

Supplemental Online Content

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eMethods. Diagnosis (*ICD-10*) and Procedure (*CPT*) Codes

eTable 1. Associated Diagnoses and Symptoms in Patients in the First (Hypercalcemia and PTH ≥ 50 pg/mL Without a Documented Diagnosis) (n = 20,176) and Second (Unexplained Hypercalcemia and No Further Workup) (n = 24,905) High-risk Groups for PHP

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eTable 9. Comparing Diagnoses and Symptoms in Patients at High Risk of PHP With Hypercalcemia and PTH ≥ 40 (n = 23,969) or 50 pg/mL (n = 20,176) Without a Documented Diagnosis With Those Diagnosed With Similar PTH Levels (n = 12,294 for PTH ≥ 40 and n = 11,968 for ≥ 50 pg/mL)

eTable 10. Comparing Diagnoses and Symptoms in Patients at High Risk of PHP With Hypercalcemia and PTH ≥ 65 (n = 14,959) or 100 pg/mL (n = 7,387) Without a Documented Diagnosis With Those Diagnosed With Similar PTH Levels (n = 11,262 for PTH ≥ 65 and n = 8,192 for ≥ 100 pg/mL)

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods. Diagnosis (*ICD-10*) and Procedure (*CPT*) Codes

Diagnosis Codes

D35.1 Benign Neoplasm of Parathyroid Gland
E21.0 Primary Hyperparathyroidism
E21.1 Secondary Hyperparathyroidism, Not Elsewhere Classified
N25.81 Secondary Hyperparathyroidism of Renal Origin
E21.2 Other Hyperparathyroidism
E21.4 Other Specified Disorders of Parathyroid Gland
C75.0 Malignant Neoplasm of Parathyroid Gland
E31.2 Multiple Endocrine Neoplasia (MEN) Syndromes
Z94.0 Kidney Transplant Status
N18.4-6 Chronic kidney disease stage 4, 5, or end stage
C73 Malignant Neoplasm of Thyroid Gland
C25 Malignant Neoplasm of Pancreas
C49 Malignant Neoplasm of Connective and Soft Tissue
C56 Malignant Neoplasm of Ovary
C61 Malignant Neoplasm of Prostate
C81-96 Malignant Neoplasms of Lymphoid, Hematopoietic, and Related Tissue
C18 Malignant Neoplasm of Colon
C19 Malignant Neoplasm of Rectosigmoid Junction
C20 Malignant Neoplasm of Rectum
C67 Malignant Neoplasm of Bladder
C50 Malignant Neoplasm of Breast
C74.1 Malignant Neoplasm of Adrenal Gland
A15-A19 Tuberculosis
D86 Sarcoidosis
E22.0 Acromegaly
E27.1 Primary Adrenocortical Insufficiency
M88 Osteitis Deformans
E05 Thyrotoxicosis (Hyperthyroidism)
E67.3 Hypervitaminosis D
E67.0 Hypervitaminosis A
M80, M81, M85.5, M85.9 Osteoporosis/Osteopenia
N20-N23 Urolithiasis
F32, F33 Major Depressive Disorder
R35 Polyuria
K59.0 Constipation
M79.1, M25.5 Myalgias/Joint Pain
R53.1 Weakness
R10.1, R10.3, R10.81, R10.84, R10.9 Abdominal pain
R53.8 Malaise and Fatigue
F41 Anxiety Disorders
G47.0 Insomnia
R41.1, R41.2, R41.3, R41.8, R41.9 Amnesia
K21 Gastroesophageal Reflux Disease
I10 Hypertension
R51 Headache
S12, S22, S32, S42, S52, S62, S72, S82, S92, M80 Fracture
R11.0 Nausea
K80, K81, K82.8 Gallstones

Procedure Codes

0GBP/0GBN Endocrine System/ Excision/ Inferior Parathyroid Gland, Left/Right
0GBM/0GBL Endocrine System/ Excision/ Superior Parathyroid Gland, Left/Right
0GBQ Endocrine System/ Excision/ Parathyroid Glands, Multiple
0GBR Endocrine System/ Excision Parathyroid Gland
0GTR Endocrine System/ Resection/ Parathyroid Gland
0GTM/0GTL Endocrine System/ Resection/ Superior Parathyroid Gland, Left/Right
0GTQ Endocrine System/ Resection/ Parathyroid Glands, Multiple
0GTP/0GTN Endocrine System/ Resection/ Inferior Parathyroid Gland, Left/Right
60500 Parathyroidectomy or Exploration of Parathyroid(s)
60505 Parathyroidectomy or Exploration of Parathyroid(s); With Mediastinal Exploration, Sternal Split or Transthoracic Approach
3E0636Z/3E0536Z/3E0336Z/3E0436Z Total Parenteral Nutrition

Laboratory Codes

8001 Glomerular Filtration Rate in Serum, Plasma, or Blood
9022 Calcium in Serum, Plasma, or Blood
38230-9/1994-4 Ionized Calcium in Blood
9039 Parathyrin in Serum or Plasma
9045 Albumin in Serum, Plasma, or Blood
9024 Creatinine in Serum, Plasma, or Blood
9034 Calcidiol in Serum or Plasma

Medication Codes

CV701 Thiazides/Related Diuretics
6448 Lithium
214342 Calcium Acetate
1897 Calcium Carbonate
1921069 Abaloparatide
32915 Teriparatide
46041 Alendronate
77655 Zoledronic Acid
115264 Ibandronate
73056 Risedronate
11473 Pamidronate
42682 Etidronate
57230 Tiludronate
407990 Cinacalcet

eTable 1: Associated Diagnoses and Symptoms in Patients in the First (Hypercalcemia and PTH ≥ 50 pg/mL Without a Documented Diagnosis) (n = 20,176) and Second (Unexplained Hypercalcemia and No Further Workup) (n = 24,905) High-risk Groups for PHP

| | Diagnosis | High-Risk PHP PTH ≥ 50 (n = 17,853 after matching) | High-Risk PHP Unexplained Hypercalcemia (n = 17,853 after matching) | Odds Ratio (95% CI) | ^a P value |
|----------------------------------------|-------------------------|---------------------------------------------------------|---------------------------------------------------------------------|---------------------|----------------------|
| 0-1 Year | Osteopenia/Osteoporosis | 2,436 (13.6%) | 1,206 (6.8%) | 2.2 (2.0-2.3) | <0.001 |
| | Fractures | 682 (3.8%) | 498 (2.8%) | 1.4 (1.2-1.6) | <0.001 |
| | Urolithiasis | 747 (4.2%) | 491 (2.8%) | 1.5 (1.4-1.7) | <0.001 |
| | MDD | 1,914 (10.7%) | 1,744 (9.8%) | 1.1 (1.0-1.2) | 0.003 |
| | Anxiety Disorders | 1,826 (10.2%) | 1,684 (9.4%) | 1.1 (1.0-1.2) | 0.01 |
| | HTN | 8,497 (47.6%) | 6,430 (36.0%) | 1.6 (1.5-1.7) | <0.001 |
| | GERD | 2,749 (15.4%) | 2,265 (12.7%) | 1.3 (1.2-1.3) | <0.001 |
| | Malaise/Fatigue | 1,959 (11.0%) | 1,494 (8.4%) | 1.3 (1.3-1.4) | <0.001 |
| | Joint Pain/Myalgias | 5,851 (32.8%) | 4,817 (27.0%) | 1.3 (1.3-1.4) | <0.001 |
| | Constipation | 1,165 (6.5%) | 950 (5.3%) | 1.2 (1.1-1.4) | <0.001 |
| | Insomnia | 837 (4.7%) | 638 (3.6%) | 1.3 (1.2-1.5) | <0.001 |
| | Polyuria | 821 (4.6%) | 651 (3.6%) | 1.3 (1.1-1.4) | <0.001 |
| | Weakness | 1,315 (7.4%) | 1,010 (5.7%) | 1.3 (1.2-1.4) | <0.001 |
| | Abdominal Pain | 2,029 (11.4%) | 2,106 (11.8%) | 1.0 (0.9-1.0) | 0.20 |
| | Headache | 1,033 (5.8%) | 918 (5.1%) | 1.1 (1.0-1.2) | 0.01 |
| | Nausea | 783 (4.4%) | 701 (3.9%) | 1.1 (1.0-1.2) | 0.03 |
| Amnesia | 687 (3.8%) | 747 (4.2%) | 0.9 (0.8-1.0) | 0.11 | |
| Gallstones | 357 (2.0%) | 313 (1.8%) | 1.1 (1.0-1.3) | 0.09 | |
| 1-2 Years | Osteopenia/Osteoporosis | 2,510 (14.1%) | 1,269 (7.1%) | 2.1 (2.0-2.3) | <0.001 |
| | Fractures | 608 (3.4%) | 421 (2.4%) | 1.5 (1.3-1.7) | <0.001 |
| | Urolithiasis | 629 (3.5%) | 359 (2.0%) | 1.8 (1.6-2.0) | <0.001 |
| | MDD | 1,832 (10.3%) | 1,463 (8.2%) | 1.3 (1.2-1.4) | <0.001 |
| | Anxiety Disorders | 1,655 (9.3%) | 1,397 (7.8%) | 1.2 (1.1-1.3) | <0.001 |
| | HTN | 8,331 (46.7%) | 5,688 (31.9%) | 1.9 (1.8-2.0) | <0.001 |
| | GERD | 2,518 (14.1%) | 1,912 (10.7%) | 1.4 (1.3-1.5) | <0.001 |
| | Malaise/Fatigue | 1,451 (8.1%) | 1,047 (5.9%) | 1.4 (1.3-1.5) | <0.001 |
| | Joint Pain/Myalgias | 3,111 (17.4%) | 2,201 (12.3%) | 1.5 (1.4-1.6) | <0.001 |
| | Constipation | 930 (5.2%) | 677 (3.8%) | 1.4 (1.3-1.5) | <0.001 |
| | Insomnia | 680 (3.8%) | 507 (2.8%) | 1.4 (1.2-1.5) | <0.001 |
| | Polyuria | 742 (4.2%) | 540 (3.0%) | 1.4 (1.2-1.6) | <0.001 |
| | Weakness | 892 (5.0%) | 687 (3.8%) | 1.3 (1.2-1.5) | <0.001 |
| | Abdominal Pain | 1,584 (8.9%) | 1,410 (7.9%) | 1.1 (1.1-1.2) | <0.001 |
| | Headache | 866 (4.9%) | 623 (3.5%) | 1.4 (1.3-1.6) | <0.001 |
| | Nausea | 555 (3.1%) | 424 (2.4%) | 1.3 (1.2-1.5) | <0.001 |
| Amnesia | 582 (3.3%) | 511 (2.9%) | 1.1 (1.0-1.3) | 0.03 | |
| Gallstones | 249 (1.4%) | 183 (1.0%) | 1.4 (1.1-1.7) | 0.001 | |
| 2-3 Years | Osteopenia/Osteoporosis | 2,699 (15.1%) | 1,386 (7.8%) | 2.1 (2.0-2.3) | <0.001 |
| | Fractures | 636 (3.6%) | 461 (2.6%) | 1.4 (1.2-1.6) | <0.001 |
| | Urolithiasis | 622 (3.5%) | 351 (2.0%) | 1.8 (1.6-2.1) | <0.001 |
| | MDD | 1,922 (10.8%) | 1,498 (8.4%) | 1.3 (1.2-1.4) | <0.001 |
| | Anxiety Disorders | 1,743 (9.8%) | 1,499 (8.4%) | 1.2 (1.1-1.3) | <0.001 |
| | HTN | 8,503 (47.6%) | 5,855 (32.8%) | 1.9 (1.8-1.9) | <0.001 |
| | GERD | 2,621 (14.7%) | 1,991 (11.2%) | 1.4 (1.3-1.5) | <0.001 |
| | Malaise/Fatigue | 1,485 (8.3%) | 1,055 (5.9%) | 1.4 (1.3-1.6) | <0.001 |
| | Joint Pain/Myalgias | 3,067 (17.2%) | 2,341 (13.1%) | 1.4 (1.3-1.5) | <0.001 |
| | Constipation | 947 (5.3%) | 711 (4.0%) | 1.4 (1.2-1.5) | <0.001 |
| | Insomnia | 727 (4.1%) | 537 (3.0%) | 1.4 (1.2-1.5) | <0.001 |
| | Polyuria | 804 (4.5%) | 519 (2.9%) | 1.6 (1.4-1.8) | <0.001 |
| | Weakness | 969 (5.4%) | 662 (3.7%) | 1.5 (1.3-1.6) | <0.001 |
| | Abdominal Pain | 1,611 (9.0%) | 1,457 (8.2%) | 1.1 (1.0-1.2) | 0.004 |
| | Headache | 790 (4.4%) | 626 (3.5%) | 1.3 (1.1-1.4) | <0.001 |
| | Nausea | 542 (3.0%) | 400 (2.2%) | 1.4 (1.2-1.6) | <0.001 |
| Amnesia | 621 (3.5%) | 554 (3.1%) | 1.1 (1.0-1.3) | 0.05 | |
| Gallstones | 252 (1.4%) | 200 (1.1%) | 1.3 (1.0-1.5) | 0.01 | |
| Entire Study Period (0-3 Years) | Osteopenia/Osteoporosis | 4,073 (22.8%) | 2,334 (13.1%) | 2.0 (1.9-2.1) | <0.001 |
| | Fractures | 1,363 (7.6%) | 1,100 (6.2%) | 1.3 (1.2-1.4) | <0.001 |
| | Urolithiasis | 1,218 (6.8%) | 865 (4.8%) | 1.4 (1.3-1.6) | <0.001 |
| | MDD | 3,063 (17.2%) | 2,684 (15.0%) | 1.2 (1.1-1.2) | <0.001 |
| | Anxiety Disorders | 2,947 (16.5%) | 2,661 (14.9%) | 1.1 (1.1-1.2) | <0.001 |
| | HTN | 10,434 (58.4%) | 8,224 (46.1%) | 1.6 (1.6-1.7) | <0.001 |
| | GERD | 4,306 (24.1%) | 3,587 (20.1%) | 1.3 (1.2-1.3) | <0.001 |
| | Malaise/Fatigue | 3,495 (19.6%) | 2,682 (15.0%) | 1.4 (1.3-1.5) | <0.001 |
| | Joint Pain/Myalgias | 5,851 (32.8%) | 4,817 (27.0%) | 1.3 (1.3-1.4) | <0.001 |
| | Constipation | 2,181 (12.2%) | 1,774 (9.9%) | 1.3 (1.2-1.3) | <0.001 |

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|--|----------------|---------------|---------------|---------------|--------|
| | Insomnia | 1,499 (8.4%) | 1,151 (6.4%) | 1.3 (1.2-1.4) | <0.001 |
| | Polyuria | 1,798 (10.1%) | 1,359 (7.6%) | 1.4 (1.3-1.5) | <0.001 |
| | Weakness | 2,387 (13.4%) | 1,897 (10.6%) | 1.3 (1.2-1.4) | <0.001 |
| | Abdominal Pain | 3,734 (20.9%) | 3,624 (20.3%) | 1.0 (1.0-1.1) | 0.15 |
| | Headache | 2,021 (11.3%) | 1,711 (9.6%) | 1.2 (1.1-1.3) | <0.001 |
| | Nausea | 1,433 (8.0%) | 1,246 (7.0%) | 1.2 (1.1-1.3) | <0.001 |
| | Amnesia | 1,369 (7.7%) | 1,380 (7.7%) | 1.0 (0.9-1.1) | 0.83 |
| | Gallstones | 671 (3.8%) | 582 (3.3%) | 1.2 (1.0-1.3) | 0.01 |

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; MDD, major depressive disorder; HTN, hypertension; GERD, gastroesophageal reflux disease; CI, confidence interval

^aStatistical significance defined as $P < 0.003$

eTable 2: Associated Diagnoses and Symptoms in Patients Diagnosed With PHP (n = 13,136) Compared to Matched Controls

| | Diagnosis | Diagnosed (n = 13,136 after matching) | Matched Controls (n = 13,136 after matching) | Odds Ratio (95% CI) | ^a P value |
|----------------------------------------|-------------------------|---------------------------------------------|----------------------------------------------------|------------------------|----------------------|
| 0-1 Year | Osteopenia/Osteoporosis | 2,839 (21.6%) | 849 (6.5%) | 4.0 (3.7-4.3) | <0.001 |
| | Fractures | 545 (4.1%) | 399 (3.0%) | 1.4 (1.2-1.6) | <0.001 |
| | Urolithiasis | 1,172 (8.9%) | 201 (1.5%) | 6.3 (5.4-7.3) | <0.001 |
| | MDD | 1,657 (12.6%) | 1,104 (8.4%) | 1.6 (1.5-1.7) | <0.001 |
| | Anxiety Disorders | 1,410 (10.7%) | 1,121 (8.5%) | 1.3 (1.2-1.4) | <0.001 |
| | HTN | 6,869 (52.3%) | 4,473 (34.1%) | 2.1 (2.0-2.2) | <0.001 |
| | GERD | 2,415 (18.4%) | 1,599 (12.2%) | 1.6 (1.5-1.7) | <0.001 |
| | Malaise/Fatigue | 1,778 (13.5%) | 1,003 (7.6%) | 1.9 (1.7-2.1) | <0.001 |
| | Joint Pain/Myalgias | 2,791 (21.2%) | 1,890 (14.4%) | 1.6 (1.5-1.7) | <0.001 |
| | Constipation | 1,025 (7.8%) | 528 (4.0%) | 2.0 (1.8-2.3) | <0.001 |
| | Insomnia | 602 (4.6%) | 391 (3.0%) | 1.6 (1.4-1.8) | <0.001 |
| | Polyuria | 791 (6.0%) | 406 (3.1%) | 2.0 (1.8-2.3) | <0.001 |
| | Weakness | 1,228 (9.3%) | 679 (5.2%) | 1.9 (1.7-2.1) | <0.001 |
| | Abdominal Pain | 1,713 (13.0%) | 1,190 (9.1%) | 1.5 (1.4-1.6) | <0.001 |
| | 1-2 Years | Headache | 927 (7.1%) | 609 (4.6%) | 1.6 (1.4-1.7) |
| Nausea | | 685 (5.2%) | 404 (3.1%) | 1.7 (1.5-2.0) | <0.001 |
| Amnesia | | 615 (4.7%) | 356 (2.7%) | 1.8 (1.5-2.0) | <0.001 |
| Gallstones | | 307 (2.3%) | 182 (1.4%) | 1.7 (1.4-2.0) | <0.001 |
| Osteopenia/Osteoporosis | | 2,836 (21.6%) | 764 (5.8%) | 4.5 (4.1-4.8) | <0.001 |
| Fractures | | 463 (3.5%) | 278 (2.1%) | 1.7 (1.5-2.0) | <0.001 |
| Urolithiasis | | 931 (7.1%) | 151 (1.1%) | 6.6 (5.5-7.8) | <0.001 |
| MDD | | 1,522 (11.6%) | 863 (6.6%) | 1.9 (1.7-2.0) | <0.001 |
| Anxiety Disorders | | 1,277 (9.7%) | 891 (6.8%) | 1.5 (1.4-1.6) | <0.001 |
| HTN | | 6,541 (49.8%) | 3,625 (27.6%) | 2.6 (2.5-2.7) | <0.001 |
| GERD | | 2,257 (17.2%) | 1,210 (9.2%) | 2.0 (1.9-2.2) | <0.001 |
| Malaise/Fatigue | | 1,340 (10.2%) | 700 (5.3%) | 2.0 (1.8-2.2) | <0.001 |
| Joint Pain/Myalgias | | 2,573 (19.6%) | 1,609 (12.2%) | 1.7 (1.6-1.9) | <0.001 |
| Constipation | | 816 (6.2%) | 330 (2.5%) | 2.6 (2.3-2.9) | <0.001 |
| 2-3 Years | | Insomnia | 541 (4.1%) | 301 (2.3%) | 1.8 (1.6-2.1) |
| | Polyuria | 660 (5.0%) | 337 (2.6%) | 2.0 (1.8-2.3) | <0.001 |
| | Weakness | 902 (6.9%) | 422 (3.2%) | 2.2 (2.0-2.5) | <0.001 |
| | Abdominal Pain | 1,438 (10.9%) | 755 (5.7%) | 2.0 (1.8-2.2) | <0.001 |
| | Headache | 707 (5.4%) | 371 (2.8%) | 2.0 (1.7-2.2) | <0.001 |
| | Nausea | 472 (3.6%) | 243 (1.8%) | 2.0 (1.7-2.3) | <0.001 |
| | Amnesia | 486 (3.7%) | 209 (1.6%) | 2.4 (2.0-2.8) | <0.001 |
| | Gallstones | 234 (1.8%) | 98 (0.7%) | 2.4 (1.9-3.1) | <0.001 |
| | Osteopenia/Osteoporosis | 3,177 (24.2%) | 915 (7.0%) | 4.3 (3.9-4.6) | <0.001 |
| | Fractures | 496 (3.8%) | 296 (2.3%) | 1.7 (1.5-2.0) | <0.001 |
| | Urolithiasis | 956 (7.3%) | 124 (0.9%) | 8.2 (6.8-9.9) | <0.001 |
| | MDD | 1,561 (11.9%) | 886 (6.7%) | 1.9 (1.7-2.0) | <0.001 |
| | Anxiety Disorders | 1,363 (10.4%) | 951 (7.2%) | 1.5 (1.4-1.6) | <0.001 |
| | HTN | 6,634 (50.5%) | 3,833 (29.2%) | 2.5 (2.4-2.6) | <0.001 |
| | GERD | 2,310 (17.6%) | 1,258 (9.6%) | 2.0 (1.9-2.2) | <0.001 |
| Entire Study Period (0-3 Years) | Malaise/Fatigue | 1,384 (10.5%) | 720 (5.5%) | 2.0 (1.8-2.2) | <0.001 |
| | Joint Pain/Myalgias | 2,619 (19.9%) | 1,610 (12.3%) | 1.8 (1.7-1.9) | <0.001 |
| | Constipation | 776 (5.9%) | 365 (2.8%) | 2.2 (1.9-2.5) | <0.001 |
| | Insomnia | 577 (4.4%) | 344 (2.6%) | 1.7 (1.5-2.0) | <0.001 |
| | Polyuria | 666 (5.1%) | 330 (2.5%) | 2.1 (1.8-2.4) | <0.001 |
| | Weakness | 846 (6.4%) | 465 (3.5%) | 1.9 (1.7-2.1) | <0.001 |
| | Abdominal Pain | 1,374 (10.5%) | 778 (5.9%) | 1.9 (1.7-2.0) | <0.001 |
| | Headache | 723 (5.5%) | 378 (2.9%) | 2.0 (1.7-2.2) | <0.001 |
| | Nausea | 476 (3.6%) | 231 (1.8%) | 2.1 (1.8-2.5) | <0.001 |
| | Amnesia | 506 (3.9%) | 274 (2.1%) | 1.9 (1.6-2.2) | <0.001 |
| | Gallstones | 227 (1.7%) | 113 (0.9%) | 2.0 (1.6-2.5) | <0.001 |
| | Osteopenia/Osteoporosis | 4,860 (37.0%) | 1,606 (12.2%) | 4.2 (4.0-4.5) | <0.001 |
| | Fractures | 1,113 (8.5%) | 786 (6.0%) | 1.5 (1.3-1.6) | <0.001 |
| | Urolithiasis | 1,913 (14.6%) | 324 (2.5%) | 6.7 (6.0-7.6) | <0.001 |
| | MDD | 2,677 (20.4%) | 1,748 (13.3%) | 1.7 (1.6-1.8) | <0.001 |
| Anxiety Disorders | 2,399 (18.3%) | 1,803 (13.7%) | 1.4 (1.3-1.5) | <0.001 | |
| HTN | 8,577 (65.3%) | 5,864 (44.6%) | 2.3 (2.2-2.5) | <0.001 | |
| GERD | 3,913 (29.8%) | 2,531 (19.3%) | 1.8 (1.7-1.9) | <0.001 | |
| Malaise/Fatigue | 3,289 (25.0%) | 1,868 (14.2%) | 2.0 (1.9-2.1) | <0.001 | |
| Joint Pain/Myalgias | 5,085 (38.7%) | 3,543 (27.0%) | 1.7 (1.6-1.8) | <0.001 | |
| Constipation | 1,923 (14.6%) | 940 (7.2%) | 2.2 (2.0-2.4) | <0.001 | |
| Insomnia | 1,150 (8.8%) | 728 (5.5%) | 1.6 (1.5-1.8) | <0.001 | |
| Polyuria | 1,669 (12.7%) | 857 (6.5%) | 2.1 (1.9-2.3) | <0.001 | |
| Weakness | 2,268 (17.3%) | 1,267 (9.6%) | 2.0 (1.8-2.1) | <0.001 | |

| | | | | | |
|--|----------------|---------------|---------------|---------------|--------|
| | Abdominal Pain | 3,300 (25.1%) | 2,128 (16.2%) | 1.7 (1.6-1.8) | <0.001 |
| | Headache | 1,794 (13.7%) | 1,109 (8.4%) | 1.7 (1.6-1.9) | <0.001 |
| | Nausea | 1,302 (9.9%) | 739 (5.6%) | 1.8 (1.7-2.0) | <0.001 |
| | Amnesia | 1,159 (8.8%) | 664 (5.1%) | 1.8 (1.6-2.0) | <0.001 |
| | Gallstones | 580 (4.4%) | 334 (2.5%) | 1.8 (1.5-2.0) | <0.001 |

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; MDD, major depressive disorder; HTN, hypertension; GERD, gastroesophageal reflux disease; CI, confidence interval

^aStatistical significance defined as $P < 0.003$

eTable 3: Associated Diagnoses and Symptoms in High-risk Group 1 (Hypercalcemia and PTH \geq 50 pg/mL) (n = 20,176) and High-risk Group 2 (Unexplained Hypercalcemia and No Further Workup) (n = 24,905) Compared to Those Diagnosed (n = 13,136)

| | Diagnosis | High-Risk PHP PTH \geq 50 (n = 12,842 after matching) | Diagnosed (n = 12,842 after matching) | Odds Ratio (95% CI) | ^a P value | High-Risk PHP Unexplained Hypercalcemia (n = 13,136 after matching) | Diagnosed (n = 13,136 after matching) | Odds Ratio (95% CI) | ^a P value |
|------------------|-------------------------|------------------------------------------------------------------|---------------------------------------------|------------------------|----------------------|------------------------------------------------------------------------------------|---------------------------------------------|------------------------|----------------------|
| 0-1 Year | Osteopenia/Osteoporosis | 1,970 (15.3%) | 2,797 (21.8%) | 0.7 (0.6-0.7) | <0.001 | 882 (6.7%) | 2,839 (21.6%) | 0.3 (0.2-0.3) | <0.001 |
| | Fractures | 551 (4.3%) | 530 (4.1%) | 1.0 (0.9-1.2) | 0.51 | 362 (2.8%) | 545 (4.1%) | 0.7 (0.6-0.7) | <0.001 |
| | Urolithiasis | 620 (4.8%) | 1,132 (8.8%) | 0.5 (0.5-0.6) | <0.001 | 374 (2.8%) | 1,172 (8.9%) | 0.3 (0.3-0.3) | <0.001 |
| | MDD | 1,585 (12.3%) | 1,606 (12.5%) | 1.0 (0.9-1.1) | 0.69 | 1,325 (10.1%) | 1,658 (12.6%) | 0.8 (0.7-0.8) | <0.001 |
| | Anxiety Disorders | 1,549 (12.1%) | 1,359 (10.6%) | 1.2 (1.1-1.3) | <0.001 | 1,344 (10.2%) | 1,410 (10.7%) | 0.9 (0.9-1.0) | 0.18 |
| | HTN | 6,804 (53.0%) | 6,761 (52.6%) | 1.0 (1.0-1.1) | 0.59 | 4,892 (37.2%) | 6,871 (52.3%) | 0.5 (0.5-0.6) | <0.001 |
| | GERD | 2,252 (17.5%) | 2,364 (18.4%) | 0.9 (0.9-1.0) | 0.07 | 1,735 (13.2%) | 2,416 (18.4%) | 0.7 (0.6-0.7) | <0.001 |
| | Malaise/Fatigue | 1,593 (12.4%) | 1,735 (13.5%) | 0.9 (0.8-1.0) | 0.008 | 1,162 (8.8%) | 1,778 (13.5%) | 0.6 (0.6-0.7) | <0.001 |
| | Joint Pain/Myalgias | 2,631 (20.5%) | 2,725 (21.2%) | 1.0 (0.9-1.0) | 0.15 | 2,057 (15.7%) | 2,791 (21.2%) | 0.7 (0.6-0.7) | <0.001 |
| | Constipation | 950 (7.4%) | 1,005 (7.8%) | 0.9 (0.9-1.0) | 0.20 | 726 (5.5%) | 1,026 (7.8%) | 0.7 (0.6-0.8) | <0.001 |
| | Insomnia | 699 (5.4%) | 583 (4.5%) | 1.2 (1.1-1.4) | <0.001 | 499 (3.8%) | 602 (4.6%) | 0.8 (0.7-0.9) | 0.002 |
| | Polyuria | 639 (5.0%) | 773 (6.0%) | 0.8 (0.7-0.9) | <0.001 | 486 (3.7%) | 791 (6.0%) | 0.6 (0.5-0.7) | <0.001 |
| | Weakness | 1,068 (8.3%) | 1,195 (9.3%) | 0.9 (0.8-1.0) | 0.005 | 794 (6.0%) | 1,228 (9.3%) | 0.6 (0.6-0.7) | <0.001 |
| | Abdominal Pain | 1,683 (13.1%) | 1,661 (12.9%) | 1.0 (0.9-1.1) | 0.68 | 1,603 (12.2%) | 1,713 (13.0%) | 0.9 (0.9-1.0) | 0.04 |
| | Headache | 856 (6.7%) | 897 (7.0%) | 1.0 (0.9-1.0) | 0.31 | 714 (5.4%) | 927 (7.1%) | 0.8 (0.7-0.8) | <0.001 |
| | Nausea | 672 (5.2%) | 660 (5.1%) | 1.0 (0.9-1.1) | 0.74 | 547 (4.2%) | 685 (5.2%) | 0.8 (0.7-0.9) | <0.001 |
| Amnesia | 557 (4.3%) | 609 (4.7%) | 0.9 (0.8-1.0) | 0.12 | 512 (3.9%) | 615 (4.7%) | 0.8 (0.7-0.9) | 0.002 | |
| Gallstones | 293 (2.3%) | 301 (2.3%) | 1.0 (0.8-1.1) | 0.74 | 255 (1.9%) | 307 (2.3%) | 0.8 (0.7-1.0) | 0.03 | |
| 1-2 Years | Osteopenia/Osteoporosis | 2,059 (16.0%) | 2,795 (21.8%) | 0.7 (0.6-0.7) | <0.001 | 927 (7.1%) | 2,836 (21.6%) | 0.3 (0.3-0.3) | <0.001 |
| | Fractures | 479 (3.7%) | 453 (3.5%) | 1.1 (0.9-1.2) | 0.39 | 305 (2.3%) | 463 (3.5%) | 0.7 (0.6-0.8) | <0.001 |
| | Urolithiasis | 518 (4.0%) | 903 (7.0%) | 0.6 (0.5-0.6) | <0.001 | 283 (2.2%) | 931 (7.1%) | 0.3 (0.3-0.3) | <0.001 |
| | MDD | 1,511 (11.8%) | 1,476 (11.5%) | 1.0 (1.0-1.1) | 0.50 | 1,120 (8.5%) | 1,522 (11.6%) | 0.7 (0.7-0.8) | <0.001 |
| | Anxiety Disorders | 1,390 (10.8%) | 1,236 (9.6%) | 1.1 (1.1-1.2) | 0.002 | 1,122 (8.5%) | 1,277 (9.7%) | 0.9 (0.8-0.9) | <0.001 |
| | HTN | 6,679 (52.0%) | 6,446 (50.2%) | 1.1 (1.0-1.1) | 0.004 | 4,345 (33.1%) | 6,541 (49.8%) | 0.5 (0.5-0.5) | <0.001 |
| | GERD | 2,058 (16.0%) | 2,211 (17.2%) | 0.9 (0.9-1.0) | 0.01 | 1,493 (11.4%) | 2,257 (17.2%) | 0.6 (0.6-0.7) | <0.001 |
| | Malaise/Fatigue | 1,206 (9.4%) | 1,306 (10.2%) | 0.9 (0.8-1.0) | 0.04 | 813 (6.2%) | 1,340 (10.2%) | 0.6 (0.5-0.6) | <0.001 |
| | Joint Pain/Myalgias | 2,548 (19.8%) | 2,506 (19.5%) | 1.0 (1.0-1.1) | 0.51 | 1,759 (13.4%) | 2,573 (19.6%) | 0.6 (0.6-0.7) | <0.001 |
| | Constipation | 747 (5.8%) | 799 (6.2%) | 0.9 (0.8-1.0) | 0.17 | 481 (3.7%) | 816 (6.2%) | 0.6 (0.5-0.6) | <0.001 |
| | Insomnia | 558 (4.3%) | 527 (4.1%) | 1.1 (0.9-1.2) | 0.34 | 381 (2.9%) | 541 (4.1%) | 0.7 (0.6-0.8) | <0.001 |
| | Polyuria | 593 (4.6%) | 643 (5.0%) | 0.9 (0.8-1.0) | 0.14 | 374 (2.8%) | 660 (5.0%) | 0.6 (0.5-0.6) | <0.001 |
| | Weakness | 732 (5.7%) | 880 (6.9%) | 0.8 (0.7-0.9) | <0.001 | 526 (4.0%) | 902 (6.9%) | 0.6 (0.5-0.6) | <0.001 |
| | Abdominal Pain | 1,290 (10.0%) | 1,394 (10.9%) | 0.9 (0.8-1.0) | 0.03 | 1,060 (8.1%) | 1,438 (10.9%) | 0.7 (0.7-0.8) | <0.001 |
| | Headache | 718 (5.6%) | 676 (5.3%) | 1.1 (1.0-1.2) | 0.25 | 484 (3.7%) | 707 (5.4%) | 0.7 (0.6-0.8) | <0.001 |
| | Nausea | 467 (3.6%) | 458 (3.6%) | 1.0 (0.9-1.2) | 0.76 | 342 (2.6%) | 472 (3.6%) | 0.7 (0.6-0.8) | <0.001 |
| Amnesia | 458 (3.6%) | 476 (3.7%) | 1.0 (0.8-1.1) | 0.55 | 346 (2.6%) | 486 (3.7%) | 0.7 (0.6-0.8) | <0.001 | |
| Gallstones | 201 (1.6%) | 229 (1.8%) | 0.9 (0.7-1.1) | 0.17 | 146 (1.1%) | 234 (1.8%) | 0.6 (0.5-0.8) | <0.001 | |
| 2-3 Years | Osteopenia/Osteoporosis | 2,198 (17.1%) | 3,132 (24.4%) | 0.6 (0.6-0.7) | <0.001 | 1,047 (8.0%) | 3,177 (24.2%) | 0.3 (0.3-0.3) | <0.001 |
| | Fractures | 506 (3.9%) | 485 (3.8%) | 1.0 (0.9-1.2) | 0.50 | 356 (2.7%) | 496 (3.8%) | 0.7 (0.6-0.8) | <0.001 |
| | Urolithiasis | 525 (4.1%) | 923 (7.2%) | 0.6 (0.5-0.6) | <0.001 | 282 (2.1%) | 956 (7.3%) | 0.3 (0.2-0.3) | <0.001 |
| | MDD | 1,583 (12.3%) | 1,509 (11.8%) | 1.1 (1.0-1.1) | 0.16 | 1,132 (8.6%) | 1,561 (11.9%) | 0.7 (0.6-0.8) | <0.001 |
| | Anxiety Disorders | 1,462 (11.4%) | 1,314 (10.2%) | 1.1 (1.0-1.2) | 0.003 | 1,183 (9.0%) | 1,363 (10.4%) | 0.9 (0.8-0.9) | <0.001 |
| | HTN | 6,796 (52.9%) | 6,538 (50.9%) | 1.1 (1.0-1.1) | 0.001 | 4,496 (34.2%) | 6,634 (50.5%) | 0.5 (0.5-0.5) | <0.001 |
| | GERD | 2,135 (16.6%) | 2,250 (17.5%) | 0.9 (0.9-1.0) | 0.06 | 1,553 (11.8%) | 2,310 (17.6%) | 0.6 (0.6-0.7) | <0.001 |
| | Malaise/Fatigue | 1,234 (9.6%) | 1,356 (10.6%) | 0.9 (0.8-1.0) | 0.01 | 833 (6.3%) | 1,384 (10.5%) | 0.6 (0.5-0.6) | <0.001 |
| | Joint Pain/Myalgias | 2,508 (19.5%) | 2,560 (19.9%) | 1.0 (0.9-1.0) | 0.41 | 1,824 (13.9%) | 2,619 (19.9%) | 0.6 (0.6-0.7) | <0.001 |
| | Constipation | 775 (6.0%) | 762 (5.9%) | 1.0 (0.9-1.1) | 0.73 | 546 (4.2%) | 776 (5.9%) | 0.7 (0.6-0.8) | <0.001 |

| | | | | | | | | | |
|----------------------------------------|-------------------------|---------------|---------------|---------------|--------|---------------|---------------|---------------|--------|
| Entire Study Period (0-3 Years) | Insomnia | 598 (4.7%) | 558 (4.3%) | 1.1 (1.0-1.2) | 0.23 | 381 (2.9%) | 577 (4.4%) | 0.7 (0.6-0.7) | <0.001 |
| | Polyuria | 628 (4.9%) | 656 (5.1%) | 1.0 (0.9-1.1) | 0.42 | 383 (2.9%) | 666 (5.1%) | 0.6 (0.5-0.6) | <0.001 |
| | Weakness | 802 (6.2%) | 828 (6.4%) | 1.0 (0.9-1.1) | 0.51 | 519 (4.0%) | 846 (6.4%) | 0.6 (0.5-0.7) | <0.001 |
| | Abdominal Pain | 1,333 (10.4%) | 1,334 (10.4%) | 1.0 (0.9-1.1) | 0.98 | 1,126 (8.6%) | 1,374 (10.5%) | 0.8 (0.7-0.9) | <0.001 |
| | Headache | 666 (5.2%) | 698 (5.4%) | 1.0 (0.9-1.1) | 0.37 | 484 (3.7%) | 723 (5.5%) | 0.7 (0.6-0.7) | <0.001 |
| | Nausea | 467 (3.6%) | 462 (3.6%) | 1.0 (0.9-1.2) | 0.87 | 332 (2.5%) | 476 (3.6%) | 0.7 (0.6-0.8) | <0.001 |
| | Amnesia | 488 (3.8%) | 498 (3.9%) | 1.0 (0.9-1.1) | 0.75 | 408 (3.1%) | 506 (3.9%) | 0.8 (0.7-0.9) | <0.001 |
| | Gallstones | 211 (1.6%) | 224 (1.7%) | 0.9 (0.8-1.1) | 0.53 | 158 (1.2%) | 227 (1.7%) | 0.7 (0.6-0.8) | <0.001 |
| | Osteopenia/Osteoporosis | 3,326 (25.9%) | 4,787 (37.3%) | 0.6 (0.6-0.6) | <0.001 | 1,746 (13.3%) | 4,860 (37.0%) | 0.3 (0.2-0.3) | <0.001 |
| | Fractures | 1,091 (8.5%) | 1,089 (8.5%) | 1.0 (0.9-1.1) | 0.96 | 813 (6.2%) | 1,113 (8.5%) | 0.7 (0.6-0.8) | <0.001 |
| | Urolithiasis | 1,010 (7.9%) | 1,847 (14.4%) | 0.5 (0.5-0.6) | <0.001 | 676 (5.1%) | 1,913 (14.6%) | 0.3 (0.3-0.3) | <0.001 |
| | MDD | 2,528 (19.7%) | 2,599 (20.2%) | 1.0 (0.9-1.0) | 0.27 | 2,060 (15.7%) | 2,678 (20.4%) | 0.7 (0.7-0.8) | <0.001 |
| | Anxiety Disorders | 2,485 (19.4%) | 2,320 (18.1%) | 1.1 (1.0-1.2) | 0.008 | 2,108 (16.0%) | 2,399 (18.3%) | 0.9 (0.8-0.9) | <0.001 |
| | HTN | 8,371 (65.2%) | 8,425 (65.6%) | 1.0 (0.9-1.0) | 0.48 | 6,261 (47.7%) | 8,579 (65.3%) | 0.5 (0.5-0.5) | <0.001 |
| | GERD | 3,515 (27.4%) | 3,823 (29.8%) | 0.9 (0.8-0.9) | <0.001 | 2,751 (20.9%) | 3,914 (29.8%) | 0.6 (0.6-0.7) | <0.001 |
| | Malaise/Fatigue | 2,859 (22.3%) | 3,208 (25.0%) | 0.9 (0.8-0.9) | <0.001 | 2,112 (16.1%) | 3,289 (25.0%) | 0.6 (0.5-0.6) | <0.001 |
| | Joint Pain/Myalgias | 4,771 (37.2%) | 4,966 (38.7%) | 0.9 (0.9-1.0) | 0.01 | 3,783 (28.8%) | 5,085 (38.7%) | 0.6 (0.6-0.7) | <0.001 |
| | Constipation | 1,779 (13.9%) | 1,887 (14.7%) | 0.9 (0.9-1.0) | 0.05 | 1,345 (10.2%) | 1,924 (14.6%) | 0.7 (0.6-0.7) | <0.001 |
| | Insomnia | 1,236 (9.6%) | 1,116 (8.7%) | 1.1 (1.0-1.2) | 0.009 | 852 (6.5%) | 1,150 (8.8%) | 0.7 (0.7-0.8) | <0.001 |
| | Polyuria | 1,432 (11.2%) | 1,634 (12.7%) | 0.9 (0.8-0.9) | <0.001 | 1,009 (7.7%) | 1,669 (12.7%) | 0.6 (0.5-0.6) | <0.001 |
| | Weakness | 1,954 (15.2%) | 2,212 (17.2%) | 0.9 (0.8-0.9) | <0.001 | 1,482 (11.3%) | 2,268 (17.3%) | 0.6 (0.6-0.7) | <0.001 |
| | Abdominal Pain | 3,075 (23.9%) | 3,203 (24.9%) | 0.9 (0.9-1.0) | 0.07 | 2,801 (21.3%) | 3,300 (25.1%) | 0.8 (0.8-0.9) | <0.001 |
| | Headache | 1,685 (13.1%) | 1,737 (13.5%) | 1.0 (0.9-1.0) | 0.34 | 1,343 (10.2%) | 1,794 (13.7%) | 0.7 (0.7-0.8) | <0.001 |
| | Nausea | 1,214 (9.5%) | 1,262 (9.8%) | 1.0 (0.9-1.0) | 0.31 | 981 (7.5%) | 1,302 (9.9%) | 0.7 (0.7-0.8) | <0.001 |
| | Amnesia | 1,104 (8.6%) | 1,140 (8.9%) | 1.0 (0.9-1.1) | 0.43 | 965 (7.3%) | 1,159 (8.8%) | 0.8 (0.7-0.9) | <0.001 |
| | Gallstones | 550 (4.3%) | 571 (4.4%) | 1.0 (0.9-1.1) | 0.52 | 474 (3.6%) | 580 (4.4%) | 0.8 (0.7-0.9) | <0.001 |

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; MDD, major depressive disorder; HTN, hypertension; GERD, gastroesophageal reflux disease; CI, confidence interval

^aStatistical significance defined as $P < 0.003$

eTable 4: Lab Values for Patient Cohorts

| Patient Cohort | Mean Calcium +/- SD (mg/dL) | Mean PTH +/- SD (pg/mL) | Mean Albumin +/- SD (g/dL) | ^a Corrected Calcium (mg/dL) |
|--------------------------------------------------------------|-----------------------------|-------------------------|----------------------------|----------------------------------------|
| High Risk PHP PTH ≥40 (n = 23,969) | 10.8 +/- 0.5 | 84 +/- 67 | 4.2 +/- 0.4 | 10.6 |
| High Risk PHP PTH ≥50 (n = 20,176) | 10.8 +/- 0.5 | 93 +/- 70 | 4.2 +/- 0.4 | 10.6 |
| High Risk PHP PTH ≥65 (n = 14,959) | 10.8 +/- 0.5 | 108 +/- 77 | 4.2 +/- 0.4 | 10.6 |
| High Risk PHP PTH ≥100 (n = 7,387) | 10.9 +/- 0.6 | 148 +/- 100 | 4.1 +/- 0.4 | 10.8 |
| Unexplained hypercalcemia and no further workup (n = 24,905) | 10.7 +/- 0.5 | - | 4.2 +/- 0.5 | 10.5 |
| All PHP Diagnosed (n = 13,136) | 10.9 +/- 0.5 | 107 +/- 101 | 4.2 +/- 0.6 | 10.7 |
| PHP Diagnosed PTH ≥40 (n = 12,294) | 10.9 +/- 0.5 | 115 +/- 100 | 4.2 +/- 0.6 | 10.7 |
| PHP Diagnosed PTH ≥50 (n = 11,968) | 10.9 +/- 0.5 | 118 +/- 100 | 4.2 +/- 0.6 | 10.7 |
| PHP Diagnosed PTH ≥65 (n = 11,262) | 10.9 +/- 0.5 | 125 +/- 103 | 4.2 +/- 0.6 | 10.7 |
| PHP Diagnosed PTH ≥100 (n = 8,192) | 10.9 +/- 0.6 | 152 +/- 116 | 4.2 +/- 0.6 | 10.7 |
| Hypercalcemia to Diagnosis ≤ 1 Year (n = 3,686) | 11.1 +/- 0.7 | 121 +/- 112 | 4.2 +/- 0.6 | 10.9 |
| Hypercalcemia to Diagnosis > 1 Year (n = 9,450) | 10.8 +/- 0.4 | 102 +/- 96 | 4.2 +/- 0.6 | 10.6 |
| Diagnosis to Surgery ≤ 1 Year (n = 3,134) | 11.0 +/- 0.6 | 135 +/- 154 | 4.3 +/- 0.6 | 10.8 |
| Diagnosis to Surgery > 1 Year (n = 748) | 10.9 +/- 0.4 | 112 +/- 72 | 4.2 +/- 0.6 | 10.7 |

^aCorrected calcium = serum calcium + 0.8 (4 – serum albumin)

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; SD, standard deviation

eTable 5: Associated Diagnoses and Symptoms in Patients at High Risk of PHP With Hypercalcemia and PTH ≥ 40 (n = 23,969) or 50 pg/mL (n = 20,176) Without a Documented Diagnosis of PHP Compared to Matched Controls

| | Diagnosis | High-Risk PHP PTH ≥ 40 (n = 23,968 after matching) | Matched Controls (n = 23,968 after matching) | Odds Ratio (95% CI) | ^a P value | High-Risk PHP PTH ≥ 50 (n = 20,175 after matching) | Matched Controls (n = 20,175 after matching) | Odds Ratio (95% CI) | ^a P value |
|------------------|-------------------------|---------------------------------------------------------------|----------------------------------------------------|------------------------|----------------------|---------------------------------------------------------------|----------------------------------------------------|------------------------|----------------------|
| 0-1 Year | Osteopenia/Osteoporosis | 3,291 (13.7%) | 1,439 (6.0%) | 2.5 (2.3-2.7) | < 0.001 | 2,662 (13.2%) | 1,099 (5.4%) | 2.6 (2.5-2.8) | < 0.001 |
| | Fractures | 904 (3.8%) | 619 (2.6%) | 1.5 (1.3-1.4) | < 0.001 | 719 (3.6%) | 478 (2.4%) | 1.5 (1.4-1.7) | < 0.001 |
| | Urolithiasis | 977 (4.1%) | 343 (1.4%) | 2.9 (2.6-3.3) | < 0.001 | 771 (3.8%) | 281 (1.4%) | 2.8 (2.5-3.2) | < 0.001 |
| | MDD | 2,478 (10.3%) | 1,677 (7.0%) | 1.5 (1.4-1.6) | < 0.001 | 2,009 (10.0%) | 1,393 (6.9%) | 1.5 (1.4-1.6) | < 0.001 |
| | Anxiety Disorders | 2,368 (9.9%) | 1,632 (6.8%) | 1.5 (1.4-1.6) | < 0.001 | 1,920 (9.5%) | 1,347 (6.7%) | 1.5 (1.4-1.6) | < 0.001 |
| | HTN | 11,179 (46.6%) | 7,494 (31.3%) | 1.9 (1.9-2.0) | < 0.001 | 9,107 (45.1%) | 6,231 (30.9%) | 1.8 (1.8-1.9) | < 0.001 |
| | GERD | 3,610 (15.1%) | 2,591 (10.8%) | 1.5 (1.4-1.5) | < 0.001 | 2,952 (14.6%) | 2,047 (10.1%) | 1.5 (1.4-1.6) | < 0.001 |
| | Malaise/Fatigue | 2,547 (10.6%) | 1,640 (6.8%) | 1.6 (1.5-1.7) | < 0.001 | 2,065 (10.2%) | 1,328 (6.6%) | 1.6 (1.5-1.3) | < 0.001 |
| | Joint Pain/ Myalgias | 4,326 (18.0%) | 2,947 (12.3%) | 1.6 (1.5-1.7) | < 0.001 | 3,461 (17.2%) | 2,385 (11.8%) | 1.5 (1.5-1.6) | < 0.001 |
| | Constipation | 1,533 (6.4%) | 847 (3.5%) | 1.9 (1.7-2.0) | < 0.001 | 1,247 (6.2%) | 719 (3.6%) | 1.8 (1.6-2.0) | < 0.001 |
| | Insomnia | 1,114 (4.6%) | 672 (2.8%) | 1.7 (1.5-1.9) | < 0.001 | 885 (4.4%) | 524 (2.6%) | 1.7 (1.5-1.9) | < 0.001 |
| | Polyuria | 1,099 (4.6%) | 619 (2.6%) | 1.8 (1.6-2.0) | < 0.001 | 874 (4.3%) | 506 (2.5%) | 1.8 (1.6-2.0) | < 0.001 |
| | Weakness | 1,719 (7.2%) | 1,118 (4.7%) | 1.6 (1.5-1.7) | < 0.001 | 1,374 (6.8%) | 872 (4.3%) | 1.6 (1.5-1.8) | < 0.001 |
| | Abdominal Pain | 2,658 (11.1%) | 1,950 (8.1%) | 1.4 (1.3-1.5) | < 0.001 | 2,142 (10.6%) | 1,573 (7.8%) | 1.4 (1.3-1.5) | < 0.001 |
| Headache | 1,407 (5.9%) | 966 (4.0%) | 1.5 (1.4-1.6) | < 0.001 | 1,104 (5.5%) | 794 (3.9%) | 1.4 (1.3-1.6) | < 0.001 | |
| Nausea | 1,049 (4.4%) | 611 (2.5%) | 1.8 (1.6-1.9) | < 0.001 | 814 (4.0%) | 498 (2.5%) | 1.7 (1.5-1.9) | < 0.001 | |
| Amnesia | 910 (3.8%) | 585 (2.4%) | 1.6 (1.4-1.8) | < 0.001 | 738 (3.7%) | 506 (2.5%) | 1.5 (1.3-1.7) | < 0.001 | |
| Gallstones | 462 (1.9%) | 320 (1.3%) | 1.5 (1.3-1.7) | < 0.001 | 373 (1.8%) | 217 (1.1%) | 1.7 (1.5-2.1) | < 0.001 | |
| 1-2 Years | Osteopenia/Osteoporosis | 3,387 (14.1%) | 1,365 (5.7%) | 2.7 (2.6-2.9) | < 0.001 | 2,718 (13.5%) | 1,070 (5.3%) | 2.8 (2.6-3.0) | < 0.001 |
| | Fractures | 844 (3.5%) | 446 (1.9%) | 1.9 (1.7-2.2) | < 0.001 | 647 (3.2%) | 367 (1.8%) | 1.8 (1.6-2.0) | < 0.001 |
| | Urolithiasis | 827 (3.5%) | 220 (0.9%) | 3.9 (3.3-4.5) | < 0.001 | 651 (3.2%) | 198 (1.0%) | 3.4 (2.9-3.9) | < 0.001 |
| | MDD | 2,329 (9.7%) | 1,395 (5.8%) | 1.7 (1.6-1.9) | < 0.001 | 1,909 (9.5%) | 1,164 (5.8%) | 1.7 (1.6-1.8) | < 0.001 |
| | Anxiety Disorders | 2,164 (9.0%) | 1,249 (5.2%) | 1.8 (1.7-1.9) | < 0.001 | 1,740 (8.6%) | 1,105 (5.5%) | 1.6 (1.5-1.8) | < 0.001 |
| | HTN | 10,967 (45.8%) | 6,132 (25.6%) | 2.5 (2.4-2.6) | < 0.001 | 8,940 (44.3%) | 5,057 (25.1%) | 2.4 (2.3-2.5) | < 0.001 |
| | GERD | 3,331 (13.9%) | 1,991 (8.3%) | 1.8 (1.7-1.9) | < 0.001 | 2,690 (13.3%) | 1,606 (8.0%) | 1.8 (1.7-1.9) | < 0.001 |
| | Malaise/Fatigue | 1,912 (8.0%) | 1,118 (4.7%) | 1.8 (1.6-1.9) | < 0.001 | 1,531 (7.6%) | 898 (4.5%) | 1.8 (1.6-1.9) | < 0.001 |
| | Joint Pain/Myalgias | 4,113 (17.2%) | 2,502 (10.4%) | 1.8 (1.7-1.9) | < 0.001 | 3,327 (16.5%) | 2,004 (9.9%) | 1.8 (1.7-1.9) | < 0.001 |
| | Constipation | 1,238 (5.2%) | 584 (2.4%) | 2.2 (2.0-2.4) | < 0.001 | 1,001 (5.0%) | 472 (2.3%) | 2.2 (2.0-2.4) | < 0.001 |
| | Insomnia | 917 (3.8%) | 508 (2.1%) | 1.8 (1.6-2.1) | < 0.001 | 725 (3.6%) | 395 (2.0%) | 1.9 (1.6-2.1) | < 0.001 |
| | Polyuria | 968 (4.0%) | 547 (2.3%) | 1.8 (1.6-2.0) | < 0.001 | 786 (3.9%) | 420 (2.1%) | 1.9 (1.7-2.2) | < 0.001 |
| | Weakness | 1,204 (5.0%) | 703 (2.9%) | 1.6 (1.6-1.9) | < 0.001 | 948 (4.7%) | 547 (2.8%) | 1.8 (1.6-2.0) | < 0.001 |
| | Abdominal Pain | 2,114 (8.8%) | 1,225 (5.1%) | 1.8 (1.7-1.9) | < 0.001 | 1,698 (8.4%) | 949 (4.7%) | 1.9 (1.7-2.0) | < 0.001 |
| | Headache | 1,183 (4.9%) | 645 (2.7%) | 1.9 (1.7-2.1) | < 0.001 | 923 (4.6%) | 505 (2.5%) | 1.9 (1.7-2.1) | < 0.001 |
| | Nausea | 765 (3.2%) | 372 (1.6%) | 2.1 (1.8-2.4) | < 0.001 | 598 (3.0%) | 292 (1.4%) | 2.1 (1.8-2.4) | < 0.001 |
| | Amnesia | 785 (3.3%) | 436 (1.8%) | 1.8 (1.6-2.1) | < 0.001 | 635 (3.1%) | 373 (1.8%) | 1.7 (1.5-2.0) | < 0.001 |
| Gallstones | 323 (1.3%) | 157 (0.7%) | 2.1 (1.7-2.5) | < 0.001 | 265 (1.3%) | 124 (0.6%) | 2.2 (1.7-2.7) | < 0.001 | |
| 2-3 Years | Osteopenia/Osteoporosis | 3,631 (15.1%) | 1,510 (6.3%) | 2.7 (2.5-2.8) | < 0.001 | 2,945 (14.6%) | 1,254 (6.2%) | 2.6 (2.4-2.8) | < 0.001 |
| | Fractures | 878 (3.7%) | 499 (2.1%) | 1.8 (1.6-2.0) | < 0.001 | 679 (3.4%) | 418 (2.1%) | 1.6 (1.5-1.9) | < 0.001 |
| | Urolithiasis | 834 (3.5%) | 212 (0.9%) | 4.0 (3.5-4.7) | < 0.001 | 644 (3.2%) | 175 (0.9%) | 3.8 (3.2-4.5) | < 0.001 |
| | MDD | 2,482 (10.4%) | 1,461 (6.1%) | 1.8 (1.7-1.9) | < 0.001 | 2,024 (10.0%) | 1,200 (5.9%) | 1.8 (1.6-1.9) | < 0.001 |
| | Anxiety Disorders | 2,253 (9.4%) | 1,419 (5.9%) | 1.6 (1.5-1.8) | < 0.001 | 1,835 (9.1%) | 1,163 (5.8%) | 1.6 (1.5-1.8) | < 0.001 |
| | HTN | 11,167 (46.6%) | 6,417 (26.8%) | 2.4 (2.3-2.5) | < 0.001 | 9,124 (45.2%) | 5,346 (26.5%) | 2.3 (2.2-2.4) | < 0.001 |
| | GERD | 3,441 (14.4%) | 2,140 (8.9%) | 1.7 (1.6-1.8) | < 0.001 | 2,800 (13.9%) | 1,760 (8.7%) | 1.7 (1.6-1.8) | < 0.001 |
| | Malaise/Fatigue | 1,972 (8.2%) | 1,122 (4.7%) | 1.8 (1.7-2.0) | < 0.001 | 1,574 (7.8%) | 917 (4.5%) | 1.8 (1.6-1.9) | < 0.001 |
| | Joint Pain/Myalgias | 4,104 (17.1%) | 2,555 (10.7%) | 1.7 (1.6-1.8) | < 0.001 | 3,285 (16.3%) | 2,082 (10.3%) | 1.7 (1.6-1.8) | < 0.001 |
| | Constipation | 1,265 (5.3%) | 612 (2.6%) | 2.1 (1.9-2.3) | < 0.001 | 1,017 (5.0%) | 511 (2.5%) | 2.0 (1.8-2.3) | < 0.001 |
| | Insomnia | 963 (4.0%) | 522 (2.2%) | 1.9 (1.7-2.1) | < 0.001 | 774 (3.8%) | 436 (2.2%) | 1.8 (1.6-2.0) | < 0.001 |

| | | | | | | | | | | |
|----------------|----------------------------------------|-------------------------|----------------|---------------|---------------|---------------|----------------|---------------|---------------|---------|
| | Polyuria | 1,036 (4.3%) | 599 (2.5%) | 1.8 (1.6-2.0) | < 0.001 | 849 (4.2%) | 511 (2.5%) | 1.7 (1.5-1.9) | < 0.001 | |
| | Weakness | 1,306 (5.4%) | 683 (2.9%) | 2.0 (1.8-2.2) | < 0.001 | 1,034 (5.1%) | 577 (2.9%) | 1.8 (1.7-2.0) | < 0.001 | |
| | Abdominal Pain | 2,146 (9.0%) | 1,241 (5.2%) | 1.8 (1.7-1.9) | < 0.001 | 1,725 (8.6%) | 1,041 (5.2%) | 1.7 (1.6-1.9) | < 0.001 | |
| | Headache | 1,089 (4.5%) | 586 (2.4%) | 1.9 (1.7-2.1) | < 0.001 | 848 (4.2%) | 480 (2.4%) | 1.8 (1.6-2.0) | < 0.001 | |
| | Nausea | 769 (3.2%) | 350 (1.5%) | 2.2 (2.0-2.5) | < 0.001 | 576 (2.9%) | 289 (1.3%) | 2.0 (1.8-2.3) | < 0.001 | |
| | Amnesia | 863 (3.6%) | 493 (2.1%) | 1.8 (1.6-2.0) | < 0.001 | 681 (3.4%) | 404 (2.0%) | 1.7 (1.5-1.9) | < 0.001 | |
| | Gallstones | 344 (1.4%) | 155 (0.6%) | 2.2 (1.8-2.7) | < 0.001 | 267 (1.3%) | 132 (0.7%) | 2.0 (1.7-2.5) | < 0.001 | |
| | Entire Study Period (0-3 Years) | Osteopenia/Osteoporosis | 5,449 (22.7%) | 2,661 (11.1%) | 2.4 (2.2-2.5) | < 0.001 | 4,447 (22.0%) | 2,221 (11.0%) | 2.3 (2.2-2.4) | < 0.001 |
| | | Fractures | 1,836 (7.7%) | 1,254 (5.2%) | 1.5 (1.4-1.6) | < 0.001 | 1,450 (7.2%) | 1,044 (5.2%) | 1.4 (1.3-1.5) | < 0.001 |
| | | Urolithiasis | 1,600 (6.7%) | 569 (2.4%) | 2.9 (2.7-3.2) | < 0.001 | 1,262 (6.3%) | 470 (2.3%) | 2.8 (2.5-3.1) | < 0.001 |
| | | MDD | 3,962 (16.5%) | 2,751 (11.5%) | 1.5 (1.4-1.6) | < 0.001 | 3,218 (16.0%) | 2,253 (11.2%) | 1.5 (1.4-1.6) | < 0.001 |
| | | Anxiety Disorders | 3,824 (16.0%) | 2,672 (11.1%) | 1.5 (1.4-1.6) | < 0.001 | 3,097 (15.4%) | 2,177 (10.8%) | 1.5 (1.4-1.6) | < 0.001 |
| | | HTN | 13,639 (56.9%) | 9,749 (40.7%) | 1.9 (1.9-2.0) | < 0.001 | 11,187 (55.5%) | 8,114 (40.2%) | 1.9 (1.8-1.9) | < 0.001 |
| | | GERD | 5,619 (23.4%) | 4,151 (17.3%) | 1.5 (1.4-1.5) | < 0.001 | 4,602 (22.8%) | 3,430 (17.0%) | 1.4 (1.4-1.5) | < 0.001 |
| | | Malaise/Fatigue | 4,565 (19.0%) | 2,947 (12.3%) | 1.7 (1.6-1.8) | < 0.001 | 3,687 (18.3%) | 2,428 (12.0%) | 1.6 (1.5-1.7) | < 0.001 |
| | | Joint Pain/Myalgias | 7,759 (32.4%) | 5,589 (23.3%) | 1.6 (1.5-1.6) | < 0.001 | 6,266 (31.1%) | 4,591 (22.8%) | 1.5 (1.5-1.6) | < 0.001 |
| Constipation | | 2,874 (12.0%) | 1,577 (6.6%) | 1.9 (1.8-2.1) | < 0.001 | 2,335 (11.6%) | 1,316 (6.5%) | 1.9 (1.7-2.0) | < 0.001 | |
| Insomnia | | 1,999 (8.3%) | 1,193 (5.0%) | 1.7 (1.6-1.9) | < 0.001 | 1,592 (7.9%) | 994 (4.9%) | 1.7 (1.5-1.8) | < 0.001 | |
| Polyuria | | 2,371 (9.9%) | 1,427 (6.0%) | 1.7 (1.6-1.9) | < 0.001 | 1,905 (9.4%) | 1,205 (6.0%) | 1.6 (1.5-1.8) | < 0.001 | |
| Weakness | | 3,145 (13.1%) | 1,992 (8.3%) | 1.7 (1.6-1.8) | < 0.001 | 2,522 (12.5%) | 1,670 (8.3%) | 1.6 (1.5-1.7) | < 0.001 | |
| Abdominal Pain | | 4,906 (20.5%) | 3,417 (14.3%) | 1.5 (1.5-1.6) | < 0.001 | 3,979 (19.7%) | 2,844 (14.1%) | 1.5 (1.4-1.6) | < 0.001 | |
| Headache | | 2,719 (11.3%) | 1,772 (7.4%) | 1.6 (1.5-1.7) | < 0.001 | 2,155 (10.7%) | 1,453 (7.2%) | 1.5 (1.4-1.7) | < 0.001 | |
| Nausea | | 1,941 (8.1%) | 1,115 (4.7%) | 1.8 (1.7-1.9) | < 0.001 | 1,518 (7.5%) | 919 (4.6%) | 1.7 (1.6-1.9) | < 0.001 | |
| Amnesia | 1,852 (7.7%) | 1,173 (4.9%) | 1.6 (1.5-1.8) | < 0.001 | 1,484 (7.4%) | 965 (4.8%) | 1.6 (1.5-1.7) | < 0.001 | | |
| Gallstones | 883 (3.7%) | 532 (2.2%) | 1.7 (1.5-1.9) | < 0.001 | 708 (3.5%) | 442 (2.2%) | 1.6 (1.4-1.8) | < 0.001 | | |

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; MDD, major depressive disorder; HTN, hypertension; GERD, gastroesophageal reflux disease; CI, confidence interval

^aStatistical significance defined as $P < 0.003$

eTable 6: Associated Diagnoses and Symptoms in Patients at High Risk of PHP With Hypercalcemia and PTH ≥ 65 (n = 14,959) or 100 (n = 7,387) pg/mL Without a Documented Diagnosis of PHP Compared to Matched Controls

| | Diagnosis | High-Risk PHP PTH ≥ 65 (n = 14,959 after matching) | Matched Controls (n = 7,386 after matching) | Odds Ratio (95% CI) | *P value | High-Risk PHP PTH ≥ 100 (n = 7,386 after matching) | Matched Controls (n = 7,386 after matching) | Odds Ratio (95% CI) | *P value |
|------------------|-------------------------|---------------------------------------------------------------|---------------------------------------------------|------------------------|------------|---------------------------------------------------------------|---------------------------------------------------|------------------------|----------|
| 0-1 Year | Osteopenia/Osteoporosis | 1,859 (12.4%) | 886 (5.9%) | 2.3 (2.1-2.5) | < 0.001 | 826 (11.2%) | 388 (5.3%) | 2.3 (2.0-2.6) | < 0.001 |
| | Fractures | 479 (3.2%) | 360 (2.4%) | 1.3 (1.2-1.5) | < 0.001 | 197 (2.7%) | 180 (2.4%) | 1.1 (0.9-1.3) | 0.38 |
| | Urolithiasis | 532 (3.6%) | 187 (1.3%) | 2.9 (2.5-3.4) | < 0.001 | 234 (3.2%) | 99 (1.3%) | 2.4 (1.9-3.1) | < 0.001 |
| | MDD | 1,395 (9.3%) | 1,047 (7.0%) | 1.4 (1.3-1.5) | < 0.001 | 583 (7.9%) | 467 (6.3%) | 1.3 (1.1-1.4) | < 0.001 |
| | Anxiety Disorders | 1,330 (8.9%) | 1,026 (6.9%) | 1.3 (1.2-1.4) | < 0.001 | 560 (7.6%) | 451 (6.1%) | 1.3 (1.1-1.4) | < 0.001 |
| | HTN | 6,433 (43.0%) | 4,232 (28.3%) | 1.9 (1.8-2.0) | < 0.001 | 2,857 (38.7%) | 2,137 (28.9%) | 1.5 (1.4-1.7) | < 0.001 |
| | GERD | 2,047 (13.7%) | 1,476 (9.9%) | 1.4 (1.3-1.6) | < 0.001 | 880 (11.9%) | 707 (9.6%) | 1.3 (1.2-1.4) | < 0.001 |
| | Malaise/Fatigue | 1,412 (9.4%) | 755 (5.0%) | 2.0 (1.8-2.1) | < 0.001 | 621 (8.4%) | 460 (6.2%) | 1.4 (1.2-1.6) | < 0.001 |
| | Joint Pain/Myalgias | 2,358 (15.8%) | 1,846 (12.3%) | 1.3 (1.2-1.4) | < 0.001 | 1,033 (14.0%) | 807 (10.9%) | 1.3 (1.2-1.5) | < 0.001 |
| | Constipation | 851 (5.7%) | 453 (3.0%) | 1.9 (1.7-2.2) | < 0.001 | 347 (4.7%) | 243 (3.3%) | 1.5 (1.2-1.7) | < 0.001 |
| | Insomnia | 584 (3.9%) | 351 (2.3%) | 1.7 (1.5-1.9) | < 0.001 | 250 (3.4%) | 194 (2.6%) | 1.3 (1.1-1.6) | 0.007 |
| | Polyuria | 599 (4.0%) | 377 (2.5%) | 1.6 (1.4-1.8) | < 0.001 | 246 (3.3%) | 191 (2.6%) | 1.3 (1.1-1.6) | 0.008 |
| | Weakness | 936 (6.3%) | 497 (3.3%) | 1.9 (1.7-2.2) | < 0.001 | 402 (5.4%) | 299 (4.0%) | 1.4 (1.2-1.6) | < 0.001 |
| | Abdominal Pain | 1,439 (9.6%) | 918 (6.1%) | 1.6 (1.5-1.8) | < 0.001 | 596 (8.1%) | 534 (7.2%) | 1.1 (1.0-1.3) | 0.06 |
| | Headache | 765 (5.1%) | 496 (3.3%) | 1.6 (1.4-1.8) | < 0.001 | 309 (4.2%) | 268 (3.6%) | 1.2 (1.0-1.4) | 0.08 |
| | Nausea | 538 (3.6%) | 275 (1.8%) | 2.0 (1.7-2.3) | < 0.001 | 226 (3.1%) | 166 (2.2%) | 1.4 (1.1-1.7) | 0.002 |
| Amnesia | 523 (3.5%) | 355 (2.4%) | 1.5 (1.3-1.7) | < 0.001 | 213 (2.9%) | 164 (2.2%) | 1.3 (1.1-1.6) | 0.01 | |
| Gallstones | 266 (1.8%) | 149 (1.0%) | 1.8 (1.5-2.2) | < 0.001 | 124 (1.7%) | 88 (1.2%) | 1.4 (1.1-1.9) | 0.01 | |
| 1-2 Years | Osteopenia/Osteoporosis | 1,914 (12.8%) | 693 (4.6%) | 3.0 (2.8-3.3) | < 0.001 | 838 (11.3%) | 379 (5.1%) | 2.4 (2.1-2.7) | < 0.001 |
| | Fractures | 418 (2.8%) | 241 (1.6%) | 1.8 (1.5-2.1) | < 0.001 | 173 (2.3%) | 137 (1.9%) | 1.3 (1.0-1.6) | 0.04 |
| | Urolithiasis | 458 (3.1%) | 135 (0.9%) | 3.5 (2.9-4.2) | < 0.001 | 212 (2.9%) | 60 (0.8%) | 3.6 (2.7-4.8) | < 0.001 |
| | MDD | 1,346 (9.0%) | 734 (4.9%) | 1.9 (1.7-2.1) | < 0.001 | 570 (7.7%) | 405 (5.5%) | 1.4 (1.3-1.6) | < 0.001 |
| | Anxiety Disorders | 1,205 (8.1%) | 721 (4.9%) | 1.8 (1.6-1.9) | < 0.001 | 512 (6.9%) | 365 (4.9%) | 1.4 (1.2-1.6) | < 0.001 |
| | HTN | 6,297 (42.1%) | 2,991 (20.0%) | 2.9 (2.8-3.1) | < 0.001 | 2,786 (37.7%) | 1,763 (23.9%) | 1.9 (1.8-2.1) | < 0.001 |
| | GERD | 1,877 (12.5%) | 1,051 (7.0%) | 1.9 (1.8-2.1) | < 0.001 | 774 (10.5%) | 542 (7.3%) | 1.5 (1.3-1.7) | < 0.001 |
| | Malaise/Fatigue | 1,058 (7.1%) | 489 (3.3%) | 2.3 (2.0-2.5) | < 0.001 | 441 (6.0%) | 327 (4.4%) | 1.4 (1.2-1.6) | < 0.001 |
| | Joint Pain/Myalgias | 2,298 (15.4%) | 1,264 (8.5%) | 2.0 (1.8-2.1) | < 0.001 | 1,007 (13.6%) | 712 (9.6%) | 1.5 (1.4-1.6) | < 0.001 |
| | Constipation | 706 (4.7%) | 298 (2.0%) | 2.4 (2.1-2.8) | < 0.001 | 295 (4.0%) | 156 (2.1%) | 1.9 (1.6-2.3) | < 0.001 |
| | Insomnia | 488 (3.3%) | 275 (1.8%) | 1.8 (1.6-2.1) | < 0.001 | 209 (2.8%) | 158 (2.1%) | 1.3 (1.1-1.6) | 0.007 |
| | Polyuria | 543 (3.6%) | 266 (1.8%) | 2.1 (1.8-2.4) | < 0.001 | 242 (3.3%) | 159 (2.2%) | 1.5 (1.3-1.9) | < 0.001 |
| | Weakness | 636 (4.3%) | 297 (2.0%) | 2.2 (1.9-2.5) | < 0.001 | 279 (3.8%) | 200 (2.7%) | 1.4 (1.2-1.7) | < 0.001 |
| | Abdominal Pain | 1,179 (7.9%) | 590 (3.9%) | 2.1 (1.9-2.3) | < 0.001 | 489 (6.6%) | 349 (4.7%) | 1.3 (1.2-1.6) | < 0.001 |
| | Headache | 644 (4.3%) | 282 (1.9%) | 2.3 (2.0-2.7) | < 0.001 | 275 (3.7%) | 181 (2.5%) | 1.5 (1.3-1.9) | < 0.001 |
| | Nausea | 400 (2.7%) | 150 (1.0%) | 2.7 (2.2-3.3) | < 0.001 | 176 (2.4%) | 113 (1.5%) | 1.6 (1.2-2.0) | < 0.001 |
| Amnesia | 459 (3.1%) | 203 (1.4%) | 2.3 (1.9-2.7) | < 0.001 | 194 (2.6%) | 125 (1.7%) | 1.6 (1.2-2.0) | < 0.001 | |
| Gallstones | 189 (1.3%) | 74 (0.5%) | 2.6 (2.0-3.4) | < 0.001 | 92 (1.2%) | 36 (0.5%) | 2.6 (1.7-3.8) | < 0.001 | |
| 2-3 Years | Osteopenia/Osteoporosis | 2,059 (13.8%) | 575 (3.8%) | 4.0 (3.6-4.4) | < 0.001 | 887 (12.0%) | 421 (5.7%) | 2.3 (2.0-2.5) | < 0.001 |
| | Fractures | 474 (3.2%) | 163 (1.1%) | 3.0 (2.5-3.6) | < 0.001 | 186 (2.5%) | 127 (1.7%) | 1.5 (1.2-1.9) | < 0.001 |
| | Urolithiasis | 438 (2.9%) | 94 (0.6%) | 4.8 (3.8-6.0) | < 0.001 | 201 (2.7%) | 61 (0.8%) | 3.4 (2.5-4.5) | < 0.001 |
| | MDD | 1,429 (9.6%) | 533 (3.6%) | 2.9 (2.6-3.2) | < 0.001 | 591 (8.0%) | 409 (5.5%) | 1.5 (1.3-1.7) | < 0.001 |
| | Anxiety Disorders | 1,272 (8.5%) | 531 (3.6%) | 2.5 (2.3-2.8) | < 0.001 | 547 (7.4%) | 502 (5.4%) | 1.4 (1.2-1.6) | < 0.001 |
| | HTN | 6,469 (43.2%) | 2,295 (15.3%) | 4.2 (4.0-4.4) | < 0.001 | 2,873 (38.9%) | 1,858 (25.2%) | 1.9 (1.8-2.0) | < 0.001 |
| | GERD | 1,911 (12.8%) | 830 (5.5%) | 2.5 (2.3-2.8) | < 0.001 | 791 (10.7%) | 609 (8.2%) | 1.3 (1.2-1.5) | < 0.001 |
| | Malaise/Fatigue | 1,101 (7.4%) | 386 (2.6%) | 3.0 (2.7-3.4) | < 0.001 | 494 (6.7%) | 304 (4.1%) | 1.7 (1.4-1.9) | < 0.001 |
| | Joint Pain/Myalgias | 2,313 (15.5%) | 952 (6.4%) | 2.7 (2.5-2.9) | < 0.001 | 972 (13.2%) | 733 (9.9%) | 1.4 (1.2-1.5) | < 0.001 |
| | Constipation | 688 (4.6%) | 246 (1.6%) | 2.9 (2.5-3.3) | < 0.001 | 280 (3.8%) | 183 (2.5%) | 1.6 (1.3-1.9) | < 0.001 |

| | | | | | | | | | |
|----------------------------------------|-------------------------|---------------|---------------|---------------|---------|---------------|---------------|---------------|---------|
| Entire Study Period (0-3 Years) | Insomnia | 516 (3.5%) | 205 (1.4%) | 2.6 (2.2-3.0) | < 0.001 | 220 (3.0%) | 165 (2.2%) | 1.3 (1.1-1.6) | 0.005 |
| | Polyuria | 584 (3.9%) | 198 (1.3%) | 3.0 (2.6-3.6) | < 0.001 | 235 (3.2%) | 160 (2.2%) | 1.5 (1.2-1.9) | < 0.001 |
| | Weakness | 699 (4.7%) | 201 (1.3%) | 3.6 (3.1-4.2) | < 0.001 | 303 (4.1%) | 185 (2.5%) | 1.7 (1.4-2.0) | < 0.001 |
| | Abdominal Pain | 1,193 (8.0%) | 474 (3.2%) | 2.6 (2.4-3.0) | < 0.001 | 497 (6.7%) | 366 (5.0%) | 1.4 (1.2-1.6) | < 0.001 |
| | Headache | 603 (4.0%) | 233 (1.6%) | 2.7 (2.3-3.1) | < 0.001 | 256 (3.5%) | 161 (2.2%) | 1.6 (1.3-2.0) | < 0.001 |
| | Nausea | 396 (2.6%) | 160 (1.1%) | 2.5 (2.1-3.0) | < 0.001 | 157 (2.1%) | 89 (1.2%) | 1.8 (1.4-2.3) | < 0.001 |
| | Amnesia | 471 (3.1%) | 174 (1.2%) | 2.8 (2.3-3.3) | < 0.001 | 175 (2.4%) | 143 (1.9%) | 1.2 (1.0-1.5) | 0.07 |
| | Gallstones | 194 (1.3%) | 70 (0.5%) | 2.8 (2.1-3.7) | < 0.001 | 81 (1.1%) | 52 (0.7%) | 1.6 (1.1-2.2) | 0.01 |
| | Osteopenia/Osteoporosis | 3,152 (21.1%) | 1,426 (9.5%) | 2.5 (2.4-2.7) | < 0.001 | 1,422 (19.3%) | 726 (9.8%) | 2.2 (2.0-2.4) | < 0.001 |
| | Fractures | 992 (6.6%) | 632 (4.2%) | 1.6 (1.5-1.8) | < 0.001 | 409 (5.5%) | 352 (4.8%) | 1.2 (1.0-1.4) | 0.03 |
| | Urolithiasis | 887 (5.9%) | 317 (2.1%) | 2.9 (2.6-3.3) | < 0.001 | 414 (5.6%) | 135 (1.8%) | 3.2 (2.6-3.9) | < 0.001 |
| | MDD | 2,252 (15.1%) | 1,468 (9.8%) | 1.6 (1.5-1.7) | < 0.001 | 923 (12.5%) | 690 (9.3%) | 1.4 (1.2-1.5) | < 0.001 |
| | Anxiety Disorders | 2,168 (4.5%) | 1,475 (9.9%) | 1.5 (1.4-1.7) | < 0.001 | 942 (12.8%) | 709 (9.6%) | 1.4 (1.2-1.5) | < 0.001 |
| | HTN | 7,944 (53.1%) | 5,039 (33.7%) | 2.2 (2.1-2.3) | < 0.001 | 3,603 (48.8%) | 2,708 (36.7%) | 1.6 (1.5-1.8) | < 0.001 |
| | GERD | 3,220 (21.5%) | 2,131 (14.6%) | 1.7 (1.6-1.8) | < 0.001 | 1,400 (19.0%) | 1,136 (15.4%) | 1.3 (1.2-1.4) | < 0.001 |
| | Malaise/Fatigue | 2,554 (17.1%) | 1,308 (8.7%) | 2.1 (2.0-2.3) | < 0.001 | 1,115 (15.1%) | 802 (10.9%) | 1.5 (1.3-1.6) | < 0.001 |
| | Joint Pain/Myalgias | 4,341 (29.0%) | 2,911 (19.5%) | 1.7 (1.6-1.8) | < 0.001 | 1,925 (26.1%) | 1,556 (21.1%) | 1.3 (1.2-1.4) | < 0.001 |
| | Constipation | 1,613 (10.8%) | 800 (5.3%) | 2.1 (2.0-2.3) | < 0.001 | 676 (9.2%) | 443 (6.0%) | 1.6 (1.4-1.8) | < 0.001 |
| | Insomnia | 1,075 (7.2%) | 612 (4.1%) | 1.8 (1.6-2.0) | < 0.001 | 457 (6.2%) | 308 (4.2%) | 1.5 (1.3-1.8) | < 0.001 |
| | Polyuria | 1,317 (8.8%) | 694 (4.6%) | 2.0 (1.8-2.2) | < 0.001 | 551 (7.5%) | 392 (5.3%) | 1.4 (1.3-1.6) | < 0.001 |
| | Weakness | 1,723 (11.5%) | 837 (5.6%) | 2.2 (2.0-2.4) | < 0.001 | 757 (10.2%) | 552 (7.5%) | 1.4 (1.3-1.6) | < 0.001 |
| | Abdominal Pain | 2,760 (18.4%) | 1,595 (10.7%) | 1.9 (1.8-2.2) | < 0.001 | 1,167 (15.8%) | 935 (12.7%) | 1.3 (1.2-1.4) | < 0.001 |
| | Headache | 1,523 (10.2%) | 855 (5.7%) | 1.9 (1.7-2.0) | < 0.001 | 635 (8.6%) | 471 (6.4%) | 1.4 (1.2-1.6) | < 0.001 |
| | Nausea | 1,027 (6.9%) | 502 (3.4%) | 2.1 (1.9-2.4) | < 0.001 | 443 (6.0%) | 331 (4.5%) | 1.4 (1.2-1.6) | < 0.001 |
| | Amnesia | 1,040 (7.0%) | 592 (4.0%) | 1.8 (1.6-2.0) | < 0.001 | 428 (5.8%) | 324 (4.4%) | 1.3 (1.2-1.6) | < 0.001 |
| | Gallstones | 510 (3.4%) | 253 (1.7%) | 2.1 (1.8-2.4) | < 0.001 | 234 (3.2%) | 157 (2.1%) | 1.5 (1.2-1.8) | < 0.001 |

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; MDD, major depressive disorder; HTN, hypertension; GERD, gastroesophageal reflux disease; CI, confidence interval

^aStatistical significance defined as $P < 0.003$

eTable 7: Comparing Diagnoses and Symptoms in Patients at High Risk of PHP With Hypercalcemia and PTH ≥ 40 (n = 23,969) or 50 pg/mL (n = 20,176) Without a Documented Diagnosis With Those Diagnosed (n = 13,136)

| | Diagnosis | High-Risk PHP PTH ≥ 40 (n = 13,119 after matching) | Diagnosed (n = 13,119 after matching) | Odds Ratio (95% CI) | ^a P value | High-Risk PHP PTH ≥ 50 (n = 12,842 after matching) | Diagnosed (n = 12,842 after matching) | Odds Ratio (95% CI) | ^a P value |
|-------------------------|-------------------------|---------------------------------------------------------|---------------------------------------|---------------------|----------------------|---------------------------------------------------------|---------------------------------------|---------------------|----------------------|
| 0-1 Year | Osteopenia/Osteoporosis | 2,011 (15.3%) | 2,837 (21.6%) | 0.7 (0.6-0.7) | <0.001 | 1,970 (15.3%) | 2,797 (21.8%) | 0.7 (0.6-0.7) | <0.001 |
| | Fractures | 556 (4.2%) | 544 (4.1%) | 1.0 (0.9-1.2) | 0.71 | 551 (4.3%) | 530 (4.1%) | 1.0 (0.9-1.2) | 0.51 |
| | Urolithiasis | 665 (5.1%) | 1,166 (8.9%) | 0.5 (0.5-0.6) | <0.001 | 620 (4.8%) | 1,132 (8.8%) | 0.5 (0.5-0.6) | <0.001 |
| | MDD | 1,684 (12.8%) | 1,657 (12.6%) | 1.0 (0.9-1.1) | 0.62 | 1,585 (12.3%) | 1,606 (12.5%) | 1.0 (0.9-1.1) | 0.69 |
| | Anxiety Disorders | 1,597 (12.2%) | 1,407 (10.7%) | 1.2 (1.1-1.2) | <0.001 | 1,549 (12.1%) | 1,359 (10.6%) | 1.2 (1.1-1.3) | <0.001 |
| | HTN | 7,081 (54.0%) | 6,863 (52.3%) | 1.1 (1.0-1.1) | 0.007 | 6,804 (53.0%) | 6,761 (52.6%) | 1.0 (1.0-1.1) | 0.59 |
| | GERD | 2,312 (17.6%) | 2,411 (18.4%) | 1.0 (0.9-1.0) | 0.11 | 2,252 (17.5%) | 2,364 (18.4%) | 0.9 (0.9-1.0) | 0.07 |
| | Malaise/Fatigue | 1,686 (12.9%) | 1,775 (13.5%) | 0.9 (0.9-1.0) | 0.10 | 1,593 (12.4%) | 1,735 (13.5%) | 0.9 (0.8-1.0) | 0.008 |
| | Joint Pain/Myalgias | 2,793 (21.3%) | 2,785 (21.2%) | 1.0 (0.9-1.1) | 0.90 | 2,631 (20.5%) | 2,725 (21.2%) | 1.0 (0.9-1.0) | 0.15 |
| | Constipation | 974 (7.4%) | 1,024 (7.8%) | 0.9 (0.9-1.0) | 0.24 | 950 (7.4%) | 1,005 (7.8%) | 0.9 (0.9-1.0) | 0.20 |
| | Insomnia | 742 (5.7%) | 602 (4.6%) | 1.2 (1.1-1.4) | <0.001 | 699 (5.4%) | 583 (4.5%) | 1.2 (1.1-1.4) | <0.001 |
| | Polyuria | 702 (5.4%) | 790 (6.0%) | 0.9 (0.8-1.0) | 0.02 | 639 (5.0%) | 773 (6.0%) | 0.8 (0.7-0.9) | <0.001 |
| | Weakness | 1,150 (8.8%) | 1,226 (9.3%) | 0.9 (0.9-1.0) | 0.10 | 1,068 (8.3%) | 1,195 (9.3%) | 0.9 (0.8-1.0) | 0.005 |
| | Abdominal Pain | 1,780 (13.6%) | 1,709 (13.0%) | 1.0 (1.0-1.1) | 0.20 | 1,683 (13.1%) | 1,661 (12.9%) | 1.0 (0.9-1.1) | 0.68 |
| | 1-2 Years | Headache | 929 (7.1%) | 926 (7.1%) | 1.0 (0.9-1.1) | 0.94 | 856 (6.7%) | 897 (7.0%) | 1.0 (0.9-1.0) |
| Nausea | | 741 (5.6%) | 684 (5.2%) | 1.1 (1.0-1.2) | 0.12 | 672 (5.2%) | 660 (5.1%) | 1.0 (0.9-1.1) | 0.74 |
| Amnesia | | 586 (4.5%) | 614 (4.7%) | 1.0 (0.8-1.1) | 0.41 | 557 (4.3%) | 609 (4.7%) | 0.9 (0.8-1.0) | 0.12 |
| Gallstones | | 294 (2.2%) | 307 (2.3%) | 1.0 (0.8-1.1) | 0.59 | 293 (2.3%) | 301 (2.3%) | 1.0 (0.8-1.1) | 0.74 |
| Osteopenia/Osteoporosis | | 2,082 (15.9%) | 2,836 (21.6%) | 0.7 (0.6-0.7) | <0.001 | 2,059 (16.0%) | 2,795 (21.8%) | 0.7 (0.6-0.7) | <0.001 |
| Fractures | | 507 (3.9%) | 463 (3.5%) | 1.1 (1.0-1.2) | 0.15 | 479 (3.7%) | 453 (3.5%) | 1.1 (0.9-1.2) | 0.39 |
| Urolithiasis | | 571 (4.4%) | 928 (7.1%) | 0.6 (0.5-0.7) | <0.001 | 518 (4.0%) | 903 (7.0%) | 0.6 (0.5-0.6) | <0.001 |
| MDD | | 1,566 (11.9%) | 1,520 (11.6%) | 1.0 (1.0-1.1) | 0.38 | 1,511 (11.8%) | 1,476 (11.5%) | 1.0 (1.0-1.1) | 0.50 |
| Anxiety Disorders | | 1,460 (11.1%) | 1,275 (9.7%) | 1.2 (1.1-1.3) | <0.001 | 1,390 (10.8%) | 1,236 (9.6%) | 1.1 (1.1-1.2) | 0.002 |
| HTN | | 6,946 (52.9%) | 6,532 (49.8%) | 1.1 (1.1-1.2) | <0.001 | 6,679 (52.0%) | 6,446 (50.2%) | 1.1 (1.0-1.1) | 0.004 |
| GERD | | 2,102 (16.0%) | 2,254 (17.2%) | 0.9 (0.9-1.0) | 0.01 | 2,058 (16.0%) | 2,211 (17.2%) | 0.9 (0.9-1.0) | 0.01 |
| Malaise/Fatigue | | 1,258 (9.6%) | 1,339 (10.2%) | 0.9 (0.9-1.0) | 0.09 | 1,206 (9.4%) | 1,306 (10.2%) | 0.9 (0.8-1.0) | 0.04 |
| Joint Pain/Myalgias | | 2,640 (20.1%) | 2,569 (19.6%) | 1.0 (1.0-1.1) | 0.27 | 2,548 (19.8%) | 2,506 (19.5%) | 1.0 (1.0-1.1) | 0.51 |
| Constipation | | 765 (5.8%) | 815 (6.2%) | 0.9 (0.8-1.0) | 0.19 | 747 (5.8%) | 799 (6.2%) | 0.9 (0.8-1.0) | 0.17 |
| Insomnia | | 620 (4.7%) | 541 (4.1%) | 1.2 (1.0-1.3) | 0.02 | 558 (4.3%) | 527 (4.1%) | 1.1 (0.9-1.2) | 0.34 |
| Polyuria | 603 (4.6%) | 659 (5.0%) | 0.9 (0.8-1.0) | 0.11 | 593 (4.6%) | 643 (5.0%) | 0.9 (0.8-1.0) | 0.14 | |
| Weakness | 792 (6.0%) | 901 (6.9%) | 0.9 (0.8-1.0) | 0.006 | 732 (5.7%) | 880 (6.9%) | 0.8 (0.7-0.9) | <0.001 | |
| Abdominal Pain | 1,385 (10.6%) | 1,435 (10.9%) | 1.0 (0.9-1.0) | 0.32 | 1,290 (10.0%) | 1,394 (10.9%) | 0.9 (0.8-1.0) | 0.03 | |
| Headache | 789 (6.0%) | 703 (5.4%) | 1.1 (1.0-1.3) | 0.02 | 718 (5.6%) | 676 (5.3%) | 1.1 (1.0-1.2) | 0.25 | |
| Nausea | 522 (4.0%) | 472 (3.6%) | 1.1 (1.0-1.3) | 0.11 | 467 (3.6%) | 458 (3.6%) | 1.0 (0.9-1.2) | 0.76 | |
| Amnesia | 487 (3.7%) | 485 (3.7%) | 1.0 (0.9-1.1) | 0.95 | 458 (3.6%) | 476 (3.7%) | 1.0 (0.8-1.1) | 0.55 | |
| Gallstones | 210 (1.6%) | 234 (1.8%) | 0.9 (0.7-1.1) | 0.25 | 201 (1.6%) | 229 (1.8%) | 0.9 (0.7-1.1) | 0.17 | |
| 2-3 Years | Osteopenia/Osteoporosis | 2,237 (17.1%) | 3,174 (24.2%) | 0.6 (0.6-0.7) | <0.001 | 2,198 (17.1%) | 3,132 (24.4%) | 0.6 (0.6-0.7) | <0.001 |
| | Fractures | 546 (4.2%) | 496 (3.8%) | 1.1 (1.0-1.3) | 0.11 | 506 (3.9%) | 485 (3.8%) | 1.0 (0.9-1.2) | 0.50 |
| | Urolithiasis | 573 (4.4%) | 952 (7.3%) | 0.6 (0.5-0.6) | <0.001 | 525 (4.1%) | 923 (7.2%) | 0.6 (0.5-0.6) | <0.001 |
| | MDD | 1,658 (12.6%) | 1,558 (11.9%) | 1.1 (1.0-1.2) | 0.06 | 1,583 (12.3%) | 1,509 (11.8%) | 1.1 (1.0-1.1) | 0.16 |
| | Anxiety Disorders | 1,518 (11.6%) | 1,361 (10.4%) | 1.1 (1.0-1.2) | 0.002 | 1,462 (11.4%) | 1,314 (10.2%) | 1.1 (1.0-1.2) | 0.003 |
| | HTN | 7,063 (53.8%) | 6,625 (50.5%) | 1.1 (1.1-1.2) | <0.001 | 6,796 (52.9%) | 6,538 (50.9%) | 1.1 (1.0-1.1) | 0.001 |
| | GERD | 2,174 (16.6%) | 2,308 (17.6%) | 0.9 (0.9-1.0) | 0.03 | 2,135 (16.6%) | 2,250 (17.5%) | 0.9 (0.9-1.0) | 0.06 |
| | Malaise/Fatigue | 1,271 (9.7%) | 1,383 (10.5%) | 0.9 (0.8-1.0) | 0.02 | 1,234 (9.6%) | 1,356 (10.6%) | 0.9 (0.8-1.0) | 0.01 |
| | Joint Pain/Myalgias | 2,637 (20.1%) | 2,615 (19.9%) | 1.0 (1.0-1.1) | 0.73 | 2,508 (19.5%) | 2,560 (19.9%) | 1.0 (0.9-1.0) | 0.41 |
| | Constipation | 785 (6.0%) | 775 (5.9%) | 1.0 (0.9-1.1) | 0.79 | 775 (6.0%) | 762 (5.9%) | 1.0 (0.9-1.1) | 0.73 |
| Insomnia | 633 (4.8%) | 577 (4.4%) | 1.1 (1.0-1.2) | 0.10 | 598 (4.7%) | 558 (4.3%) | 1.1 (1.0-1.2) | 0.23 | |

| | | | | | | | | | |
|----------------------------------------|-------------------------|---------------|---------------|---------------|------------|---------------|---------------|---------------|--------|
| | Polyuria | 657 (5.0%) | 665 (5.1%) | 1.0 (0.9-1.1) | 0.82 | 628 (4.9%) | 656 (5.1%) | 1.0 (0.9-1.1) | 0.42 |
| | Weakness | 841 (6.4%) | 845 (6.4%) | 1.0 (0.9-1.1) | 0.92 | 802 (6.2%) | 828 (6.4%) | 1.0 (0.9-1.1) | 0.51 |
| | Abdominal Pain | 1,410 (10.7%) | 1,369 (10.4%) | 1.0 (1.0-1.1) | 0.41 | 1,333 (10.4%) | 1,334 (10.4%) | 1.0 (0.9-1.1) | 0.98 |
| | Headache | 753 (5.7%) | 721 (5.5%) | 1.0 (0.9-1.2) | 0.39 | 666 (5.2%) | 698 (5.4%) | 1.0 (0.9-1.1) | 0.37 |
| | Nausea | 509 (3.9%) | 475 (3.6%) | 1.1 (0.9-1.2) | 0.27 | 467 (3.6%) | 462 (3.6%) | 1.0 (0.9-1.2) | 0.87 |
| | Amnesia | 511 (3.9%) | 506 (3.9%) | 1.0 (0.9-1.1) | 0.87 | 488 (3.8%) | 498 (3.9%) | 1.0 (0.9-1.1) | 0.75 |
| | Gallstones | 227 (1.7%) | 226 (1.7%) | 1.0 (0.8-1.2) | 0.96 | 211 (1.6%) | 224 (1.7%) | 0.9 (0.8-1.1) | 0.53 |
| Entire Study Period (0-3 Years) | Osteopenia/Osteoporosis | 3,355 (25.6%) | 4,856 (37.0%) | 0.6 (0.6-0.6) | <0.001 | 3,326 (25.9%) | 4,787 (37.3%) | 0.6 (0.6-0.6) | <0.001 |
| | Fractures | 1,141 (8.7%) | 1,112 (8.5%) | 1.0 (0.9-1.1) | 0.52 | 1,091 (8.5%) | 1,089 (8.5%) | 1.0 (0.9-1.1) | 0.96 |
| | Urolithiasis | 1,101 (8.4%) | 1,905 (14.5%) | 0.5 (0.5-0.6) | <0.001 | 1,010 (7.9%) | 1,847 (14.4%) | 0.5 (0.5-0.6) | <0.001 |
| | MDD | 2,646 (20.2%) | 2,675 (20.4%) | 1.0 (0.9-1.0) | 0.66 | 2,528 (19.7%) | 2,599 (20.2%) | 1.0 (0.9-1.0) | 0.27 |
| | Anxiety Disorders | 2,589 (19.7%) | 2,395 (18.3%) | 1.1 (1.0-1.2) | 0.002 | 2,485 (19.4%) | 2,320 (18.1%) | 1.1 (1.0-1.2) | 0.008 |
| | HTN | 8,623 (65.7%) | 8,568 (65.3%) | 1.0 (1.0-1.1) | 0.47 | 8,371 (65.2%) | 8,425 (65.6%) | 1.0 (0.9-1.0) | 0.48 |
| | GERD | 3,573 (27.2%) | 3,906 (29.8%) | 0.9 (0.8-0.9) | <0.001 | 3,515 (27.4%) | 3,823 (29.8%) | 0.9 (0.8-0.9) | <0.001 |
| | Malaise/Fatigue | 2,986 (22.8%) | 3,286 (25.0%) | 0.9 (0.8-0.9) | <0.001 | 2,859 (22.3%) | 3,208 (25.0%) | 0.9 (0.8-0.9) | <0.001 |
| | Joint Pain/Myalgias | 4,968 (37.9%) | 5,076 (38.7%) | 1.0 (0.9-1.0) | 0.17 | 4,771 (37.2%) | 4,966 (38.7%) | 0.9 (0.9-1.0) | 0.01 |
| | Constipation | 1,801 (13.7%) | 1,922 (14.7%) | 0.9 (0.9-1.0) | 0.03 | 1,779 (13.9%) | 1,887 (14.7%) | 0.9 (0.9-1.0) | 0.05 |
| | Insomnia | 1,320 (10.1%) | 1,150 (8.8%) | 1.2 (1.1-1.3) | <0.001 | 1,236 (9.6%) | 1,116 (8.7%) | 1.1 (1.0-1.2) | 0.009 |
| | Polyuria | 1,514 (11.5%) | 1,666 (12.7%) | 0.9 (0.8-1.0) | 0.004 | 1,432 (11.2%) | 1,634 (12.7%) | 0.9 (0.8-0.9) | <0.001 |
| | Weakness | 2,065 (15.7%) | 2,266 (17.3%) | 0.9 (0.8-1.0) | <0.001 | 1,954 (15.2%) | 2,212 (17.2%) | 0.9 (0.8-0.9) | <0.001 |
| | Abdominal Pain | 3,221 (24.6%) | 3,292 (25.1%) | 1.0 (0.9-1.0) | 0.31 | 3,075 (23.9%) | 3,203 (24.9%) | 0.9 (0.9-1.0) | 0.07 |
| | Headache | 1,822 (13.9%) | 1,789 (13.6%) | 1.0 (1.0-1.1) | 0.55 | 1,685 (13.1%) | 1,737 (13.5%) | 1.0 (0.9-1.0) | 0.34 |
| | Nausea | 1,324 (10.1%) | 1,301 (9.9%) | 1.0 (0.9-1.1) | 0.64 | 1,214 (9.5%) | 1,262 (9.8%) | 1.0 (0.9-1.0) | 0.31 |
| | Amnesia | 1,170 (8.9%) | 1,157 (8.8%) | 1.0 (0.9-1.1) | 0.78 | 1,104 (8.6%) | 1,140 (8.9%) | 1.0 (0.9-1.1) | 0.43 |
| Gallstones | 567 (4.3%) | 579 (4.4%) | 1.0 (0.9-1.1) | 0.72 | 550 (4.3%) | 571 (4.4%) | 1.0 (0.9-1.1) | 0.52 | |

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; MDD, major depressive disorder; HTN, hypertension; GERD, gastroesophageal reflux disease; CI, confidence interval

^aStatistical significance defined as $P < 0.003$

eTable 8: Comparing Diagnoses and Symptoms in Patients at High Risk of PHP With Hypercalcemia and PTH ≥ 65 (n = 14,959) or 100 pg/mL (n = 7,387) Without a Documented Diagnosis With Those Diagnosed (n = 13,136)

| | Diagnosis | High-Risk PHP PTH ≥ 65 (n = 11,076 after matching) | Diagnosed (n = 11,076 after matching) | Odds Ratio (95% CI) | *P value | High-Risk PHP PTH ≥ 100 (n = 5,686 after matching) | Diagnosed (n = 5,686 after matching) | Odds Ratio (95% CI) | *P value |
|------------------|-------------------------|---------------------------------------------------------|---------------------------------------|---------------------|------------|---------------------------------------------------------|--------------------------------------|---------------------|----------|
| 0-1 Year | Osteopenia/Osteoporosis | 1,698 (15.3%) | 2,464 (22.2%) | 0.6 (0.6-0.7) | <0.001 | 809 (14.2%) | 1,250 (22.0%) | 0.6 (0.5-0.6) | <0.001 |
| | Fractures | 434 (3.9%) | 462 (4.2%) | 0.9 (0.8-1.1) | 0.34 | 191 (3.4%) | 242 (4.3%) | 0.8 (0.6-0.9) | 0.01 |
| | Urolithiasis | 496 (4.5%) | 944 (8.5%) | 0.5 (0.4-0.6) | <0.001 | 227 (4.0%) | 445 (7.8%) | 0.5 (0.4-0.6) | <0.001 |
| | MDD | 1,275 (11.5%) | 1,353 (12.2%) | 0.9 (0.9-1.0) | 0.11 | 569 (10.0%) | 665 (11.7%) | 0.8 (0.7-0.9) | 0.004 |
| | Anxiety Disorders | 1,229 (11.1%) | 1,159 (10.5%) | 1.1 (1.0-1.2) | 0.13 | 547 (9.6%) | 599 (10.5%) | 0.9 (0.8-1.0) | 0.11 |
| | HTN | 5,854 (52.9%) | 5,945 (53.7%) | 1.0 (0.9-1.0) | 0.22 | 2,803 (49.3%) | 3,100 (54.5%) | 0.8 (0.8-0.9) | <0.001 |
| | GERD | 1,875 (16.9%) | 2,049 (18.5%) | 0.9 (0.8-1.0) | 0.002 | 860 (15.1%) | 1,047 (18.4%) | 0.8 (0.7-0.9) | <0.001 |
| | Malaise/Fatigue | 1,302 (11.8%) | 1,505 (13.6%) | 0.8 (0.8-0.9) | <0.001 | 604 (10.6%) | 774 (13.6%) | 0.8 (0.7-0.8) | <0.001 |
| | Joint Pain/Myalgias | 2,122 (19.2%) | 2,352 (21.2%) | 0.9 (0.8-0.9) | <0.001 | 1,009 (17.7%) | 1,159 (20.4%) | 0.8 (0.8-0.9) | <0.001 |
| | Constipation | 776 (7.0%) | 883 (8.0%) | 0.9 (0.8-1.0) | 0.006 | 341 (6.0%) | 468 (8.2%) | 0.7 (0.6-0.8) | <0.001 |
| | Insomnia | 531 (4.8%) | 504 (4.6%) | 1.1 (0.9-1.2) | 0.39 | 242 (4.3%) | 267 (4.7%) | 0.9 (0.8-1.1) | 0.26 |
| | Polyuria | 542 (4.9%) | 681 (6.1%) | 0.8 (0.7-0.9) | <0.001 | 243 (4.3%) | 347 (6.1%) | 0.7 (0.6-0.8) | <0.001 |
| | Weakness | 860 (7.8%) | 1,040 (9.4%) | 0.8 (0.7-0.9) | <0.001 | 394 (6.9%) | 538 (9.5%) | 0.7 (0.6-0.8) | <0.001 |
| | Abdominal Pain | 1,302 (11.8%) | 1,423 (12.8%) | 0.9 (0.8-1.0) | 0.01 | 575 (10.1%) | 702 (12.3%) | 0.8 (0.7-0.9) | <0.001 |
| Headache | 695 (6.3%) | 769 (6.9%) | 0.9 (0.8-1.0) | 0.05 | 299 (5.3%) | 388 (6.8%) | 0.8 (0.6-0.9) | <0.001 | |
| Nausea | 512 (4.6%) | 560 (5.1%) | 0.9 (0.8-1.0) | 0.13 | 221 (3.9%) | 282 (5.0%) | 0.8 (0.6-0.9) | 0.005 | |
| Amnesia | 480 (4.3%) | 536 (4.8%) | 0.9 (0.8-1.0) | 0.07 | 209 (3.7%) | 286 (5.0%) | 0.7 (0.6-0.9) | <0.001 | |
| Gallstones | 239 (2.2%) | 253 (2.3%) | 0.9 (0.8-1.1) | 0.52 | 118 (2.1%) | 130 (2.3%) | 0.9 (0.7-1.2) | 0.44 | |
| 1-2 Years | Osteopenia/Osteoporosis | 1,760 (15.9%) | 2,462 (22.2%) | 0.7 (0.6-0.7) | <0.001 | 827 (14.5%) | 1,243 (21.9%) | 0.6 (0.6-0.7) | <0.001 |
| | Fractures | 377 (3.4%) | 386 (3.5%) | 1.0 (0.8-1.1) | 0.74 | 171 (3.0%) | 185 (3.3%) | 0.9 (0.7-1.1) | 0.45 |
| | Urolithiasis | 431 (3.9%) | 756 (6.8%) | 0.6 (0.5-0.6) | <0.001 | 207 (3.6%) | 366 (6.4%) | 0.5 (0.5-0.7) | <0.001 |
| | MDD | 1,234 (11.1%) | 1,262 (11.4%) | 1.0 (0.9-1.1) | 0.55 | 555 (9.8%) | 620 (10.9%) | 0.9 (0.8-1.0) | 0.05 |
| | Anxiety Disorders | 1,111 (10.0%) | 1,055 (9.5%) | 1.1 (1.0-1.2) | 0.21 | 505 (8.9%) | 532 (9.4%) | 0.9 (0.8-1.1) | 0.38 |
| | HTN | 5,727 (51.7%) | 5,670 (51.2%) | 1.0 (1.0-1.1) | 0.44 | 2,733 (48.1%) | 2,913 (51.2%) | 0.9 (0.8-0.9) | <0.001 |
| | GERD | 1,705 (15.4%) | 1,897 (17.1%) | 0.9 (0.8-0.9) | <0.001 | 756 (13.3%) | 993 (17.5%) | 0.7 (0.7-0.8) | <0.001 |
| | Malaise/Fatigue | 961 (8.7%) | 1,145 (10.3%) | 0.8 (0.8-0.9) | <0.001 | 432 (7.6%) | 566 (10.0%) | 0.7 (0.7-0.8) | <0.001 |
| | Joint Pain/Myalgias | 2,083 (18.8%) | 2,166 (19.6%) | 1.0 (0.9-1.0) | 0.16 | 985 (17.3%) | 1,116 (19.6%) | 0.9 (0.8-0.9) | 0.002 |
| | Constipation | 643 (5.8%) | 709 (6.4%) | 0.9 (0.8-1.0) | 0.06 | 290 (5.1%) | 370 (6.5%) | 0.8 (0.7-0.9) | 0.001 |
| | Insomnia | 447 (4.0%) | 457 (4.1%) | 1.0 (0.9-1.1) | 0.73 | 205 (3.6%) | 243 (4.3%) | 0.8 (0.7-1.0) | 0.07 |
| | Polyuria | 497 (4.5%) | 574 (5.2%) | 0.9 (0.8-1.0) | 0.02 | 236 (4.2%) | 285 (5.0%) | 0.8 (0.7-1.0) | 0.03 |
| | Weakness | 580 (5.2%) | 776 (7.0%) | 0.7 (0.7-0.8) | <0.001 | 271 (4.8%) | 391 (6.9%) | 0.7 (0.6-0.8) | <0.001 |
| | Abdominal Pain | 1,062 (9.6%) | 1,208 (10.9%) | 0.9 (0.8-0.9) | 0.001 | 475 (8.4%) | 632 (11.1%) | 0.7 (0.6-0.8) | <0.001 |
| | Headache | 587 (5.3%) | 582 (5.3%) | 1.0 (0.9-1.1) | 0.88 | 270 (4.7%) | 296 (5.2%) | 0.9 (0.8-1.1) | 0.26 |
| | Nausea | 372 (3.4%) | 385 (3.5%) | 1.0 (0.8-1.1) | 0.63 | 173 (3.0%) | 200 (3.5%) | 0.9 (0.7-1.1) | 0.16 |
| | Amnesia | 417 (3.8%) | 429 (3.9%) | 1.0 (0.8-1.1) | 0.67 | 190 (3.3%) | 242 (4.3%) | 0.8 (0.6-0.9) | 0.01 |
| Gallstones | 170 (1.5%) | 204 (1.8%) | 0.8 (0.7-1.0) | 0.07 | 88 (1.5%) | 118 (2.1%) | 0.7 (0.6-1.0) | 0.03 | |
| 2-3 Years | Osteopenia/Osteoporosis | 1,888 (17.0%) | 2,747 (24.8%) | 0.6 (0.6-0.7) | <0.001 | 874 (15.4%) | 1,396 (24.6%) | 0.6 (0.5-0.6) | <0.001 |
| | Fractures | 429 (3.9%) | 427 (3.9%) | 1.0 (0.9-1.2) | 0.94 | 182 (3.2%) | 216 (3.8%) | 0.8 (0.7-1.0) | 0.08 |
| | Urolithiasis | 411 (3.7%) | 767 (6.9%) | 0.5 (0.5-0.6) | <0.001 | 195 (3.4%) | 361 (6.3%) | 0.5 (0.4-0.6) | <0.001 |
| | MDD | 1,307 (11.8%) | 1,290 (11.6%) | 1.0 (0.9-1.1) | 0.72 | 574 (10.1%) | 639 (11.2%) | 0.9 (0.8-1.0) | 0.05 |
| | Anxiety Disorders | 1,182 (10.7%) | 1,118 (10.1%) | 1.1 (1.0-1.2) | 0.16 | 536 (9.4%) | 556 (9.8%) | 1.0 (0.8-1.1) | 0.52 |
| | HTN | 5,858 (52.9%) | 5,780 (52.2%) | 1.0 (1.0-1.1) | 0.29 | 2,813 (49.5%) | 2,991 (52.6%) | 0.9 (0.8-0.9) | <0.001 |
| | GERD | 1,741 (15.7%) | 1,951 (17.6%) | 0.9 (0.8-0.9) | <0.001 | 773 (13.6%) | 1,009 (17.7%) | 0.7 (0.7-0.8) | <0.001 |
| | Malaise/Fatigue | 1,009 (9.1%) | 1,174 (10.6%) | 0.8 (0.8-0.9) | <0.001 | 484 (8.5%) | 607 (10.7%) | 0.8 (0.7-0.9) | <0.001 |
| | Joint Pain/Myalgias | 2,099 (19.0%) | 2,209 (19.9%) | 0.9 (0.9-1.0) | 0.06 | 953 (16.8%) | 1,150 (20.2%) | 0.8 (0.7-0.9) | <0.001 |
| | Constipation | 608 (5.5%) | 684 (6.2%) | 0.9 (0.8-1.0) | 0.03 | 271 (4.8%) | 358 (6.3%) | 0.7 (0.6-0.9) | <0.001 |
| Insomnia | 473 (4.3%) | 480 (4.3%) | 1.0 (0.9-1.1) | 0.82 | 214 (3.8%) | 262 (4.6%) | 0.8 (0.7-1.0) | 0.02 | |

| | | | | | | | | | |
|----------------------------------------|-------------------------|---------------|---------------|---------------|------------|---------------|---------------|---------------|--------|
| | Polyuria | 532 (4.8%) | 584 (5.3%) | 0.9 (0.8-1.0) | 0.11 | 230 (4.0%) | 308 (5.4%) | 0.7 (0.6-0.9) | <0.001 |
| | Weakness | 641 (5.8%) | 721 (6.5%) | 0.9 (0.8-1.0) | 0.03 | 293 (5.2%) | 374 (6.6%) | 0.8 (0.7-0.9) | 0.001 |
| | Abdominal Pain | 1,076 (9.7%) | 1,147 (10.4%) | 0.9 (0.9-1.0) | 0.11 | 482 (8.5%) | 573 (10.1%) | 0.8 (0.7-0.9) | 0.003 |
| | Headache | 544 (4.9%) | 593 (5.4%) | 0.9 (0.8-1.0) | 0.14 | 248 (4.4%) | 299 (5.3%) | 0.8 (0.7-1.0) | 0.03 |
| | Nausea | 364 (3.3%) | 384 (3.5%) | 0.9 (0.8-1.1) | 0.46 | 152 (2.7%) | 205 (3.6%) | 0.7 (0.6-0.9) | 0.004 |
| | Amnesia | 419 (3.8%) | 440 (4.0%) | 1.0 (0.8-1.1) | 0.46 | 170 (3.0%) | 242 (4.3%) | 0.7 (0.6-0.8) | <0.001 |
| | Gallstones | 174 (1.6%) | 188 (1.7%) | 0.9 (0.8-1.1) | 0.46 | 78 (1.4%) | 105 (1.8%) | 0.7 (0.6-1.0) | 0.04 |
| Entire Study Period (0-3 Years) | Osteopenia/Osteoporosis | 2,893 (26.1%) | 4,201 (37.9%) | 0.6 (0.5-0.6) | <0.001 | 1,399 (24.6%) | 2,132 (37.5%) | 0.5 (0.5-0.6) | <0.001 |
| | Fractures | 903 (8.2%) | 938 (8.5%) | 1.0 (0.9-1.1) | 0.39 | 400 (7.0%) | 471 (8.3%) | 0.8 (0.7-1.0) | 0.01 |
| | Urolithiasis | 827 (7.5%) | 1,556 (14.0%) | 0.5 (0.5-0.5) | <0.001 | 401 (7.1%) | 756 (13.3%) | 0.5 (0.4-0.6) | <0.001 |
| | MDD | 2,058 (18.6%) | 2,210 (20.0%) | 0.9 (0.9-1.0) | 0.01 | 898 (15.8%) | 1,097 (19.3%) | 0.8 (0.7-0.9) | <0.001 |
| | Anxiety Disorders | 2,005 (18.1%) | 1,981 (17.9%) | 1.0 (0.9-1.1) | 0.67 | 923 (16.2%) | 1,012 (17.8%) | 0.9 (0.8-1.0) | 0.03 |
| | HTN | 7,215 (65.1%) | 7,378 (66.6%) | 0.9 (0.9-1.0) | 0.02 | 3,528 (62.0%) | 3,826 (67.3%) | 0.8 (0.7-0.9) | <0.001 |
| | GERD | 2,933 (26.5%) | 3,286 (29.7%) | 0.9 (0.8-0.9) | <0.001 | 1,370 (24.1%) | 1,704 (30.0%) | 0.7 (0.7-0.8) | <0.001 |
| | Malaise/Fatigue | 2,337 (21.1%) | 2,778 (25.1%) | 0.8 (0.8-0.9) | <0.001 | 1,088 (19.1%) | 1,408 (24.8%) | 0.7 (0.7-0.8) | <0.001 |
| | Joint Pain/Myalgias | 3,931 (35.5%) | 4,274 (38.6%) | 0.9 (0.8-0.9) | <0.001 | 1,882 (33.1%) | 2,149 (37.8%) | 0.8 (0.8-0.9) | <0.001 |
| | Constipation | 1,459 (13.2%) | 1,669 (15.1%) | 0.9 (0.8-0.9) | <0.001 | 661 (11.6%) | 883 (15.5%) | 0.7 (0.6-0.8) | <0.001 |
| | Insomnia | 974 (8.8%) | 969 (8.7%) | 1.0 (0.9-1.1) | 0.91 | 445 (7.8%) | 519 (9.1%) | 0.8 (0.7-1.0) | 0.01 |
| | Polyuria | 1,203 (10.9%) | 1,448 (13.1%) | 0.8 (0.7-0.9) | <0.001 | 539 (9.5%) | 742 (13.0%) | 0.7 (0.6-0.8) | <0.001 |
| | Weakness | 1,573 (14.2%) | 1,926 (17.4%) | 0.8 (0.7-0.8) | <0.001 | 736 (12.9%) | 981 (17.3%) | 0.7 (0.6-0.8) | <0.001 |
| | Abdominal Pain | 2,503 (22.6%) | 2,754 (24.9%) | 0.9 (0.8-0.9) | <0.001 | 1,131 (19.9%) | 1,398 (24.6%) | 0.8 (0.7-0.8) | <0.001 |
| | Headache | 1,387 (12.5%) | 1,478 (13.3%) | 0.9 (0.9-1.0) | 0.07 | 619 (10.9%) | 740 (13.0%) | 0.8 (0.7-0.9) | <0.001 |
| | Nausea | 955 (8.6%) | 1,064 (9.6%) | 0.9 (0.8-1.0) | 0.01 | 432 (7.6%) | 549 (9.7%) | 0.8 (0.7-0.9) | <0.001 |
| | Amnesia | 946 (8.5%) | 1,008 (9.1%) | 0.9 (0.8-1.0) | 0.14 | 420 (7.4%) | 547 (9.6%) | 0.7 (0.7-0.9) | <0.001 |
| Gallstones | 455 (4.1%) | 487 (4.4%) | 0.9 (0.8-1.1) | 0.29 | 225 (4.0%) | 266 (4.7%) | 0.8 (0.7-1.0) | 0.06 | |

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; MDD, major depressive disorder; HTN, hypertension; GERD, gastroesophageal reflux disease; CI, confidence interval

^aStatistical significance defined as $P < 0.003$

eTable 9: Comparing Diagnoses and Symptoms in Patients at High Risk of PHP With Hypercalcemia and PTH ≥ 40 (n = 23,969) or 50 pg/mL (n = 20,176) Without a Documented Diagnosis With Those Diagnosed With Similar PTH Levels (n = 12,294 for PTH ≥ 40 and n = 11,968 for ≥ 50 pg/mL)

| | Diagnosis | High-Risk PHP PTH ≥ 40 (n = 12,277 after matching) | Diagnosed PTH ≥ 40 (n = 12,277 after matching) | Odds Ratio (95% CI) | ^a P value | High-Risk PHP PTH ≥ 50 (n = 11,876 after matching) | Diagnosed PTH ≥ 50 (n = 11,876 after matching) | Odds Ratio (95% CI) | ^a P value |
|---------------------|-------------------------|---------------------------------------------------------|-----------------------------------------------------|---------------------|----------------------|---------------------------------------------------------|-----------------------------------------------------|---------------------|----------------------|
| 0-1 Year | Osteopenia/Osteoporosis | 1,900 (15.5%) | 2,677 (21.8%) | 0.7 (0.6-0.7) | <0.001 | 1,826 (15.4%) | 2,589 (21.8%) | 0.7 (0.6-0.7) | <0.001 |
| | Fractures | 515 (4.2%) | 509 (4.1%) | 1.0 (0.9-1.1) | 0.85 | 511 (4.3%) | 492 (4.1%) | 1.0 (0.9-1.2) | 0.54 |
| | Urolithiasis | 621 (5.1%) | 1,099 (9.0%) | 0.5 (0.5-0.6) | <0.001 | 576 (4.9%) | 1,043 (8.8%) | 0.5 (0.5-0.6) | <0.001 |
| | MDD | 1,567 (12.8%) | 1,560 (12.7%) | 1.0 (0.9-1.1) | 0.89 | 1,481 (12.5%) | 1,510 (12.7%) | 1.0 (0.9-1.1) | 0.57 |
| | Anxiety Disorders | 1,501 (12.2%) | 1,328 (10.8%) | 1.1 (1.1-1.2) | <0.001 | 1,453 (12.2%) | 1,273 (10.7%) | 1.2 (1.1-1.3) | <0.001 |
| | HTN | 6,607 (53.8%) | 6,357 (51.8%) | 1.1 (1.0-1.1) | 0.001 | 6,272 (52.8%) | 6,153 (51.8%) | 1.0 (1.0-1.1) | 0.12 |
| | GERD | 2,167 (17.7%) | 2,259 (18.4%) | 1.0 (0.9-1.0) | 0.13 | 2,082 (17.5%) | 2,185 (18.4%) | 0.9 (0.9-1.0) | 0.08 |
| | Malaise/Fatigue | 1,566 (12.8%) | 1,673 (13.6%) | 0.9 (0.9-1.0) | 0.04 | 1,484 (12.5%) | 1,581 (13.3%) | 0.9 (0.9-1.0) | 0.06 |
| | Joint Pain/Myalgias | 2,617 (21.3%) | 2,592 (21.1%) | 1.0 (1.0-1.1) | 0.70 | 2,442 (20.6%) | 2,509 (21.1%) | 1.0 (0.9-1.0) | 0.28 |
| | Constipation | 915 (7.5%) | 958 (7.8%) | 1.0 (0.9-1.0) | 0.30 | 879 (7.4%) | 919 (7.7%) | 1.0 (0.9-1.0) | 0.33 |
| | Insomnia | 705 (5.7%) | 562 (4.6%) | 1.3 (1.1-1.4) | <0.001 | 651 (5.5%) | 544 (4.6%) | 1.2 (1.1-1.4) | 0.001 |
| | Polyuria | 659 (5.4%) | 740 (6.0%) | 0.9 (0.8-1.0) | 0.03 | 581 (4.9%) | 714 (6.0%) | 0.8 (0.7-0.9) | <0.001 |
| | Weakness | 1,072 (8.7%) | 1,146 (9.3%) | 0.9 (0.9-1.0) | 0.10 | 990 (8.3%) | 1,090 (9.2%) | 0.9 (0.8-1.0) | 0.02 |
| | Abdominal Pain | 1,668 (13.6%) | 1,601 (13.0%) | 1.0 (1.0-1.1) | 0.21 | 1,568 (13.2%) | 1,541 (13.0%) | 1.0 (0.9-1.1) | 0.60 |
| | Headache | 866 (7.1%) | 859 (7.0%) | 1.0 (0.9-1.1) | 0.86 | 798 (6.7%) | 823 (6.9%) | 1.0 (0.9-1.1) | 0.52 |
| | Nausea | 690 (5.6%) | 640 (5.2%) | 1.1 (1.0-1.2) | 0.16 | 628 (5.3%) | 604 (5.1%) | 1.0 (0.9-1.2) | 0.48 |
| | Amnesia | 544 (4.4%) | 572 (4.7%) | 0.9 (0.8-1.1) | 0.39 | 503 (4.2%) | 549 (4.6%) | 0.9 (0.8-1.0) | 0.15 |
| Gallstones | 274 (2.2%) | 291 (2.4%) | 0.9 (0.8-1.1) | 0.47 | 275 (2.3%) | 281 (2.4%) | 1.0 (0.8-1.2) | 0.80 | |
| 1-2 Years | Osteopenia/Osteoporosis | 1,975 (16.1%) | 2,665 (21.7%) | 0.7 (0.6-0.7) | <0.001 | 1,903 (16.0%) | 2,586 (21.8%) | 0.7 (0.6-0.7) | <0.001 |
| | Fractures | 482 (3.9%) | 431 (3.5%) | 1.1 (1.0-1.3) | 0.09 | 446 (3.8%) | 412 (3.5%) | 1.1 (0.9-1.2) | 0.24 |
| | Urolithiasis | 529 (4.3%) | 875 (7.1%) | 0.6 (0.5-0.7) | <0.001 | 473 (4.0%) | 831 (7.0%) | 0.6 (0.5-0.6) | <0.001 |
| | MDD | 1,462 (11.9%) | 1,440 (11.7%) | 1.0 (0.9-1.1) | 0.66 | 1,404 (11.8%) | 1,391 (11.7%) | 1.0 (0.9-1.1) | 0.79 |
| | Anxiety Disorders | 1,384 (11.3%) | 1,208 (9.8%) | 1.2 (1.1-1.3) | <0.001 | 1,296 (10.9%) | 1,160 (9.8%) | 1.1 (1.0-1.2) | 0.004 |
| | HTN | 6,483 (52.8%) | 6,082 (49.5%) | 1.1 (1.1-1.2) | <0.001 | 6,178 (52.0%) | 5,890 (49.6%) | 1.1 (1.0-1.2) | <0.001 |
| | GERD | 1,987 (16.2%) | 2,125 (17.3%) | 0.9 (0.9-1.0) | 0.02 | 1,902 (16.0%) | 2,056 (17.3%) | 0.9 (0.9-1.0) | 0.007 |
| | Malaise/Fatigue | 1,180 (9.6%) | 1,264 (10.3%) | 0.9 (0.9-1.0) | 0.07 | 1,124 (9.5%) | 1,204 (10.1%) | 0.9 (0.9-1.0) | 0.08 |
| | Joint Pain/Myalgias | 2,471 (20.1%) | 2,418 (19.7%) | 1.0 (1.0-1.1) | 0.40 | 2,368 (19.9%) | 2,326 (19.6%) | 1.0 (1.0-1.1) | 0.49 |
| | Constipation | 710 (5.8%) | 771 (6.3%) | 0.9 (0.8-1.0) | 0.10 | 684 (5.8%) | 744 (6.3%) | 0.9 (0.8-1.0) | 0.10 |
| | Insomnia | 582 (4.7%) | 504 (4.1%) | 1.2 (1.0-1.3) | 0.02 | 523 (4.4%) | 486 (4.1%) | 1.1 (1.0-1.2) | 0.23 |
| | Polyuria | 556 (4.5%) | 612 (5.0%) | 0.9 (0.8-1.0) | 0.09 | 528 (4.4%) | 588 (5.0%) | 0.9 (0.8-1.0) | 0.07 |
| | Weakness | 742 (6.0%) | 841 (6.9%) | 0.9 (0.8-1.0) | 0.01 | 686 (5.8%) | 799 (6.7%) | 0.8 (0.8-0.9) | 0.002 |
| | Abdominal Pain | 1,286 (10.5%) | 1,328 (10.8%) | 1.0 (0.9-1.0) | 0.38 | 1,204 (10.1%) | 1,280 (10.8%) | 0.9 (0.9-1.0) | 0.11 |
| | Headache | 734 (6.0%) | 650 (5.3%) | 1.1 (1.0-1.3) | 0.02 | 665 (5.6%) | 616 (5.2%) | 1.1 (1.0-1.2) | 0.16 |
| | Nausea | 485 (4.0%) | 437 (3.6%) | 1.1 (1.0-1.3) | 0.11 | 441 (3.7%) | 418 (3.5%) | 1.1 (0.9-1.2) | 0.42 |
| | Amnesia | 470 (3.8%) | 450 (3.7%) | 1.0 (0.9-1.2) | 0.50 | 419 (3.5%) | 433 (3.6%) | 1.0 (0.8-1.1) | 0.63 |
| Gallstones | 197 (1.6%) | 225 (1.8%) | 0.9 (0.7-1.1) | 0.17 | 182 (1.5%) | 219 (1.8%) | 0.8 (0.7-1.0) | 0.06 | |
| 2-3 Years | Osteopenia/Osteoporosis | 2,107 (17.2%) | 2,992 (24.4%) | 0.6 (0.6-0.7) | <0.001 | 2,039 (17.2%) | 2,898 (24.4%) | 0.6 (0.6-0.7) | <0.001 |
| | Fractures | 519 (4.2%) | 460 (3.7%) | 1.1 (1.0-1.3) | 0.05 | 475 (4.0%) | 444 (3.7%) | 1.1 (0.9-1.2) | 0.30 |
| | Urolithiasis | 527 (4.3%) | 872 (7.1%) | 0.6 (0.5-0.7) | <0.001 | 474 (4.0%) | 833 (7.0%) | 0.6 (0.5-0.6) | <0.001 |
| | MDD | 1,545 (12.6%) | 1,477 (12.0%) | 1.1 (1.0-1.1) | 0.19 | 1,479 (12.5%) | 1,431 (12.0%) | 1.0 (1.0-1.1) | 0.34 |
| | Anxiety Disorders | 1,426 (11.6%) | 1,290 (10.5%) | 1.1 (1.0-1.2) | 0.006 | 1,368 (11.5%) | 1,243 (10.5%) | 1.1 (1.0-1.2) | 0.01 |
| | HTN | 6,581 (53.6%) | 6,189 (50.4%) | 1.1 (1.1-1.2) | <0.001 | 6,271 (52.8%) | 5,991 (50.4%) | 1.1 (1.0-1.2) | <0.001 |
| | GERD | 2,026 (16.5%) | 2,169 (17.7%) | 0.9 (0.9-1.0) | 0.02 | 1,978 (16.7%) | 2,090 (17.6%) | 0.9 (0.9-1.0) | 0.05 |
| | Malaise/Fatigue | 1,191 (9.7%) | 1,299 (10.6%) | 0.9 (0.8-1.0) | 0.02 | 1,151 (9.7%) | 1,246 (10.5%) | 0.9 (0.8-1.0) | 0.04 |
| Joint Pain/Myalgias | 2,467 (20.1%) | 2,458 (20.0%) | 1.0 (0.9-1.1) | 0.89 | 2,327 (19.6%) | 2,373 (20.0%) | 1.0 (0.9-1.0) | 0.45 | |

| | | | | | | | | | |
|----------------------------------------|-------------------------|---------------|---------------|---------------|--------|---------------|---------------|---------------|--------|
| | Constipation | 727 (5.9%) | 734 (6.0%) | 1.0 (0.9-1.1) | 0.85 | 712 (6.0%) | 712 (6.0%) | 1.0 (0.9-1.1) | 1.0 |
| | Insomnia | 598 (4.9%) | 531 (4.3%) | 1.1 (1.0-1.3) | 0.04 | 560 (4.7%) | 514 (4.3%) | 1.1 (1.0-1.2) | 0.15 |
| | Polyuria | 607 (4.9%) | 623 (5.1%) | 1.0 (0.9-1.1) | 0.64 | 576 (4.9%) | 600 (5.1%) | 1.0 (0.9-1.1) | 0.47 |
| | Weakness | 792 (6.5%) | 796 (6.5%) | 1.0 (0.9-1.1) | 0.92 | 750 (6.3%) | 756 (6.4%) | 1.0 (0.9-1.1) | 0.87 |
| | Abdominal Pain | 1,313 (10.7%) | 1,277 (10.4%) | 1.0 (1.0-1.1) | 0.45 | 1,240 (10.4%) | 1,229 (10.3%) | 1.0 (0.9-1.1) | 0.82 |
| | Headache | 697 (5.7%) | 670 (5.5%) | 1.0 (0.9-1.2) | 0.45 | 621 (5.2%) | 645 (5.4%) | 1.0 (0.9-1.1) | 0.49 |
| | Nausea | 474 (3.9%) | 445 (3.6%) | 1.1 (0.9-1.2) | 0.33 | 424 (3.6%) | 427 (3.6%) | 1.0 (0.9-1.1) | 0.92 |
| | Amnesia | 480 (3.9%) | 471 (3.8%) | 1.0 (0.9-1.2) | 0.77 | 456 (3.8%) | 455 (3.8%) | 1.0 (0.9-1.1) | 0.97 |
| | Gallstones | 213 (1.7%) | 215 (1.8%) | 1.0 (0.8-1.2) | 0.92 | 198 (1.7%) | 210 (1.8%) | 0.9 (0.8-1.1) | 0.54 |
| Entire Study Period (0-3 Years) | Osteopenia/Osteoporosis | 3,159 (25.7%) | 4,584 (37.3%) | 0.6 (0.6-0.6) | <0.001 | 3,064 (25.8%) | 4,438 (37.4%) | 0.6 (0.6-0.6) | <0.001 |
| | Fractures | 1,073 (8.7%) | 1,032 (8.4%) | 1.0 (1.0-1.1) | 0.35 | 1,017 (8.6%) | 997 (8.4%) | 1.0 (0.9-1.1) | 0.64 |
| | Urolithiasis | 1,021 (8.3%) | 1,787 (14.6%) | 0.5 (0.5-0.6) | <0.001 | 925 (7.8%) | 1,710 (14.4%) | 0.5 (0.5-0.5) | <0.001 |
| | MDD | 2,469 (20.1%) | 2,520 (20.5%) | 1.0 (0.9-1.0) | 0.42 | 2,357 (19.8%) | 2,438 (20.5%) | 1.0 (0.9-1.0) | 0.19 |
| | Anxiety Disorders | 2,447 (19.9%) | 2,256 (18.4%) | 1.1 (1.0-1.2) | 0.002 | 2,332 (19.6%) | 2,172 (18.3%) | 1.1 (1.0-1.2) | 0.008 |
| | HTN | 8,052 (65.6%) | 7,983 (65.0%) | 1.0 (1.0-1.1) | 0.35 | 7,732 (65.1%) | 7,734 (65.1%) | 1.0 (0.9-1.1) | 0.98 |
| | GERD | 3,355 (27.3%) | 3,670 (29.9%) | 0.9 (0.8-0.9) | <0.001 | 3,258 (27.4%) | 3,549 (29.9%) | 0.9 (0.8-0.9) | <0.001 |
| | Malaise/Fatigue | 2,791 (22.7%) | 3,087 (25.1%) | 0.9 (0.8-0.9) | <0.001 | 2,655 (22.4%) | 2,957 (24.9%) | 0.9 (0.8-0.9) | <0.001 |
| | Joint Pain/Myalgias | 4,660 (38.0%) | 4,733 (38.6%) | 1.0 (0.9-1.0) | 0.34 | 4,437 (37.4%) | 4,562 (38.4%) | 1.0 (0.9-1.0) | 0.09 |
| | Constipation | 1,688 (13.7%) | 1,804 (14.7%) | 0.9 (0.9-1.0) | 0.03 | 1,641 (13.8%) | 1,739 (14.6%) | 0.9 (0.9-1.0) | 0.07 |
| | Insomnia | 1,241 (10.1%) | 1,068 (8.7%) | 1.2 (1.1-1.3) | <0.001 | 1,154 (9.7%) | 1,030 (8.7%) | 1.1 (1.0-1.2) | 0.005 |
| | Polyuria | 1,408 (11.5%) | 1,559 (12.7%) | 0.9 (0.8-1.0) | 0.003 | 1,306 (11.0%) | 1,505 (12.7%) | 0.9 (0.8-0.9) | <0.001 |
| | Weakness | 1,935 (15.8%) | 2,113 (17.2%) | 0.9 (0.8-1.0) | 0.002 | 1,823 (15.4%) | 2,032 (17.1%) | 0.9 (0.8-0.9) | <0.001 |
| | Abdominal Pain | 3,021 (24.6%) | 3,078 (25.1%) | 1.0 (0.9-1.0) | 0.40 | 2,865 (24.1%) | 2,963 (24.9%) | 1.0 (0.9-1.0) | 0.14 |
| | Headache | 1,694 (13.8%) | 1,655 (13.5%) | 1.0 (1.0-1.1) | 0.47 | 1,577 (13.3%) | 1,592 (13.4%) | 1.0 (0.9-1.1) | 0.77 |
| | Nausea | 1,234 (10.1%) | 1,216 (9.9%) | 1.0 (0.9-1.1) | 0.70 | 1,135 (9.6%) | 1,163 (9.8%) | 1.0 (0.9-1.1) | 0.54 |
| | Amnesia | 1,099 (9.0%) | 1,081 (8.8%) | 1.0 (0.9-1.1) | 0.69 | 1,010 (8.5%) | 1,046 (8.8%) | 1.0 (0.9-1.1) | 0.41 |
| | Gallstones | 535 (4.4%) | 550 (4.5%) | 1.0 (0.9-1.1) | 0.64 | 511 (4.3%) | 534 (4.5%) | 1.0 (0.8-1.1) | 0.47 |

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; MDD, major depressive disorder; HTN, hypertension; GERD, gastroesophageal reflux disease; CI, confidence interval

*Statistical significance defined as $P < 0.003$

eTable 10: Comparing Diagnoses and Symptoms in Patients at High Risk of PHP With Hypercalcemia and PTH ≥ 65 (n = 14,959) or 100 pg/mL (n = 7,387) Without a Documented Diagnosis With Those Diagnosed With Similar PTH Levels (n = 11,262 for PTH ≥ 65 and n = 8,192 for ≥ 100 pg/mL)

| | Diagnosis | High-Risk PHP PTH ≥ 65 (n = 10,336 after matching) | Diagnosed PTH ≥ 65 (n = 10,336 after matching) | Odds Ratio (95% CI) | ^a P value | High-Risk PHP PTH ≥ 100 (n = 5,578 after matching) | Diagnosed PTH ≥ 100 (n = 5,578 after matching) | Odds Ratio (95% CI) | ^a P value |
|------------------|-------------------------|------------------------------------------------------------|--------------------------------------------------------|---------------------|----------------------|------------------------------------------------------------|--------------------------------------------------------|---------------------|----------------------|
| 0-1 Year | Osteopenia/Osteoporosis | 1,565 (15.1%) | 2,303 (22.3%) | 0.6 (0.6-0.7) | <0.001 | 799 (14.3%) | 1,256 (22.5%) | 0.6 (0.5-0.6) | <0.001 |
| | Fractures | 400 (3.9%) | 421 (4.1%) | 0.9 (0.8-1.1) | 0.45 | 190 (3.4%) | 223 (4.0%) | 0.8 (0.7-1.0) | 0.10 |
| | Urolithiasis | 476 (4.6%) | 872 (8.4%) | 0.5 (0.5-0.6) | <0.001 | 226 (4.1%) | 453 (8.1%) | 0.5 (0.4-0.6) | <0.001 |
| | MDD | 1,227 (11.9%) | 1,283 (12.4%) | 1.0 (0.9-1.0) | 0.23 | 562 (10.1%) | 641 (11.5%) | 0.9 (0.8-1.0) | 0.02 |
| | Anxiety Disorders | 1,159 (11.2%) | 1,093 (10.6%) | 1.1 (1.0-1.2) | 0.14 | 543 (9.7%) | 553 (9.9%) | 1.0 (0.9-1.1) | 0.75 |
| | HTN | 5,433 (52.6%) | 5,430 (52.5%) | 1.0 (0.9-1.1) | 0.97 | 2,769 (49.6%) | 2,995 (53.7%) | 0.9 (0.8-0.9) | <0.001 |
| | GERD | 1,752 (17.0%) | 1,900 (18.4%) | 0.9 (0.8-1.0) | 0.007 | 852 (15.3%) | 1,007 (18.1%) | 0.8 (0.7-0.9) | <0.001 |
| | Malaise/Fatigue | 1,232 (11.9%) | 1,366 (13.2%) | 0.9 (0.8-1.0) | 0.005 | 600 (10.8%) | 723 (13.0%) | 0.8 (0.7-0.9) | <0.001 |
| | Joint Pain/Myalgias | 1,974 (19.1%) | 2,191 (21.2%) | 0.9 (0.8-0.9) | <0.001 | 1,001 (17.9%) | 1,165 (20.9%) | 0.8 (0.8-0.9) | <0.001 |
| | Constipation | 719 (7.0%) | 804 (7.8%) | 0.9 (0.8-1.0) | 0.02 | 339 (6.1%) | 434 (7.8%) | 0.8 (0.7-0.9) | <0.001 |
| | Insomnia | 514 (5.0%) | 456 (4.4%) | 1.1 (1.0-1.3) | 0.06 | 239 (4.3%) | 247 (4.4%) | 1.0 (0.8-1.2) | 0.71 |
| | Polyuria | 504 (4.9%) | 628 (6.1%) | 0.8 (0.7-0.9) | <0.001 | 240 (4.3%) | 338 (6.1%) | 0.7 (0.6-0.8) | <0.001 |
| | Weakness | 810 (7.8%) | 953 (9.2%) | 0.8 (0.8-0.9) | <0.001 | 392 (7.0%) | 501 (9.0%) | 0.8 (0.7-0.9) | <0.001 |
| | Abdominal Pain | 1,227 (11.9%) | 1,325 (12.8%) | 0.9 (0.8-1.0) | 0.04 | 569 (10.2%) | 700 (12.5%) | 0.8 (0.7-0.9) | <0.001 |
| | Headache | 648 (6.3%) | 697 (6.7%) | 0.9 (0.8-1.0) | 0.17 | 297 (5.3%) | 380 (6.8%) | 0.8 (0.7-0.9) | <0.001 |
| | Nausea | 476 (4.6%) | 505 (4.9%) | 0.9 (0.8-1.1) | 0.34 | 221 (4.0%) | 262 (4.7%) | 0.8 (0.7-1.0) | 0.06 |
| | Amnesia | 450 (4.4%) | 485 (4.7%) | 0.9 (0.8-1.1) | 0.24 | 206 (3.7%) | 263 (4.7%) | 0.8 (0.6-0.9) | 0.007 |
| Gallstones | 227 (2.2%) | 246 (2.4%) | 0.9 (0.8-1.1) | 0.38 | 115 (2.1%) | 133 (2.4%) | 0.9 (0.7-1.1) | 0.25 | |
| 1-2 Years | Osteopenia/Osteoporosis | 1,622 (15.7%) | 2,304 (22.3%) | 0.6 (0.6-0.7) | <0.001 | 812 (14.6%) | 1,215 (21.8%) | 0.6 (0.6-0.7) | <0.001 |
| | Fractures | 354 (3.4%) | 354 (3.4%) | 1.0 (0.9-1.2) | 1.0 | 168 (3.0%) | 188 (3.4%) | 0.9 (0.7-1.1) | 0.28 |
| | Urolithiasis | 414 (4.0%) | 704 (6.8%) | 0.6 (0.5-0.6) | <0.001 | 206 (3.7%) | 360 (6.5%) | 0.6 (0.5-0.7) | <0.001 |
| | MDD | 1,183 (11.4%) | 1,190 (11.5%) | 1.0 (0.9-1.1) | 0.88 | 549 (9.8%) | 614 (11.0%) | 0.9 (0.8-1.0) | 0.04 |
| | Anxiety Disorders | 1,060 (10.3%) | 999 (9.7%) | 1.1 (1.0-1.2) | 0.16 | 503 (9.0%) | 512 (9.2%) | 1.0 (0.9-1.1) | 0.77 |
| | HTN | 5,305 (51.3%) | 5,185 (50.2%) | 1.0 (1.0-1.1) | 0.10 | 2,696 (48.3%) | 2,809 (50.4%) | 0.9 (0.9-1.0) | 0.03 |
| | GERD | 1,605 (15.5%) | 1,795 (17.4%) | 0.9 (0.8-0.9) | <0.001 | 746 (13.4%) | 915 (16.4%) | 0.8 (0.7-0.9) | <0.001 |
| | Malaise/Fatigue | 924 (8.9%) | 1,037 (10.0%) | 0.9 (0.8-1.0) | 0.007 | 428 (7.7%) | 529 (9.5%) | 0.8 (0.7-0.9) | <0.001 |
| | Joint Pain/Myalgias | 1,959 (19.0%) | 2,018 (19.5%) | 1.0 (0.9-1.0) | 0.30 | 975 (17.5%) | 1,091 (19.6%) | 0.9 (0.8-1.0) | 0.005 |
| | Constipation | 602 (5.8%) | 653 (6.3%) | 0.9 (0.8-1.0) | 0.14 | 286 (5.1%) | 336 (6.0%) | 0.8 (0.7-1.0) | 0.04 |
| | Insomnia | 435 (4.2%) | 420 (4.1%) | 1.0 (0.9-1.2) | 0.60 | 201 (3.6%) | 231 (4.1%) | 0.9 (0.7-1.0) | 0.14 |
| | Polyuria | 457 (4.4%) | 522 (5.1%) | 0.9 (0.8-1.0) | 0.03 | 231 (4.1%) | 244 (4.4%) | 0.9 (0.8-1.1) | 0.54 |
| | Weakness | 552 (5.3%) | 700 (6.8%) | 0.8 (0.7-0.9) | <0.001 | 268 (4.8%) | 336 (6.0%) | 0.8 (0.7-0.9) | 0.004 |

| | | | | | | | | | | |
|---------------------|----------------------------------------|-------------------------|---------------|---------------|---------------|---------------|---------------|---------------|---------------|--------|
| | Abdominal Pain | 999 (9.7%) | 1,097 (10.6%) | 0.9 (0.8-1.0) | 0.02 | 468 (8.4%) | 568 (10.2%) | 0.8 (0.7-0.9) | 0.001 | |
| | Headache | 557 (5.4%) | 520 (5.0%) | 1.1 (1.0-1.2) | 0.25 | 267 (4.8%) | 266 (4.8%) | 1.0 (0.8-1.2) | 0.96 | |
| | Nausea | 353 (3.4%) | 351 (3.4%) | 1.0 (0.9-1.2) | 0.94 | 171 (3.1%) | 179 (3.2%) | 1.0 (0.8-1.2) | 0.66 | |
| | Amnesia | 394 (3.8%) | 376 (3.6%) | 1.0 (0.9-1.2) | 0.51 | 188 (3.4%) | 217 (3.9%) | 0.9 (0.7-1.1) | 0.14 | |
| | Gallstones | 160 (1.5%) | 189 (1.8%) | 0.8 (0.7-1.0) | 0.12 | 82 (1.5%) | 99 (1.8%) | 0.8 (0.6-1.1) | 0.20 | |
| 2-3 Years | Osteopenia/Osteoporosis | 1,748 (16.9%) | 2,551 (24.7%) | 0.6 (0.6-0.7) | <0.001 | 862 (15.5%) | 1,332 (23.9%) | 0.6 (0.5-0.6) | <0.001 | |
| | Fractures | 395 (3.8%) | 384 (3.7%) | 1.0 (0.9-1.2) | 0.69 | 178 (3.2%) | 193 (3.5%) | 0.9 (0.7-1.1) | 0.43 | |
| | Urolithiasis | 399 (3.9%) | 712 (6.9%) | 0.5 (0.5-0.6) | <0.001 | 192 (3.4%) | 357 (6.4%) | 0.5 (0.4-0.6) | <0.001 | |
| | MDD | 1,243 (12.0%) | 1,228 (11.9%) | 1.0 (0.9-1.1) | 0.75 | 567 (10.2%) | 630 (11.3%) | 0.9 (0.8-1.0) | 0.05 | |
| | Anxiety Disorders | 1,123 (10.9%) | 1,068 (10.3%) | 1.1 (1.0-1.2) | 0.21 | 531 (9.5%) | 513 (9.2%) | 1.0 (0.9-1.2) | 0.56 | |
| | HTN | 5,427 (52.5%) | 5,311 (51.4%) | 1.0 (1.0-1.1) | 0.11 | 2,774 (49.7%) | 2,883 (51.7%) | 0.9 (0.9-1.0) | 0.04 | |
| | GERD | 1,648 (15.9%) | 1,835 (17.8%) | 0.9 (0.8-0.9) | <0.001 | 762 (13.7%) | 947 (17.0%) | 0.8 (0.7-0.9) | <0.001 | |
| | Malaise/Fatigue | 952 (9.2%) | 1,083 (10.5%) | 0.9 (0.8-0.9) | 0.002 | 478 (8.6%) | 589 (10.6%) | 0.8 (0.7-0.9) | <0.001 | |
| | Joint Pain/Myalgias | 1,955 (18.9%) | 2,077 (20.1%) | 0.9 (0.9-1.0) | 0.03 | 940 (16.9%) | 1,094 (19.6%) | 0.8 (0.8-0.9) | <0.001 | |
| | Constipation | 566 (5.5%) | 613 (5.9%) | 0.9 (0.8-1.0) | 0.16 | 266 (4.8%) | 313 (5.6%) | 0.8 (0.7-1.0) | 0.04 | |
| | Insomnia | 451 (4.4%) | 444 (4.3%) | 1.0 (0.9-1.2) | 0.81 | 211 (3.8%) | 223 (4.0%) | 0.9 (0.8-1.1) | 0.56 | |
| | Polyuria | 496 (4.8%) | 538 (5.2%) | 0.9 (0.8-1.0) | 0.18 | 229 (4.1%) | 279 (5.0%) | 0.8 (0.7-1.0) | 0.02 | |
| | Weakness | 591 (5.7%) | 671 (6.5%) | 0.9 (0.8-1.0) | 0.02 | 290 (5.2%) | 348 (6.2%) | 0.8 (0.7-1.0) | 0.02 | |
| | Abdominal Pain | 986 (9.5%) | 1,070 (10.4%) | 0.9 (0.8-1.0) | 0.05 | 477 (8.6%) | 565 (10.1%) | 0.8 (0.7-0.9) | 0.004 | |
| | Headache | 517 (5.0%) | 556 (5.4%) | 0.9 (0.8-1.0) | 0.22 | 245 (4.4%) | 275 (4.9%) | 0.9 (0.7-1.1) | 0.18 | |
| | Nausea | 337 (3.3%) | 363 (3.5%) | 0.9 (0.8-1.1) | 0.32 | 150 (2.7%) | 171 (3.1%) | 0.9 (0.7-1.1) | 0.23 | |
| | Amnesia | 389 (3.8%) | 405 (3.9%) | 1.0 (0.8-1.1) | 0.56 | 169 (3.0%) | 220 (3.9%) | 0.8 (0.6-0.9) | 0.008 | |
| | Gallstones | 166 (1.6%) | 177 (1.7%) | 0.9 (0.8-1.2) | 0.55 | 77 (1.4%) | 90 (1.6%) | 0.9 (0.6-1.2) | 0.31 | |
| | Entire Study Period (0-3 Years) | Osteopenia/Osteoporosis | 2,673 (25.9%) | 3,911 (37.8%) | 0.6 (0.5-0.6) | <0.001 | 1,382 (24.8%) | 2,104 (37.7%) | 0.5 (0.5-0.6) | <0.001 |
| | | Fractures | 834 (8.1%) | 876 (8.5%) | 0.9 (0.9-1.0) | 0.29 | 393 (7.0%) | 462 (8.3%) | 0.8 (0.7-1.0) | 0.01 |
| Urolithiasis | | 795 (7.7%) | 1,452 (14.0%) | 0.5 (0.5-0.6) | <0.001 | 398 (7.1%) | 756 (13.6%) | 0.5 (0.4-0.6) | <0.001 | |
| MDD | | 1,968 (19.0%) | 2,082 (20.1%) | 0.9 (0.9-1.0) | 0.05 | 888 (15.9%) | 1,098 (19.7%) | 0.8 (0.7-0.9) | <0.001 | |
| Anxiety Disorders | | 1,895 (18.3%) | 1,873 (18.1%) | 1.0 (0.9-1.1) | 0.69 | 916 (16.4%) | 963 (17.3%) | 0.9 (0.9-1.0) | 0.23 | |
| HTN | | 6,694 (64.8%) | 6,809 (65.9%) | 1.0 (0.9-1.0) | 0.09 | 3,485 (62.5%) | 3,742 (67.1%) | 0.8 (0.8-0.9) | <0.001 | |
| GERD | | 2,756 (26.7%) | 3,102 (30.0%) | 0.8 (0.8-0.9) | <0.001 | 1,354 (24.3%) | 1,647 (29.5%) | 0.8 (0.7-0.8) | <0.001 | |
| Malaise/Fatigue | | 2,210 (21.4%) | 2,566 (24.8%) | 0.8 (0.8-0.9) | <0.001 | 1,079 (19.3%) | 1,377 (24.7%) | 0.7 (0.7-0.8) | <0.001 | |
| Joint Pain/Myalgias | | 3,670 (35.5%) | 3,987 (38.6%) | 0.9 (0.8-0.9) | <0.001 | 1,860 (33.3%) | 2,132 (38.2%) | 0.8 (0.7-0.9) | <0.001 | |
| Constipation | | 1,361 (13.2%) | 1,522 (14.7%) | 0.9 (0.8-1.0) | 0.001 | 654 (11.7%) | 805 (14.4%) | 0.8 (0.7-0.9) | <0.001 | |
| Insomnia | | 940 (9.1%) | 888 (8.6%) | 1.1 (1.0-1.2) | 0.20 | 439 (7.9%) | 469 (8.4%) | 0.9 (0.8-1.1) | 0.30 | |
| Polyuria | | 1,124 (10.9%) | 1,332 (12.9%) | 0.8 (0.8-0.9) | <0.001 | 531 (9.5%) | 696 (12.5%) | 0.7 (0.7-0.8) | <0.001 | |
| Weakness | | 1,474 (14.3%) | 1,779 (17.2%) | 0.8 (0.7-0.9) | <0.001 | 730 (13.1%) | 933 (16.7%) | 0.7 (0.7-0.8) | <0.001 | |
| Abdominal Pain | | 2,334 (22.6%) | 2,565 (24.8%) | 0.9 (0.8-0.9) | <0.001 | 1,118 (20.0%) | 1,352 (24.2%) | 0.8 (0.7-0.9) | <0.001 | |

| | | | | | | | | | |
|--|------------|------------------|------------------|-------------------|------|-------------|-------------|-------------------|-------|
| | Headache | 1,303 (12.6%) | 1,357 (13.1%) | 1.0 (0.9- 1.0) | 0.26 | 612 (11.0%) | 714 (12.8%) | 0.8 (0.7- 0.9) | 0.003 |
| | Nausea | 889 (8.6%) | 983 (9.5%) | 0.9 (0.8- 1.0) | 0.02 | 429 (7.7%) | 490 (8.8%) | 0.9 (0.8- 1.0) | 0.04 |
| | Amnesia | 885 (8.6%) | 922 (8.9%) | 1.0 (0.9- 1.1) | 0.36 | 417 (7.5%) | 508 (9.1%) | 0.8 (0.7- 0.9) | 0.002 |
| | Gallstones | 431 (4.2%) | 471 (4.6%) | 0.9 (0.8- 1.0) | 0.17 | 218 (3.9%) | 242 (4.3%) | 0.9 (0.7- 1.1) | 0.25 |

Abbreviations: PHP, primary hyperparathyroidism; PTH, parathyroid hormone; MDD, major depressive disorder; HTN, hypertension; GERD, gastroesophageal reflux disease; CI, confidence interval

*Statistical significance defined as $P < 0.003$