Agreement Between 40-Year-Old and 65-Year-Old Age Thresholds\***

Indication for surgical referral	Referral thresholds†								Agreement between age 40 and 65 thresholds (%)		
	40-year-old patient				65-year-old patient				40-year- old had lower referral threshold	Both age groups had same referral threshold	65-year- old had lower referral threshold
	Low (%)	Middle (%)	High (%)	Not sufficient alone (%)	Low (%)	Middle (%)	High (%)	Not sufficient alone (%)			
Test abnormalities											
Intact PTH level	19	6	6	70	9	9	5	77	14	80	6
Serum calcium level	25	<b>39</b>	31	4	8	<b>48</b>	39	4	25	68	8
Urine calcium level	17	17	<b>34</b>	32	9	25	<b>35</b>	31	17	71	12
Creatinine clearance	17	37	<b>19</b>	28	5	38	<b>27</b>	30	29	62	9
Z-score	10	25	<b>30</b>	35	3	22	<b>34</b>	42	23	69	8
Nonspecific symptoms											
Psychiatric symptoms	19	15	15	51	12	16	20	52	14	77	10
Neuromuscular weakness	59	...	...	41	50	...	...	50	12	82	5
GI symptoms or PUD	20	36	12	33	12	35	14	39	17	79	3
PHPT symptoms											
Pancreatitis	...	<b>59</b>	25	17	...	<b>51</b>	26	23	16	76	8
Fracture	...	<b>77</b>	4	20	...	<b>74</b>	4	21	8	86	6
Nephrolithiasis	...	<b>67</b>	24	9	...	<b>61</b>	29	10	14	79	7

\*GI = gastrointestinal; PHPT = primary hyperparathyroidism; PTH = parathyroid hormone; PUD = peptic ulcer disease.

†Boltzmann numbers are the thresholds for which the National Institutes of Health panel reached consensus for surgical referral. Substantial variation existed in referral thresholds among respondents. Although, as expected, some respondents had lower thresholds for younger patients with PHPT, most respondents had the same thresholds for 40-year-old and 65-year-old patients. A few had lower thresholds for 65-year-old patients. No significant differences were found in referral thresholds between high- and low-volume physicians (data shown are for all physicians).

have also found incomplete or ineffective impact on changing clinical practice by NIH consensus panel recommendations (19,20). Because of difficulties in changing physician behavior, multisociety sponsorship and increased guideline promotion and dissemination may be required.

## CONCLUSION

The results of this national study of endocrinologists indicate that many endocrinologists were unaware of the 1990 NIH guidelines for management of asymptomatic PHPT and that actual clinical practice varies considerably, with even highly experienced physicians not following many guideline recommendations. With the development of newly revised recommendations for management of asymptomatic PHPT, professional societies may need to develop strategies to increase recognition of these guidelines if clinical care of affected patients is to be improved.

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