Research Article

*For reprint orders, please contact: info@becaris.com*

Journal of **Comparative Effectiveness Research**

# Clinical and economic burden among older adults with acromegaly in the United States

Tiffany P Quock*[,1], Eunice Chang[2], Ashis K Das[2], Amanda Speller[2], Marian H Tarbox[2], Stacy K Rattana[1], Ingrid E Paulson[1] & Michael S Broder[2]

[1]Crinetics Pharmaceuticals, San Diego, CA 92121, USA

[2]ADVI Health, LLC, Washington, DC 20004, USA

*Author for correspondence: tquock@crinetics.com

**Aim:** To compare healthcare resource utilization (HCRU) and costs between older adults with and without acromegaly. **Materials & methods:** Using 2017–2022 100% Medicare Research Identifiable Files, we identified beneficiaries (≥65 years) with prevalent cases of acromegaly. A randomly selected claim with an acromegaly diagnosis was the index date. Beneficiaries were required to have continuous enrollment in Medicare fee-for-service and Part D for the 1-year post-index period (observation period). Beneficiaries with acromegaly were matched 1:1 (age, sex, race, US geographic region) to acromegaly-free beneficiaries (reference group). The beneficiaries in the reference group were assigned the same index date as their matched beneficiary with acromegaly and met the same enrollment criteria. Outcomes of interest, measured during the observation period, included all-cause and acromegaly-related HCRU and costs (adjusted to 2022 US dollars). **Results:** We identified 3491 beneficiaries with acromegaly and 3491 without acromegaly. The mean age was 73.1 years and the majority of beneficiaries were female and non-Hispanic White. Beneficiaries with acromegaly had more HCRU than those without acromegaly, including a greater proportion with hospitalizations (27.6 vs 14.9%), ED visits (31.8 vs 22.8%), use of skilled nursing facility care (7.3 vs 3.5%) and home health agency visits (18.1 vs 8.4%) ($p < 0.001$ for all). Total all-cause healthcare costs were higher among beneficiaries with acromegaly versus those without acromegaly ($45,830 vs $18,922, $p < 0.001$). The majority of beneficiaries with acromegaly (69.6%) did not have evidence of acromegaly treatment. **Conclusion:** Medicare beneficiaries with acromegaly have substantial HCRU and costs compared with controls without acromegaly; this indicates a high burden of illness which may be lessened by new and effective therapeutic options for those with acromegaly.

**Plain language summary: Burden & costs associated with acromegaly in older US adults**

**What is this article about?** There is little research on healthcare costs and healthcare resource utilization (HCRU) focused specifically on US Medicare beneficiaries diagnosed with acromegaly. We examined HCRU and costs among US Medicare beneficiaries with acromegaly compared with beneficiaries without acromegaly.

**What were the results?** In this retrospective, matched cohort analysis, we used Medicare claims data from the past to observe healthcare costs and utilization among beneficiaries with acromegaly and compared them to reference cases who did not have acromegaly. The reference cases were chosen so that their population characteristics matched the population characteristics of the beneficiaries diagnosed with acromegaly. Beneficiaries with acromegaly had higher rates of HCRU than reference cases without acromegaly. Total all-cause healthcare costs were more than double among beneficiaries with acromegaly relative to reference cases without acromegaly ($45,830 vs $18,922, $p < 0.001$). Most beneficiaries with acromegaly (69.6%) did not have evidence of acromegaly treatment.

**What do the results mean?** High rates of healthcare utilization and greater healthcare costs compared with references cases without acromegaly, along with the low proportion of beneficiaries with acromegaly treatment, indicate that there is still a need for more effective therapy options for beneficiaries with acromegaly.

First draft submitted: 20 May 2025; Accepted for publication: 24 June 2025; Published online: 8 July 2025

**Keywords:** acromegaly • burden • costs • healthcare utilization • matched analysis • Medicare

Acromegaly is a rare acquired endocrine disease associated with excessive production of growth hormone (GH), characterized by progressive somatic disfigurement and systemic manifestations [1]. The goals of acromegaly treatment include the normalization of GH and insulin-like growth factor 1 (IGF-1) levels and the resolution of tumor-induced mass effects, acromegaly-related symptoms and associated comorbidities [2]. Diagnosis of acromegaly usually occurs in the third or fourth decade of life [3]. Clinical diagnosis of acromegaly is often delayed for several reasons, including overlapping symptoms with other common conditions and the slow progression of symptoms [4–9]. This can be especially challenging in older adults due to symptoms that overlap with comorbidities associated with aging [10–12].

Delayed diagnosis and age at onset are factors that increase the risk of mortality; however, recent data suggest a reduction in acromegaly mortality due to improvements in diagnostic approaches, monitoring, surgical techniques and medical therapies [2,12–15]. These improvements, along with general increased life expectancy, are expected to lead to an increased prevalence of older patients with acromegaly [12,15–17]. Current management options for patients with acromegaly include pituitary surgery, medical therapy and radiation therapy. Medications for acromegaly treatment include somatostatin analogs (octreotide, lanreotide, pasireotide), dopamine agonists (cabergoline, bromocriptine) and pegvisomant.

It has also been shown that acromegaly can exacerbate the aging process by negatively impacting cognitive function, malnutrition risk, physical performance and mood [12,15,18] and that comorbidity burden is higher; thereby increasing burden in an older population. Acromegaly is associated with greater healthcare utilization and higher healthcare costs, but the real-world burden of acromegaly has not been examined in Medicare beneficiaries [19–21]. Current real-world evidence rarely focused on older adults, a population generally at higher risk for economic and disease-related burden and who are often underrepresented in clinical trials and commercial data [12,22–26]. Furthermore, published literature is limited by small sample sizes, limited considerations of healthcare costs, or did not include all treatment options such as surgery or oral octreotide (US FDA approved in 2020) [19–21,27]. A few international retrospective studies have examined clinical characteristics and disease management among older adults with acromegaly and found a higher comorbidity burden compared with younger adults and that acromegaly-related burden (e.g., cardiovascular) and an older age increase the risk of mortality; however, costs were not examined [11,17]. To fill this gap in US real-world literature, we utilized a large database that provides coverage to all US citizens who are at least 65 years old to quantify and compared healthcare resource utilization and costs among Medicare beneficiaries with and without acromegaly.

## Materials & methods

### Study design & data source

This retrospective cohort study examined the burden of acromegaly among Medicare beneficiaries in the US. The analysis used the five most recent years of available data (1 January 2017–31 December 2022) from the 100% Medicare Research Identifiable Files (RIFs). The RIF database is the most comprehensive Medicare database covering 100% of Medicare beneficiaries from all census regions and includes patient-level demographic, enrollment and fee-for-service administrative claims data across all places of service (e.g., emergency departments [ED], inpatient and outpatient facilities, skilled nursing and hospice facilities and home health agencies). The RIF database is an ideal data source for capturing older adults with rare diseases such as acromegaly as Medicare is the predominant health insurance provider to US citizens and qualifying permanent residents aged 65 years and older and also to those less than 65 years old who have other qualifying circumstances (e.g., have received disability benefits from Social Security for at least 24 months). This study received approval for full waiver of Health Insurance Portability and Accountability Act authorization from the Western Institutional Review Board.

### Patient identification

This study included Medicare beneficiaries who were at least 65 years old with existing or newly diagnosed acromegaly during the identification period (1 January 2017–31 December 2021). As our goal was to include patients at varying stages of disease, existing and newly diagnosed beneficiaries were included with prevalent

cases of acromegaly, defined as individuals diagnosed at any time in the past, including recent and long-standing diagnoses. An acromegaly diagnosis was based on having at least two medical claims for acromegaly (International Classification of Diseases, 10th Revision, Clinical Modification [ICD-10-CM] diagnosis code: E22.0) in any diagnosis field or at least one medical claim for an acromegaly diagnosis code in combination with one other claim for a pituitary tumor, pituitary surgery (hypophysectomy) or cranial stereotactic radiosurgery. In order to have a representative sample that reflects disease burden across various stages of the disease, a randomly selected claim with an acromegaly diagnosis was the index date. All beneficiaries were followed for 1 year from the index date (observation period). Beneficiaries were also required to have continuous enrollment in Medicare fee-for-service (FFS) and Part D (voluntary prescription drug coverage offered to Medicare beneficiaries by insurance companies and other private companies approved by Medicare [28]) during the 1-year observation period. To serve as reference cases, we identified an acromegaly-free reference group drawn from a 5% random sample of Medicare beneficiaries who lacked any diagnosis of acromegaly during the study period and matched 1:1 to patients with acromegaly beneficiaries based on the common cofounders age, sex, race and US geographic region. The acromegaly-free beneficiaries were assigned the same index date as the matched beneficiaries with acromegaly and met the same enrollment criteria.

### Study measures

We reported beneficiary age, sex, race and US geographic region at index. Disease burden was assessed during the observation period by measuring comorbidities, healthcare utilization and healthcare costs between beneficiaries with and without acromegaly. Comorbidity burden was measured by the Charlson Comorbidity Index and specific comorbidities of interest. All-cause and acromegaly-related (defined below) healthcare utilization included inpatient admissions, ED visits, office visits, use of therapies (i.e., somatostatin analogs, dopamine agonists, pegvisomant, radiation therapy; stratified by route of administration), use of laboratory and imaging tests (i.e., IGF-1, glucose tolerance, and GH tests and pituitary MRI), total healthcare costs, medical costs (inpatient hospitalization, ED service and non-ED outpatient services costs) and treatment costs. Acromegaly-related medical healthcare use and costs were estimated based on medical claims with acromegaly as any diagnosis. Costs were adjusted to 2022 US dollars using the medical component of the Consumer Price Index [29].

### Statistical analysis

Descriptive statistics were conducted to examine patient characteristics and healthcare utilization (all-cause and acromegaly-related). Means and standard deviations (SD) were used to summarize continuous variables. Frequencies and percentages were used to summarize categorical variables. All outcome measures for matched beneficiaries with acromegaly and acromegaly-free beneficiaries were compared using *t*-tests or Chi-square tests for continuous and categorical variables, respectively. All data transformations and statistical analyses were performed using SAS® version 9.4.

## Results

### Patient identification & demographics

We identified 5551 beneficiaries with existing or newly diagnosed acromegaly during the ID period (1 January 2017–31 December 2021). After excluding beneficiaries less than 65 years old and without Medicare (fee-for-service Part A/B and Part D) coverage during the 1-year observation period, 3491 beneficiaries with acromegaly remained (Figure 1). The final sample consisted of 3491 beneficiaries with acromegaly and 3491 acromegaly-free beneficiaries (reference group).

The mean (SD) age was 73.1 (6.3) years with the highest proportion of beneficiaries in the 65–74 age group (64.3%). More beneficiaries were female (53.0%), non-Hispanic White (82.6%) and from the South (32.0%) (Table 1). Beneficiaries with acromegaly had more comorbidity burden compared with beneficiaries without acromegaly (mean Charlson Comorbidity Index score: 3.2 vs 2.2, $p < 0.001$), including greater proportions of beneficiaries with musculoskeletal (47.7 vs 33.1%), cardiovascular (85.5 vs 74.8%) and endocrine/metabolic (83.6 vs 63.0%) comorbidities of interest ($p < 0.001$ for all) (Table 2).

### Healthcare utilization & costs

Beneficiaries with acromegaly had more healthcare utilization than beneficiaries without acromegaly, including a greater proportion with an inpatient hospitalization (27.6 vs 14.9%), ED visits (31.8 vs 22.8%), use of skilled

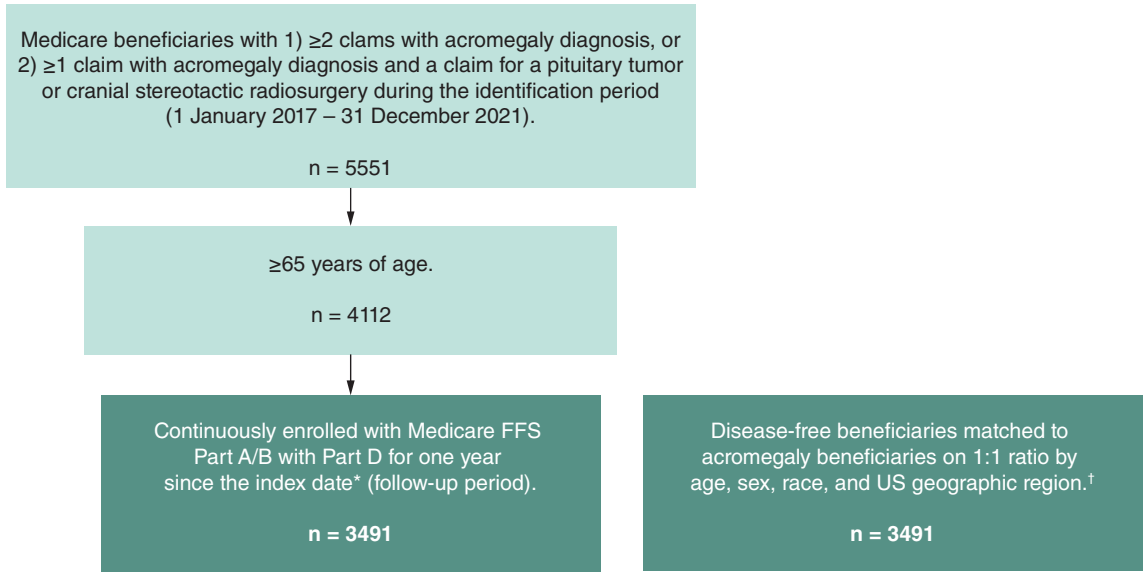


**Figure 1. Patient attrition.**
*A randomly selected claim with acromegaly diagnosis was the index date.
†Drawn from a 5% random sample of Medicare beneficiaries. Assigned the same index date as the matched acromegaly beneficiaries and met the same enrollment criteria.

**Table 1. Patient demographics.**

| | Acromegaly patients (n = 3491) | Matched disease-free references† (n = 3491) |
|---|---|---|
| **Age, year, mean (SD)** | 73.1 (6.3) | 73.1 (6.3) |
| 65–74, n (%) | 2244 (64.3%) | 2244 (64.3%) |
| 75–84 | 1026 (29.4%) | 1026 (29.4%) |
| 85+ | 221 (6.3%) | 221 (6.3%) |
| **Female, n (%)** | 1851 (53.0%) | 1851 (53.0%) |
| **Race, n (%)** | | |
| Asian/Pacific Islander | 89 (2.5%) | 89 (2.5%) |
| Black (or African–American) | 186 (5.3%) | 186 (5.3%) |
| Hispanic | 189 (5.4%) | 189 (5.4%) |
| Non-Hispanic White | 2883 (82.6%) | 2883 (82.6%) |
| Other | 44 (1.3%) | 44 (1.3%) |
| Unknown | 100 (2.9%) | 100 (2.9%) |
| **Region, n (%)** | | |
| Midwest | 878 (25.2%) | 878 (25.2%) |
| Northeast | 802 (23.0%) | 802 (23.0%) |
| South | 1116 (32.0%) | 1116 (32.0%) |
| West | 695 (19.9%) | 695 (19.9%) |
| **Year of index date, n (%)** | | |
| 2017 | 661 (18.9%) | 661 (18.9%) |
| 2018 | 642 (18.4%) | 642 (18.4%) |
| 2019 | 710 (20.3%) | 710 (20.3%) |
| 2020 | 674 (19.3%) | 674 (19.3%) |
| 2021 | 804 (23.0%) | 804 (23.0%) |

†Disease-free beneficiaries were drawn from a 5% random sample of Medicare beneficiaries and matched to acromegaly beneficiaries on a 1:1 ratio by age, sex, race and US geographic region. The disease-free controls were assigned with the same index date as the matched acromegaly beneficiaries and met the same enrollment criteria.
SD: Standard deviation.

Table 2. Comorbidities.

| | Acromegaly patients (n = 3491) | Matched disease-free references† (n = 3491) | p-value |
|---|---|---|---|
| **Charlson Comorbidity Index, mean (SD)** | 3.2 (3.0) | 2.2 (2.7) | <0.001 |
| 0, n (%) | 677 (19.4%) | 1205 (34.5%) | |
| 1 | 596 (17.1%) | 634 (18.2%) | |
| 2 | 503 (14.4%) | 483 (13.8%) | |
| 3+ | 1715 (49.1%) | 1169 (33.5%) | |
| **Musculoskeletal, n (%)** | 1665 (47.7%) | 1156 (33.1%) | <0.001 |
| Osteoarthritis | 1345 (38.5%) | 892 (25.6%) | <0.001 |
| Arthropathy/arthralgia/synovitis | 286 (8.2%) | 180 (5.2%) | <0.001 |
| Kyphosis and scoliosis | 49 (1.4%) | 22 (0.6%) | 0.001 |
| Vertebral fracture | 91 (2.6%) | 46 (1.3%) | <0.001 |
| Carpal tunnel syndrome | 109 (3.1%) | 70 (2.0%) | 0.003 |
| Myopathy/myalgia | 323 (9.3%) | 224 (6.4%) | <0.001 |
| **Cardiovascular, n (%)** | 2985 (85.5%) | 2613 (74.8%) | <0.001 |
| Hypertension | 2793 (80.0%) | 2473 (70.8%) | <0.001 |
| Cardiomyopathy | 245 (7.0%) | 138 (4.0%) | <0.001 |
| Cardiac hypertrophy | 336 (9.6%) | 150 (4.3%) | <0.001 |
| Congestive heart failure | 562 (16.1%) | 387 (11.1%) | <0.001 |
| Valvular heart disease | 765 (21.9%) | 445 (12.7%) | <0.001 |
| Cardiac dysrhythmia/arrhythmia | 1175 (33.7%) | 749 (21.5%) | <0.001 |
| **Endocrine/metabolic, n (%)** | 2917 (83.6%) | 2199 (63.0%) | <0.001 |
| Diabetes (including impaired glucose intolerance) | 1687 (48.3%) | 1086 (31.1%) | <0.001 |
| Obesity | 1235 (35.4%) | 856 (24.5%) | <0.001 |
| Galactorrhea | – ‡ | 0 (0.0%) | 0.157 |
| Conditions related to the female reproductive system§ | 29 (0.8%) | 27 (0.8%) | 0.788 |
| Impaired libido/impotence | 839 (24.0%) | 654 (18.7%) | <0.001 |
| Hypothyroidism | 1584 (45.4%) | 769 (22.0%) | <0.001 |
| **Chronic obstructive pulmonary disease, n (%)** | 517 (14.8%) | 495 (14.2%) | 0.455 |
| **Sleep apnea (obstructive and central), n (%)** | 1111 (31.8%) | 457 (13.1%) | <0.001 |
| **Solid tumor without metastasis, n (%)** | 2506 (71.8%) | 1202 (34.4%) | <0.001 |
| **Deficiency anemias, n (%)** | 645 (18.5%) | 395 (11.3%) | <0.001 |
| **Psychoses, n (%)** | 30 (0.9%) | 31 (0.9%) | 0.898 |
| **Depression, n (%)** | 799 (22.9%) | 581 (16.6%) | <0.001 |

†Disease-free beneficiaries were drawn from a 5% random sample of Medicare beneficiaries and matched to acromegaly beneficiaries on a 1:1 ratio by age, sex, race and US geographic region. The disease-free controls were assigned with the same index date as the matched acromegaly beneficiaries and met the same enrollment criteria.
‡Reported per CMS cell size suppression policy (<11).
§Conditions related to the female reproductive system include: postmenopausal bleeding, premenopausal menorrhagia, postmenopausal menorrhagia, excessive bleeding in the premenopausal period, other abnormal uterine and vaginal bleeding and other menstrual disorders.
CMS: Centers for Medicare & Medicaid Services; SD: Standard deviation.

nursing facility care (7.3 vs 3.5%), a home health agency (HHA) visit (18.1 vs 8.4%) and a higher number of mean office visits (20.2 vs 12.8) and non-ED outpatient visits (8.5 vs 4.8) ($p < 0.001$ for all) (Table 3). Total healthcare costs were higher among beneficiaries with acromegaly compared with those without ($45,830 vs $18,922, $p < 0.001$). Medical (non-outpatient pharmacy) costs accounted for $28,696 of total costs and of these, outpatient services (including durable medical equipment, HHA, office, ED and other outpatient facilities) were the largest contributor ($17,947) (Table 3).

The majority of beneficiaries with acromegaly (69.6%) did not have evidence of acromegaly treatment (medical, pituitary surgery or radiation therapy) (Table 4) during the 1-year observation period. Thirty percent of beneficiaries received acromegaly therapy and 17.2% were treated with somatostatin analogs (octreotide, lanreotide and pasireotide). Acromegaly-related inpatient hospitalization or ED visits were not common and only observed in 9.8% and 3.5% of beneficiaries with acromegaly, respectively; 5.1% of beneficiaries had an acromegaly-related

Table 3. All-cause healthcare utilization and costs.

| | Acromegaly patients (n = 3491) | Matched disease-free references† (n = 3491) | p-value |
|---|---|---|---|
| **Utilization** | | | |
| **Had an inpatient hospitalization, n (%)** | 963 (27.6%) | 521 (14.9%) | <0.001 |
| **Inpatient hospitalizations, n (%)** | | | |
| 0 | 2528 (72.4%) | 2970 (85.1%) | <0.001 |
| 1 | 628 (18.0%) | 327 (9.4%) | <0.001 |
| 2+ | 335 (9.6%) | 194 (5.6%) | <0.001 |
| Length of stay (days) among utilizers, mean (SD) | 8.1 (11.6) | 8.9 (15.2) | 0.281 |
| **Has an ED service, n (%)** | 1110 (31.8%) | 795 (22.8%) | <0.001 |
| **ED services, n (%)** | | | |
| 0 | 2381 (68.2%) | 2696 (77.2%) | <0.001 |
| 1 | 693 (19.9%) | 512 (14.7%) | <0.001 |
| 2 | 223 (6.4%) | 163 (4.7%) | <0.001 |
| 3+ | 194 (5.6%) | 120 (3.4%) | <0.001 |
| **Outpatient hospital service (non-ED), mean (SD)** | 8.5 (10.0) | 4.8 (6.7) | <0.001 |
| **Physician office visits, mean (SD)** | 20.2 (17.1) | 12.8 (13.2%) | <0.001 |
| **Any SNF care, n (%)** | 256 (7.3%) | 123 (3.5%) | <0.001 |
| **Any HHA visit, n (%)** | 633 (18.1%) | 293 (8.4%) | <0.001 |
| **Any hospice service, n (%)** | 37 (1.1%) | 24 (0.7%) | 0.095 |
| **Healthcare costs** | | | |
| **Total healthcare costs, mean (SD)** | $45,830 (60,846.0) | $18,922 (37,464.4) | <0.001 |
| Costs of medical claims, mean (SD) | $28,696 (41,887.1) | $14,871 (32,865.6) | <0.001 |
| Costs of inpatient services (including inpatient hospitalizations, SNF and hospice), mean (SD) | $10,749 (27,753.4) | $5888 (22,470.7) | <0.001 |
| Costs of inpatient hospitalizations, mean (SD) | $8618 (22,937.2) | $4647 (19,201.1) | <0.001 |
| Costs of outpatient services (including DME, HHA, office, ED and other outpatient facilities), mean (SD) | $17,947 (27,202.9) | $8982 (20,064.8) | <0.001 |
| Costs of ED visits, mean (SD) | $760 (2003.7) | $454 (1336.9) | <0.001 |
| Costs of non-ED outpatient services, mean (SD) | $17,187 (26,845.6) | $8529 (19,846.3) | <0.001 |
| Costs of outpatient hospital services (excluding ED visits), mean (SD) | $7967 (20,845.6) | $3133 (11,220.6) | <0.001 |
| Costs of office visits, mean (SD) | $5125 (13,514.3) | $3059 (14,208.9) | <0.001 |
| **Outpatient pharmacy costs, mean (SD)** | $17,134 (42,912.6) | $4051 (15,118.9) | <0.001 |

†Disease-free beneficiaries were drawn from a 5% random sample of Medicare beneficiaries and matched to acromegaly beneficiaries on a 1:1 ratio by age, sex, race and US geographic region. The disease-free controls were assigned with the same index date as the matched acromegaly beneficiaries and met the same enrollment criteria.
DME: Durable medical equipment; ED: Emergency department; HHA: Home health agency; SD: Standard deviation; SNF: Skilled nursing facility.

HHA visit. Beneficiaries with acromegaly had a mean (SD) number of endocrinologist office visits of 1.7 (3.0) (Table 4). Acromegaly therapy costs ($15,487) accounted for the majority of the mean total acromegaly-related healthcare costs ($19,889) (Table 4).

## Discussion

Medicare beneficiaries with acromegaly use significantly more healthcare services and have higher healthcare costs than beneficiaries without acromegaly. Skilled nursing facility care, HHA visits, and non-ED outpatient visits are around two-times more common among beneficiaries with acromegaly than among those without acromegaly. Total all-cause healthcare costs are more than double among Medicare beneficiaries with acromegaly compared with beneficiaries without acromegaly. Outpatient pharmacy costs are the largest contributor to the cost differences between those with and without acromegaly.

Comorbidity burden was higher among Medicare beneficiaries with acromegaly than what has been published in commercially insured acromegaly populations [20]. This result is not surprising as adults older than 65 years old typically have higher rates of comorbidities compared with adults less than 65 years old [30]. Additionally, we observed that older patients with acromegaly have higher rates of comorbidities relative to a matched ref-

Table 4. Acromegaly-related healthcare utilization and costs†.

| | Acromegaly patients (n = 3491) |
|---|---|
| **Utilization** | |
| **Laboratory or imaging test, n (%)** | 2560 (73.3%) |
| IGF-1 test | 2140 (61.3%) |
| Glucose tolerance test | 406 (11.6%) |
| GH test | 1020 (29.2%) |
| Pituitary MRI | 1043 (29.9%) |
| **Acromegaly therapy (medical, pituitary surgery and radiation therapy), n (%)** | 1063 (30.4%) |
| Somatostatin analogs (octreotide, lanreotide, pasireotide) | 599 (17.2%) |
| Dopamine receptor agonists (cabergoline, bromocriptine) | 369 (10.6%) |
| GH receptor antagonist (pegvisomant) | 141 (4.0%) |
| Pituitary surgery (hypophysectomy) | 115 (3.3%) |
| Radiation therapy | 26 (0.7%) |
| **Had an acromegaly-related inpatient hospitalization, n (%)** | 342 (9.8%) |
| **Acromegaly-related inpatient hospitalizations, n (%)** | 3149 (90.2%) |
| 0 | |
| 1 | 295 (8.5%) |
| 2+ | 47 (1.3%) |
| Length of stay (days) among utilizers, mean (SD) | 5.3 (6.0) |
| **Has an acromegaly-related ED service, n (%)** | 123 (3.5%) |
| **Acromegaly-related outpatient hospital services (excluding ED visits), mean (SD)** | 1.7 (3.4) |
| **Acromegaly-related office visits, mean (SD)** | 2.3 (3.7) |
| **Endocrinologist office visits, mean (SD)** | 1.7 (3.0) |
| **Any acromegaly-related SNF care, n (%)** | 60 (1.7%) |
| **Any acromegaly-related HHA visit, n (%)** | 179 (5.1%) |
| **Any acromegaly-related hospice service, n (%)** | – ‡ |
| **Healthcare costs** | |
| **Total acromegaly-related healthcare costs, mean (SD)** | $19,889 (42,523.4) |
| Costs of acromegaly-related non-therapy medical claims | $4401 (12,956.1) |
| Costs of acromegaly-related inpatient services | $2255 (11,669.1) |
| Costs of acromegaly-related inpatient hospitalizations | $1885 (10,780.1) |
| Costs of acromegaly-related outpatient services | $1468 (3948.6) |
| Costs of acromegaly-related ED visits | $81 (599.4) |
| Costs of non-ED acromegaly-related outpatient services | $1387 (3840.3) |
| Costs of non-ED acromegaly-related outpatient hospital services | $552 (3113.5) |
| Costs of acromegaly-related office visits | $374 (1393.8) |
| **Acromegaly therapy costs, mean (SD)** | $15,487 (40,040.8) |
| Somatostatin analogs costs | $9696 (26,113.2) |
| Dopamine receptor agonists costs | $144 (636.2) |
| GH receptor antagonist costs | $4772 (27,977.7) |
| Radiation therapy costs | $52 (753.5) |
| Pituitary surgery costs | $824 (4791.7) |

†Medical claims with acromegaly diagnosis in any diagnosis field.
‡Reported per CMS cell size suppression policy (<11).
CMS: Centers for Medicare & Medicaid Services; ED: Emergency department; GH: Growth hormone; HHA: Home health agency; IGF-1: Insulin-like growth factor 1; SD: Standard deviation; SNF: Skilled nursing facility.

erence cohort of older patients without acromegaly. Broder *et al.* found that acromegaly-related complications (i.e., colon neoplasms, musculoskeletal, cardiovascular disease, sleep apnea and hypopituitarism) and cardiovascular risk factors (i.e., diabetes, hypertension, hypertriglyceridemia) were associated with statistically significant increases in overall healthcare costs and odds of hospitalization and emergency department visits [31]. Address-

ing symptoms and disease progression through more effective treatment options could be an area of potential cost-savings.

Overall, the rates of HCRU and costs found in the current work were similar to published real-world studies. Published HCRU ranged from 4.0–34.6% of patients with inpatient hospitalization and 0.6–28.3% with ED visits [19–21]; however, these studies used commercial data and did not examine burden among Medicare beneficiaries. The only published article which analyzed all-cause and acromegaly-related utilization and costs reported that in a commercially insured population, 18.8% of patients had acromegaly-related inpatient hospitalization and 1.8% had acromegaly-related ED visits [20], comparable to what we found in the current study (9.8 and 3.5%, respectively).

There is some potential for statistically significant differences between patients with acromegaly and the disease-free references to be false positives due to our reporting of multiple hypothesis tests. However, most of the outcomes tested were found to be significant at $p < 0.001$; therefore, it is unlikely that the significance of those findings would change following the implementation of a multiple comparisons correction method. Outcomes for which lower p-values are reported should be interpreted with additional caution as a p-value adjustment for those outcomes is more likely to impact the study's findings.

The proportion of patients with pituitary surgery in the current study (3.3%) was lower than in previous claims-based analyses (5.3–31.8%) [20,31,32]. Rates of surgery in claims-based analyses, particularly those conducted in the US setting, are lower than reported in medical registries (92.0–92.7%) or patient surveys (71–81%) because claims data rarely cover the lifetime medical history of a patient [18,33,34]. The current study analyzed Medicare claims data and reported the proportion of prevalent acromegaly cases among Medicare beneficiaries who had surgery during a 1-year observation period. Among previous claims-based analyses, differences in the observed proportion of patients who received pituitary surgery may be attributable to differences in the studies' designs. First, previous studies included patients under the age of 65 and patients who are 65 years old or older only make up about 10% of those cohorts [20,31,32]. Older patients are likely to have different rates of surgery compared with younger patients due to patient preferences for surgery and more contraindications for surgery among older patients relative to younger patients [35,36]. Second, in the current study, a randomly selected claim with an acromegaly diagnosis was used as the index date over a 5-year identification period; therefore, the current study's cohort is composed of patients in various states of the acromegaly disease course. One strength of the current study's design is that it observed the pituitary surgery rate for Medicare beneficiaries diagnosed with acromegaly during 1 year across the full spectrum of the disease course. Conversely, in the studies authored by Broder *et al.* and Burton *et al.* the first observed acromegaly diagnosis was used as the index date and their cohorts are biased toward patients who are both younger (due to their patient cohorts which contains patients from 1 year old to 65+ years old) and earlier in the acromegaly disease course (due to their study protocols which selected the first observed diagnosis as the index date) [31,32]. Therefore, Broder *et al.* and Burton *et al.* were more likely to observe surgeries under their study designs relative to the current study design [31,32].

Medicare beneficiaries without surgery may also have had milder disease, which is not uncommon in older patients with acromegaly [12,17,37]. Lower rates of surgery in our cohort relative to younger cohorts are in line with conservative disease management practices related to the documented higher risk of mortality and poor post-surgery outcomes in an older population [38,39]. Ceccato *et al.* compared acromegaly surgical rates, using medical records from an endocrinology unit in Italy, among patients for whom the age of onset was less than 65 years old and those 65 years and older and found more than double the proportion of patients with surgery in the younger age group (86 vs 31%) [17]. As this published source using data other than claims also shows lower rates of surgery among older adults, it is unlikely that the current study's lower rates were due to missing data. Additionally, because all of the patients in this study can have their healthcare reimbursed by Medicare, it is unlikely that beneficiaries would have paid for surgery out-of-pocket and any surgery reimbursed by Medicare was available in the data used in the current study. New medical therapies may be especially valuable for maintaining disease control among older patients with acromegaly for whom surgical intervention is less common.

Similar to the current study, a high rate of nontreatment was also seen in published sources, ranging from 55.2% and 49.1% of patients without treatment [20,32]. Beneficiaries who were not on medications during the observation period may have acromegaly that is in remission, had a surgery that successfully reduced IGF-1 and GH levels, or discontinued therapy due to cost, healthcare barriers or patient dissatisfaction with current treatment options [40]. For example, Medicare beneficiaries with mild disease may have opted out of current available treatment due to preferred route of administration (e.g., preferred an oral medication over an injectable medication) or avoidance of adverse

events associated with available treatments [12,41]. Studies show that 58–81% of patients with acromegaly have disease recurrence following medication discontinuation [42,43]. Furthermore, other studies have linked treatment dissatisfaction with low treatment adherence [44,45]. Future studies focusing on treatment satisfaction among older patients with acromegaly and treatment patterns and the proportion of older patients who achieve biochemical control and symptom management with or without treatment could provide further insight into the high rates of nontreatment.

The current study's total costs (all-cause and acromegaly-related) were comparable to those published in previous studies using older commercial data, which ranged from $24,900 to $48,341 [19,20,31,32,42,43]. Placzek *et al.* reported acromegaly-related total costs (medical + pharmacy) of $14,470 (inflation-adjusted to 2023 USD), slightly less than the $19,889 found in the current study. The main driver of the difference between that cost and the current study appears to be related to therapy costs, as Placzek *et al.* reported prescription (pharmacy) costs of $8158 (inflation-adjusted to 2023 USD) compared with the $15,487 we found; additionally, our therapy costs also included surgery and radiation [20].

## Limitations

This retrospective cohort study uses claims data to estimates of healthcare utilization and costs associated with acromegaly in US Medicare beneficiaries 65 years and older. Patient identification was based on diagnosis and procedure codes, rather than being clinically validated, so misdiagnosis of acromegaly was possible. Results from common acromegaly diagnostic testing, such as IGF-1 serum or pituitary MRI, are not available in claims data. Using a linked data source, such as linked electronic health records (EHR) and claims data, may offer additional and valuable clinical detail [44–50]. However, linked EHR and claims data can be limited in their usefulness due to variations in data quality and completeness based on differences in data structure and collection methods, terminology, and definitions across providers, sites and systems [44,45,47,48,51]. Additionally, while lab data can be found in linked EHR and claims data, it can still be limited in its availability and usefulness due to differences in the lab tests and codes used by different local laboratories and a lack of consistency in how and when results are recorded and interpreted [45,49,51]. Sample size, which was a key consideration in the current study as acromegaly is a rare disease, is another potential limiting factor in the usefulness of linked EHR and claims data [44,45,49]. As described earlier, Medicare RIFs are an ideal, large data source for capturing older adults with rare diseases such as acromegaly due to wide coverage in the US, and the methodology for patient identification used in the current study has been utilized in other published work [31,32]. While a 1-year observation/follow-up period is a commonly used time frame in real-world studies [17,19,20,43], restricting the analysis to a 1-year time frame limits the study's ability to inform whether beneficiaries were ever on any medications. However, 1-year evaluations of HCRU and costs provide valuable insights for patients, physicians, and payers and this information is relevant for budgeting, staffing and resource allocation for each stakeholder. As this study relied on insurance claims for services provided, undiagnosed patients or patients not seeking acromegaly-related care would not have been captured. This could have resulted in underestimated utilization and costs. Additionally, we only measured direct healthcare costs and did not examine indirect healthcare costs that may add to the burden among older adults with acromegaly, such as loss of productivity, caregiver burden and reduced quality of life. Lastly, results may not be generalizable to different populations with acromegaly, such as those lacking healthcare coverage and patients under the age of 65 years. Results may also not be generalizable to beneficiaries with incident cases of acromegaly as the cohort included patients at varying stages of disease progression.

## Conclusion

Medicare beneficiaries with acromegaly have substantial healthcare resource use and costs compared with controls without acromegaly. The higher rates of utilization, costs and comorbidities among beneficiaries with acromegaly compared with their counterparts without acromegaly indicates a need for additional effective therapeutic options for patients with acromegaly. Effective disease management, through biochemical control and symptom alleviation, may reduce the utilization and cost burden associated with acromegaly. Future studies examining the impact of treatment choices and patterns on utilization and costs could provide more insight into this unmet need.

## Summary points

- Acromegaly can exacerbate the aging process in older adults.
- There is limited real-world data estimating the burden associated with acromegaly in older adults.
- This retrospective cohort study used 2017–2022 data from the 100% Medicare Research Identifiable Files to compare healthcare utilization and costs between Medicare beneficiaries with acromegaly and matched disease-free references without acromegaly.
- The final study sample included 3491 beneficiaries with acromegaly and 3491 beneficiaries without acromegaly, and the majority of patients were female and non-Hispanic White.
- Beneficiaries with acromegaly had more healthcare utilization and higher costs compared with beneficiaries without acromegaly, including more than double the total healthcare costs ($45,830 vs $18,922, $p < 0.001$).
- The majority of beneficiaries with acromegaly did not have evidence of acromegaly treatment during the 1-year observation period.
- Among the 30.4% of beneficiaries with acromegaly treatment, somatostatin analogs were the most common treatment (17.2% of beneficiaries with acromegaly treatment).
- The higher rate of utilization and greater costs among beneficiaries with acromegaly compared with beneficiaries without acromegaly indicates an unmet need among older adults with acromegaly.

### Author contributions

TP Quock, SK Rattana, IE Paulson: Acquisition of data; design of the work; interpretation of data; revising the work for important intellectual content; final approval. E Chang, AK Das, A Speller, MH Tarbox, MS Broder: Design of the work; analysis of data; interpretation of data; drafting and revising the work for important intellectual content; final approval.

### Financial disclosure

Funding for this study and publication-related fees was received from Crinetics Pharmaceuticals.

### Competing interests disclosure

TP Quock, SK Rattana, IE Paulson are employees of and hold stock in Crinetics Pharmaceuticals, Inc. at the time of this study. At the time this research was conducted, E Chang, AK Das, A Speller, MH Tarbox and MS Broder were employees of Partnership for Health Analytic Research, LLC (now ADVI Health), which was paid by Crinetics to perform the research described in this manuscript. PHAR also discloses financial relationships with the following commercial entities outside of the submitted work: Abbvie, Akcea, Amgen, Astellas, AstraZeneca, Delfi Diagnostics, Dompe, Exact Sciences Corporation, Genentech, Gilead, GRAIL, Ionis, Janssen, Nobelpharma, Novartis, Pfizer, Recordati, Regeneron and Sanofi US Services. The authors have no other competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript apart from those disclosed.

### Writing disclosure

No funded writing assistance was utilized in the production of this manuscript.

### Ethical conduct of research

This study received approval for full waiver of Health Insurance Portability and Accountability Act (HIPAA) authorization from the Western Institutional Review Board.



## References

Papers of special note have been highlighted as: • of interest

1. Orphanet. Acromegaly (2024). Available at: https://www.orpha.net/en/disease/detail/963
2. Ershadinia N, Tritos NA. Diagnosis and treatment of acromegaly: an update. *Mayo Clin. Proc.* 97(2), 333–346 (2022).
3. Adigun OO, Nguyen M, Fox TJ, Anastasopoulou C. Acromegaly. In: *StatPearls*. StatPearls Publishing, FL, USA (2024).
4. Chanson P, Salenave S. Acromegaly. *Orphanet J. Rare Dis.* 3(1), 17 (2008).

5. Chanson P, Salenave S, Kamenicky P, Cazabat L, Young J. Acromegaly. *Best Pract. Res. Clin. Endocrinol. Metab.* 23(5), 555–574 (2009).
6. Melmed S. Acromegaly. *N. Engl. J. Med.* 355(24), 2558–2573 (2006).
7. Esposito D, Ragnarsson O, Johannsson G, Olsson DS. Prolonged diagnostic delay in acromegaly is associated with increased morbidity and mortality. *Eur. J. Endocrinol.* 182(6), 523–531 (2020).
8. Siegel S, Streetz-van der Werf C, Schott JS, Nolte K, Karges W, Kreitschmann-Andermahr I. Diagnostic delay is associated with psychosocial impairment in acromegaly. *Pituitary* 16(4), 507–514 (2013).
9. Wang K, Guo X, Yu S *et al.* Patient-identified problems and influences associated with diagnostic delay of acromegaly: a nationwide cross-sectional study. *Front. Endocrinol.* 12, 704496 (2021).
10. Pekic DS, Stojanovic M, Doknic M *et al.* Acromegaly in the elderly: additional challenges in timely recognizing. *Endocr. Abstr.* 90, P426 (2023).

- **Diagnosis of acromegaly in older adults may be challenging and delay can occur due to milder symptoms overlapping with aging and comorbidities.**

11. Gasco V, Prencipe N, Cuboni D *et al.* Diagnostic delay, older age, and hormonal levels at diagnosis affect disease burden and mortality in acromegaly. *J. Endocrinol. Invest.* 48(4), 919–929 (2024).

- **This retrospective analysis of patients treated at an Italian Neuroendocrinology clinic found that older age was associated with greater cardiometabolic burden, mortality, and longer diagnostic delay.**

12. Jallad RS, Bronstein MD. Acromegaly in the elderly patient. *Arch. Endocrinol. Metab.* 63(6), 638–645 (2020).
13. Tritos NA, Mattsson AF, Vila G *et al.* All-cause mortality in patients with acromegaly treated with pegvisomant: an ACROSTUDY analysis. *Eur. J. Endocrinol.* 182(3), 285–292 (2020).
14. Găloiu S, Toma I-D, Tănasie DI *et al.* High mortality risk among women with acromegaly still persists. *Front. Endocrinol.* 15, 1348972 (2024).
15. Gagliardi I, Chiloiro S, Vallillo M *et al.* Multidimensional geriatric evaluation in acromegaly: a comparative cross-sectional study. *BMC Geriatr.* 21(1), 598 (2021).
16. Yamamoto N, Urai S, Fukuoka H *et al.* The effect of aging on quality of life in acromegaly patients under treatment. *Front. Endocrinol.* 13, 819330 (2022).
17. Ceccato F, Barbot M, Lizzul L *et al.* Clinical presentation and management of acromegaly in elderly patients. *Horm. Athens Greece* 20(1), 143–150 (2021).

- **This retrospective study of medical records found that elderly patients with acromegaly are not uncommon and surgery is less common among patients diagnosed at 65 years and older compared with those less than 65 years of age.**

18. Hatipoglu E, Yuruyen M, Keskin E *et al.* Acromegaly and aging: a comparative cross-sectional study. *Growth Horm. IGF Res.* 25(1), 47–52 (2015).
19. Ribeiro-Oliveira A, Brook RA, Munoz KA *et al.* Burden of acromegaly in the United States: increased health services utilization, location of care, and costs of care. *J. Med. Econ.* 24(1), 432–439 (2021).

- **This retrospective analysis using a US employer database found that total costs were five-fold higher in patients with acromegaly compared to matched references; however, this study was conducted before the US FDA approval of octreotide and did not focus on older adults.**

20. Placzek H, Xu Y, Mu Y, Begelman SM, Fisher M. Clinical and economic burden of commercially insured patients with acromegaly in the United States: a retrospective analysis. *J. Manag. Care Spec. Pharm.* 21(12), 1106–1112 (2015).
21. Fleseriu M, Barkan A, Brue T *et al.* Treatment patterns, adherence, persistence, and health care resource utilization in acromegaly: a real-world analysis. *J. Endocr. Soc.* 7(10), bvad104 (2023).

- **This study used administrative claims data from MarketScan (2010–2022) and found that patient demographic characteristics are associated with treatment adherence, persistence and dosing patterns.**

22. Lau SWJ, Huang Y, Hsieh J *et al.* Participation of older adults in clinical trials for new drug applications and biologics license applications from 2010 through 2019. *JAMA Netw. Open* 5(10), e2236149 (2022).
23. Marum RJ. Underrepresentation of the elderly in clinical trials, time for action. *Br. J. Clin. Pharmacol.* 86(10), 2014–2016 (2020).
24. Merative. *MarketScan Research Databases for life sciences research*. Merative, MI, USA (2022).
25. Herrera AP, Snipes SA, King DW, Torres-Vigil I, Goldberg DS, Weinberg AD. Disparate inclusion of older adults in clinical trials: priorities and opportunities for policy and practice change. *Am. J. Public Health* 100(Suppl. 1), S105–S112 (2010).
26. Biagetti B, Iglesias P, Villar-Taibo R *et al.* Factors associated with therapeutic response in acromegaly diagnosed in the elderly in Spain. *Front. Endocrinol.* 13, 984877 (2022).
27. Daniel CP, Wagner MJ, Borne GE *et al.* Acromegaly: pathophysiological considerations and treatment options including the evolving role of oral somatostatin analogs. *Pathophysiol. Off. J. Int. Soc. Pathophysiol.* 30(3), 377–388 (2023).
28. US Centers for Medicare and Medicaid Services. What's Medicare drug coverage (Part D)? (2025). Available at: https://www.medicare.gov/health-drug-plans/part-d

29. U.S. Bureau of Labor Statistics, Division of Consumer Prices and Price Indexes. Consumer Price Index (2021). Available at: https://www.bls.gov/cpi/
30. Adams ML. Differences between younger and older US adults with multiple chronic conditions. *Prev. Chronic. Dis.* 14, E76 (2017).
31. Broder MS, Neary MP, Chang E, Cherepanov D, Katznelson L. Treatments, complications, and healthcare utilization associated with acromegaly: a study in two large United States databases. *Pituitary* (2013).

- **This real-world evidence study assessed the burden of acromegaly by reporting the additional healthcare resource utilization and costs associated with complications of the disease.**

32. Burton T, Le Nestour E, Bancroft T, Neary M. Real-world comorbidities and treatment patterns of patients with acromegaly in two large US health plan databases. *Pituitary* 16(3), 354–362 (2013).

- **This real-world evidence study found lower than expected rates of acromegaly treatment, considering that remission rates from surgery alone remain low.**

33. Pennlund A, Esposito D, Bontell TO *et al.* Long-term clinical outcome of 103 patients with acromegaly after pituitary surgery. *Pituitary* 28(2), 33 (2025).
34. Salvatori R, Woodmansee WW, Molitch M, Gordon MB, Lomax KG. Lanreotide extended-release aqueous-gel formulation, injected by patient, partner or healthcare provider in patients with acromegaly in the United States: 1-year data from the SODA registry. *Pituitary* 17(1), 13–21 (2014).
35. Marquez Y, Tuchman A, Zada G. Surgery and radiosurgery for acromegaly: a review of indications, operative techniques, outcomes, and complications. *Int. J. Endocrinol.* 2012, 386401 (2012).
36. De Roo AC, Vitous CA, Rivard SJ *et al.* High-risk surgery among older adults: not-quite shared decision-making. *Surgery* 170(3), 756–763 (2021).
37. Bogusławska A, Gilis-Januszewska A, Godlewska M, Nowak A, Starzyk J, Hubalewska-Dydejczyk A. Gender and age differences among patients with acromegaly. *Pol. Arch. Intern. Med.* (2022).
38. Freda PU, Bruce JN. Surgery: risks of pituitary surgery in the elderly. *Nat. Rev. Endocrinol.* 6(11), 606–608 (2010).
39. Puchner MJA, Knappe UJ, Lüdecke DK. Pituitary surgery in elderly patients with acromegaly. *Neurosurgery* 36(4), 677–684 (1995).
40. Liu S, Xu Y, Begelman SM, Shi L. Barriers to treatment adherence associated with acromegaly in the United States: provider's perspective. *Value Health* 18(3), A64 (2015).
41. Ogedegbe OJ, Cheema AY, Khan MA *et al.* A comprehensive review of four clinical practice guidelines of acromegaly. *Cureus* 14(9), e28722 (2022).
42. Yuen KCJ, Munoz KA, Brook RA *et al.* Health benefit costs and absenteeism among employed patients with acromegaly. *Endocr. Pract.* 27(10), 1034–1039 (2021).
43. Chuang C-C, Bhurke S, Chen S-Y, Dinet J, Brulais S, Gabriel S. Treatment patterns and economic burden in patients treated for acromegaly in the USA. *Drugs – Real World Outcomes* 2(3), 299–309 (2015).
44. Sentinel Community Building and Outreach Center (CBOC). Strengths and limits of claims and EHR-based data sources. *Sentinel Initiative.*
45. West SL, Johnson W, Visscher W, Kluckman M, Qin Y, Larsen A. The challenges of linking health insurer claims with electronic medical records. *Health Informatics J.* 20(1), 22–34 (2014).
46. Verana Health. Strengths and limitations of real-world data from electronic health records and claims, and the value of combining data from these sources to inform research. *Verana Health* (2025).
47. NashBio. Claims Data vs EHRs: Distinct but United in Real-World Research (2023). Available at: https://nashbio.com/blog/ehr/claims-data-vs-ehrs/
48. Swaleh R, McGuckin T, Campbell-Scherer D, Setchell B, Senior P, Yeung RO. Real world challenges in integrating electronic medical record and administrative health data for regional quality improvement in diabetes: a retrospective cross-sectional analysis. *BMC Health Serv. Res.* 23(1), 1 (2023).
49. LaBrec PA. *Linking healthCAre claims and electronic health records (EHR) for patient management – Diabetes Case Study*. 3M Health Information Solutions, CA, USA (2014).
50. Eisinger-Mathason TSK, Leshin J, Lahoti V, Fridsma DB, Mucaj V, Kho AN. Data linkage multiplies research insights across diverse healthcare sectors. *Commun. Med.* 5(1), 58 (2025).
51. Ehrenstein V, Kharrazi H, Lehmann H, Overby Taylor C. Obtaining data from electronic health records. In: *Tools and Technologies for Registry Interoperability, Registries for Evaluating Patient Outcomes: A User's Guide (Volume Addendum 2 (3rd Edition))*. Agency for Healthcare Research and Quality, MD, USA (2019).