US Growth Hormone Use in the Idiopathic Short Stature Era: Trends in Insurer Payments and Patient Financial Burden

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Objective: To investigate trends in prevalence and expenditures of growth hormone (GH) use by US youth in the last 15 years, a period during which the US Food and Drug Administration (FDA) approved GH treatment of idiopathic short stature (ISS), and insurers imposed greater barriers to GH treatment reimbursements.

Design: With the use of 2001 to 2016 OptumInsight commercial claims data, we analyzed trends in claims of GH drugs among beneficiaries aged 0 to 18 years (n = 38,857 beneficiaries receiving GH). Outcome measures included annual prevalence of GH claims and annual total insurer and total patient payments for GH claims. Tests were used for linear time trends in outcomes. The percentage of beneficiaries switching GH brands also was calculated.

Results: The number of members with GH claims per 10,000 beneficiaries under age 18 rose steadily from 5.1 in 2001 to 14.6 in 2016, without a dramatic change around 2003, the ISS approval date. Mean total GH expenditures decreased (~26% in constant dollars), as did the estimated insurance paid amount (~28%). However, mean total patient spending increased by 163%. Beneficiaries switching GH brands in the year ranged from 1.4% to 3.6% in 2001 to 2007 and from 5.1% to 8.8% after, with 25.6% switching in 2009 and 13.9% switching in 2015.

Conclusions: The FDA ISS approval was not a watershed event in the steady increase in GH use by US youth. Progressive restrictions on coverage and formulary preference coverage strategies appear to have succeeded in lowering total expenditures and insurer burden of GH treatment per beneficiary. However, those savings were not passed on to patients who bore greater burdens financially and from brand switches.

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Abbreviations: FDA, US Food and Drug Administration; GH, growth hormone; ISS, idiopathic short stature.
In 2003, the US Food and Drug Administration (FDA) approved growth hormone (GH) treatment of idiopathic short stature (ISS), expanding potential eligibility for GH treatment from 1:3500 children with GH deficiency [1] to the shortest 1.2% of the US population [2]. Based on the 74,181,467 population under age 18 years counted in the 2010 US Census, that translates to increasing potential GH eligibility from an estimated 21,000 youth with GH deficiency to ~890,000 youth with height meeting the ISS criterion, for an increment of ~869,000 more potential GH recipients nationally [3]. ISS was the first FDA indication that emphasized height rather than underlying pathology as the qualifying criterion for treatment, and GH became a paradigm of “expansive biotechnology,” wherein a biomedical technology originally designed for treatment of disease (GH deficiency) expanded, with the encouragement of physicians and support of industry, into treatment of conditions that blur the boundary between disease and variation [4].

In response, over the last dozen years, the insurance industry has been instituting progressive restrictions on coverage for GH treatment. Insurance providers adopted formulary preference-coverage strategies as a cost-containing measure. Because the preferred brand may change when patients change their insurance provider or when insurance providers renegotiate their contracts with the various GH manufacturers, the formulary preference strategy may result in brand switches during the long-term course of pediatric GH treatment, sometimes with untoward consequences [5]. More recently, many insurance providers instituted more stringent coverage rules, including adoption of plan-specific criteria more stringent than those recommended by the guidelines of the Pediatric Endocrine Society for treatment of GH deficiency [6] and denial of any coverage for GH treatment of ISS.

Thus, we sought to investigate how the prevalence of GH use by US youth changed in the last 15 years, focusing on the date of FDA ISS approval and general secular trends in insurer payments and patient spending, as insurers imposed greater barriers to GH reimbursements. We also examined trends in GH brand switching.

1. Materials and Methods

A. Data

We used 2001 to 2016 OptumInsight administrative claims data (Clinformatics DataMart™ 7.0, 2017; Optum, Eden Prairie, MN), which covers an annual 15 to 18 million individuals enrolled in US commercial health plans. OptumInsight is a large health care commercial claims database, widely used in health services research [7]. With diverse population coverage in all 50 states, the database is considered to be representative of the national commercially insured population.

The analytic sample consisted of beneficiaries aged 0 to 18 years with insurance coverage for 6 or more months and had at least one claim for GH that year (n = 38,857). GH drugs were identified as those with the active ingredient somatropin and included the branded drugs Genotropin, Humatrope, Norditropin, Nutropin, Saizen, and Tev-Tropin and the biosimilars Omnitrope and Zomacton.

B. Outcomes

As a prevalence measure, we calculated the annual number of beneficiaries with at least one GH drug claim per 10,000 beneficiaries under age 18 years. We examined sex, race/ethnicity (white/black/Asian; Hispanic/non-Hispanic), and age composition of beneficiaries with GH claims.

For confidentiality reasons, Optum does not report the actual insurer paid amount but averages allowed payments across health plans and provider contracts. We used this standardized allowed payment as an estimated measure of the insurer paid amount. As a measure of patient spending, we computed annual total patient payments for coinsurance, copayment, dispensing fee, and deductible associated with GH claims for each beneficiary.
Total GH spending was calculated as the sum of the estimated insurer paid amount and total patient payments. Because of the long time frame covered, we computed payments in both nominal dollars and in constant dollars, deflating nominal amounts by the Consumer Price Index to 2004 dollars [8].

To determine switching frequency, we calculated the percentage of members with GH claims whose GH brand was switched at least once in that year.

C. Statistical Analysis

Descriptive analyses were conducted in graphical and tabular form. t Tests were used to test for linear time trends in prevalence, GH patient demographics, and financial burden.

2. Results

A. Traits of GH Recipients

The number of members with GH claims per 10,000 beneficiaries under age 18 years rose steadily from 5.1 in 2001 to 14.6 in 2016 (P < 0.001) without a dramatic change around 2003, the ISS approval date (Fig. 1). To put these rates in perspective, the estimated prevalence of GH deficiency corresponds to 2.857 per 10,000 [1], and the prevalence of 120 per 10,000 beneficiaries would be applicable if every child meeting the FDA height criterion for ISS were to be treated.

From 2001 to 2016, the proportion of girls receiving GH treatment dropped (34% to 28%, P < 0.001; Fig. 2), as did the proportion of white youth (80% to 77%), whereas proportions of black (3% to 4%) and Asian (1% to 4%) youth increased (all P < 0.001). Proportions of Hispanic youth did not change during this time (9% to 10% throughout). Mean and median ages remained stable at 12 to 13 years.

![Figure 1. Rising prevalence of GH claims from 2001 to 2016. For comparison, the estimated 1:3500 prevalence of GH deficiency (GHD) [1] is indicated with the horizontal line.](image-url)
B. GH Expenditures

As shown in Tables 1 and 2, mean total GH expenditures decreased in both nominal dollars (−6%, \( P < 0.001 \)) and in 2004 constant dollars (−26%, \( P < 0.001 \)), as did mean estimated insurance-paid amounts (−8% in nominal dollars, \( P < 0.001 \); −28% in constant dollars, \( P < 0.001 \)). However, mean total patient financial burden increased (234% in nominal dollars, \( P < 0.001 \); 163% in constant dollars, \( P < 0.001 \)). These dollar changes translated to an increase of 2.5 percentage points in mean patient share of spending, rising from 1.4% in 2004 to 3.9% in 2016.

Table 1. Trends in Insurance and Patient Financial Burden for GH Use in Youth <18 Years Old: Nominal Dollars

| Year   | Total Expenditure, $ | Insurer Burden, $ | Patient Burden, $ |
|--------|---------------------|-------------------|-------------------|
|        | Mean    | SD     | Median  | IQR\(^{a}\) | Mean    | Median  | Mean    | Median  |
| 2004   | 35,427  | 28,459 | 28,296  | 34,106   | 35,099  | 27,827  | 329     | 200     |
| 2005   | 36,161  | 28,604 | 28,900  | 34,696   | 35,810  | 28,750  | 351     | 220     |
| 2006   | 36,383  | 27,576 | 29,789  | 34,047   | 35,880  | 29,328  | 503     | 230     |
| 2007   | 34,349  | 26,167 | 27,886  | 32,333   | 33,734  | 27,387  | 615     | 235     |
| 2008   | 34,296  | 26,484 | 28,596  | 33,093   | 33,628  | 27,641  | 640     | 250     |
| 2009   | 34,820  | 25,894 | 28,535  | 32,973   | 34,147  | 27,490  | 673     | 260     |
| 2010   | 33,258  | 25,574 | 27,160  | 31,040   | 32,545  | 25,919  | 714     | 270     |
| 2011   | 33,081  | 25,817 | 27,204  | 31,560   | 32,234  | 25,946  | 850     | 300     |
| 2012   | 32,313  | 24,933 | 26,518  | 30,848   | 31,373  | 25,742  | 941     | 330     |
| 2013   | 30,617  | 23,342 | 25,358  | 29,648   | 29,554  | 24,580  | 1064    | 370     |
| 2014   | 32,642  | 24,486 | 27,516  | 32,816   | 31,584  | 26,486  | 1059    | 375     |
| 2015   | 33,563  | 23,964 | 28,553  | 31,605   | 32,488  | 27,341  | 1075    | 360     |
| 2016   | 33,304  | 23,661 | 28,805  | 31,383   | 32,206  | 27,341  | 1099    | 385     |

\(^{a}\)Interquartile range (IQR): 75th – 25th percentile.
2016 (Table 3). Median insurer and patient spending and shares followed similar patterns (Tables 1 to 3).

C. GH Brand Switches

As shown in Fig. 3, between 2001 and 2007, the percentage of beneficiaries whose GH brand was switched at least once in the year ranged from 1.4% to 3.6% (mean 2.7%). After 2007, the mean annual percentage of beneficiaries whose GH brand was switched was 9.4%, with the greatest frequency occurring around 2008 to 2009 (25.6% switching) and 2014 to 2015 (13.9% switching). In 2008 to 2009, there was high switching activity from Genotropin, Humatrope, and Norditropin to Nutropin and Saizen; in 2014 to 2015, there was high switching activity

Table 2. Trends in Insurance and Patient Financial Burden for GH Use in Youth <18 Years Old: Constant Dollars (Base = 2004)

| Year   | Total Expenditures, $ | Insurer Burden, $ | Patient Burden, $ |
|--------|-----------------------|-------------------|-------------------|
|        | Mean     | SD       | Median  | IQR       | Mean     | Median  | Mean     | Median  |
| 2004   | 35,427   | 28,459   | 28,296  | 34,106    | 35,099   | 27,827  | 329     | 200     |
| 2005   | 35,265   | 27,895   | 28,184  | 33,836    | 34,923   | 28,038  | 342     | 215     |
| 2006   | 34,057   | 25,815   | 27,885  | 31,871    | 33,586   | 27,453  | 471     | 215     |
| 2007   | 31,310   | 23,852   | 25,419  | 29,472    | 30,750   | 24,964  | 561     | 214     |
| 2008   | 29,765   | 23,005   | 24,840  | 28,746    | 29,211   | 24,010  | 556     | 217     |
| 2009   | 30,623   | 22,773   | 25,095  | 28,999    | 30,031   | 24,176  | 592     | 229     |
| 2010   | 28,925   | 22,242   | 23,621  | 26,996    | 28,305   | 22,542  | 621     | 235     |
| 2011   | 27,797   | 21,694   | 22,859  | 26,519    | 27,086   | 21,802  | 714     | 252     |
| 2012   | 26,710   | 20,610   | 21,920  | 25,499    | 25,933   | 21,279  | 778     | 273     |
| 2013   | 24,881   | 19,969   | 20,608  | 24,094    | 24,018   | 19,975  | 865     | 301     |
| 2014   | 25,992   | 19,497   | 21,910  | 26,130    | 25,149   | 21,090  | 843     | 299     |
| 2015   | 26,674   | 19,045   | 22,693  | 25,118    | 25,820   | 21,729  | 854     | 286     |
| 2016   | 26,195   | 18,610   | 22,656  | 24,684    | 25,331   | 21,505  | 864     | 303     |

2004 to 2016 change: 

-26 and -20
-28 and -23
163 and 51

*a IQR: 75th – 25th percentile.

Table 3. Trends in Insurance and Patient Financial Burden for GH Use in Youth <18 Years Old: Shares of Insurance and Patient Expenditures

| Year   | Insurer Share, % | Patient Share, % |
|--------|------------------|------------------|
| Mean   | Median           | Mean             | Median           |
| 2004   | 98.6             | 99.3             | 1.4              | 0.7              |
| 2005   | 98.6             | 99.3             | 1.4              | 0.7              |
| 2006   | 98.1             | 99.3             | 1.9              | 0.7              |
| 2007   | 97.6             | 99.2             | 2.4              | 0.8              |
| 2008   | 97.4             | 99.1             | 2.6              | 0.9              |
| 2009   | 97.5             | 99.1             | 2.5              | 0.9              |
| 2010   | 97.2             | 99.0             | 2.8              | 1.0              |
| 2011   | 96.7             | 98.9             | 3.3              | 1.1              |
| 2012   | 96.4             | 98.7             | 3.6              | 1.3              |
| 2013   | 95.8             | 98.5             | 4.2              | 1.5              |
| 2014   | 95.9             | 98.6             | 4.2              | 1.4              |
| 2015   | 96.0             | 98.7             | 4.0              | 1.3              |
| 2016   | 96.1             | 98.6             | 3.9              | 1.4              |
| 2004 to 2016 change | -2.5        | -0.7        | +2.5         | +0.7          |
from Tev-Tropin, which was eventually discontinued, as well as from Saizen and Genotropin, toward Nutropin. Excluding these two spikes, the mean prevalence of post-2007 GH brand switching was 6.0%.

3. Discussion

In summary, the FDA ISS approval was not a watershed event in the steady increase in GH use by US youth. Progressive restrictions on coverage and formulary preference coverage strategies appear to have succeeded in lowering total spending and insurer burden of GH treatment per beneficiary. However, those savings were not passed onto patients who bore higher burdens financially and from brand switches.

Several factors likely contributed to the lack of major impact of the FDA approval for the ISS indication in 2003 on the rising trend of US pediatric GH use seen in this study. The rise preceded 2003, likely because of off-label prescriptions for GH treatment of ISS and other conditions. Review of the Pfizer International Growth Study database revealed substantial numbers of US patients treated for ISS since the inception of the postmarketing surveillance study in 1987 (introduced in the United States in 1996) and in Europe, despite lack of approval by the European Medicines Agency [9]. The prevalence of GH claims from 2001 to 2016 in the current study always exceeded the 1:3500 prevalence of GH deficiency [1], contributed to, at least in part, by the other FDA-approved indications for pediatric GH treatment: chronic renal insufficiency (1993), Turner syndrome (1996), Prader-Willi syndrome (2000), small-for-gestational age without catch-up growth (2001), SHOX gene haploinsufficiency (2007), and Noonan syndrome (2008) [4]. However, the prevalence of GH claims never came close to the 1.2% height threshold for the FDA ISS indication [2]. Some of the deficit may be a result of the progressively stringent insurance coverage rules, including in toto denial of coverage for ISS treatment. Some may be instead a result of incomplete access to health care or lack of interest in GH treatment of ISS by some patient-families and/or their endocrinologists. The most recent Pediatric Endocrine Society guidelines recommended “against the
The routine use of GH in every child with height SD score \( \leq -2.25 \)”, but rather suggested a shared decision-making approach on a case-by-case basis after assessment of physical and psychological burdens and discussion of potential risks and benefits [6].

The traits of GH recipients in this study were consistent with other studies. The predominance of male [9–12] and white [11, 12] GH recipients was previously reported from GH postmarketing surveillance studies. The drop in percentage of female GH recipients over time in this study likely reflects increasing treatment of ISS, as the male/female ratio across the four US pediatric GH registries was 2:1 for all indications but 3:1 for ISS [10]. The age distribution in this study also resembled previous reports [10].

The patterns in GH expenditures seen in this study are consistent with broader US trends in patient out-of-pocket spending and insurance coverage. Total and per-capita out-of-pocket spending in health care has been increasing over the last 15 years, primarily as a result of higher deductibles, increased patient exposure to rising health care costs, and a greater share of individuals covered by plans with high out-of-pocket costs [13, 14]. For specialty drugs, in particular, commercial insurers have been aggressively using prior authorization, formularies, and coverage restrictions to limit their exposure to high drug prices and temper rising drug spending [15, 16]. These insurer strategies, as well as frequent changes in formularies—based on changes in prices negotiated with manufacturers—also are driving brand switching.

Whereas use of the OptumInsight database provided payment information on a large, national sample of US pediatric GH recipients over a longer time frame of interest, its use also introduced some limitations. Reliance on insurance claim payments by commercial health plans does not shed light on actual prices, on the total number of prescriptions initially submitted, or on the proportion that was denied. The prices listed represent “standard prices” that combine information across all health plans and provider contracts. Although not an exact measure of paid amounts, they should provide a reasonable proxy measure for comparisons over time. These allowed payment amounts, however, do not reflect rebates offered by GH manufacturers to pharmacy benefit managers for granting formulary preference status to their products and likely overstate the insurer contribution. Also missing are data on coupons and other subsidies provided by manufacturer patient assistance programs and data on patients who pay for GH treatment completely out of pocket or are covered by state or federal government insurance plans. The OptumInsight database includes lives covered by commercial providers with Medicare contracts (e.g., Medicare Advantage members) but does not include lives covered by Medicaid managed care. Because Medicare Advantage members are aged 65+, this coverage inclusion does not materially affect our analysis.

Furthermore, whereas this study design allowed collection of financial costs, hidden costs—to all stakeholders—were unavailable for analysis. The study quantified brand switches at the group level but did not capture their impact on patient-families [5]. Because the different GH brands are delivered in different injection devices, insurance-mandated brand switches during the years a patient is treated with GH require retraining on proper administration (i.e., more complicated than simply switching from one pill to another). Hidden costs are also borne by the insurance providers who incur salary burdens as well as time and training of staff to review the ever-growing numbers of preauthorization forms and denial appeals and to render and write decisions. Missing altogether from these analyses are the hidden costs and professional impact to pediatric endocrine practices. Unreimbursed time and effort have been increasing over the years, from insurance appeals and frequent form submission, rewriting prescriptions with every formulary change, training patient-families on new devices with each brand change, and reassuring patient-families and answering their questions when anxious about their new products or potential interruptions in treatment [5]. The growing unreimbursed bureaucratic burden to endocrinology practices is compounded by a loss of patient-physician decision making autonomy that combined, contribute to the high rate of clinician burnout [17]. Increasing clinician burnout can itself adversely affect the quality of patient care [18].
In conclusion, whereas use of GH drugs by US youth seems to have increased over the past 15 years, the rise has not been as high as we might have thought; neither FDA approval of ISS treatment nor introduction of biosimilars led to big increases (the latter just led to brand switching). Nonetheless, GH use has increased, despite the increasing insurance-driven barriers and physician burden. Overall per-capita GH spending has moderated, but those gains have accrued primarily to insurers, who also do not bear the intangible burdens that befall the clinicians and patients. Patients additionally have been incurring increasing financial burden for GH, in terms of both share and dollar amounts. These patterns are consistent with broader US trends of increased patient cost-sharing and aggressive use of formularies and coverage restrictions to limit insurer exposure to high specialty drug prices. These trends are perhaps most visibly illustrated by insulin, for which rising patient costs in the United States have emerged recently as an important health care concern [19], prompting Congressional hearings and legislative review.

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Additional Information

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Disclosure Summary: A.G. serves on the Steering Committee of the Pfizer International Growth Study (KIGS) database.

Data Availability: Restrictions apply to the availability of data generated or analyzed during this study to preserve patient confidentiality or because they were used under license. The corresponding author will on request detail the restrictions and any conditions under which access to some data may be provided.

References and Notes

1. Lindsay R, Feldkamp M, Harris D, Robertson J, Rallison M. Utah Growth Study: growth standards and the prevalence of growth hormone deficiency. J Pediatr. 1994;125(1):29–35.
2. Food and Drug Administration. NDA 19-640S-033: NDA approval letter. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/appletter/2003/19640se1-033ltr.pdf. Accessed 5 April 2019.
3. United States Census Bureau. American Fact Finder. Available at: https://factfinder.census.gov/faces/nav/jsf/pages/index.xhtml. Accessed 24 June 2019.
4. Grimberg A, Allen DB. Growth hormone treatment for growth hormone deficiency and idiopathic short stature: new guidelines shaped by the presence and absence of evidence. Curr Opin Pediatr. 2017;29(4):466–471.
5. Grimberg A, Feudtner C, Gordon CM. Consequences of brand switches during the course of pediatric growth hormone treatment. Endocr Pract. 2012;18(3):307–316.
6. Grimberg A, DiVall SA, Polychronakos C, Allen DB, Cohen LE, Quintos JB, Rossi WC, Feudtner C, Murad MH; Drug and Therapeutics Committee and Ethics Committee of the Pediatric Endocrine Society. Guidelines for growth hormone and insulin-like growth factor-I treatment in children and adolescents: growth hormone deficiency, idiopathic short stature, and primary insulin-like growth factor-I deficiency. Horm Res Paediatr. 2016;86(6):361–397.
7. Wallace PJ, Shah ND, Dennen T, Bleicher PA, Crown WH. Optum Labs: building a novel node in the learning health care system [published correction appears in Health Aff (Millwood). 2014;33(9):1703]. Health Aff (Millwood). 2014;33(7):1187–1194 https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2014.0038.
8. United States Department of Labor; Bureau of Labor Statistics. Top picks. Available at: https://data.bls.gov/cgi-bin/surveymost?cu. Accessed 10 August 2019.
9. Grimberg A, Stewart E, Wajnrajch MP. Gender of pediatric recombinant human growth hormone recipients in the United States and globally. *J Clin Endocrinol Metab.* 2008;93(6):2050–2056.
10. Grimberg A, Huerta-Saenz L, Grundmeier R, Ramos MJ, Pati S, Cucchiara AJ, Stallings VA. Gender bias in U.S. pediatric growth hormone treatment. *Sci Rep.* 2015;5(1):11099.
11. August GP, Lippe BM, Blethen SL, Rosenfeld RG, Seelig SA, Johanson AJ, Compton PG, Frane JW, McClellan BH, Sherman BM. Growth hormone treatment in the United States: demographic and diagnostic features of 2331 children. *J Pediatr.* 1990;116(6):899–903.
12. Grimberg A, Lindberg A, Wajnrajch M, Cucchiara AJ, Camacho-Hübner C. Racial/ethnic disparities in US pediatric growth hormone treatment. *Horm Res Pediatr.* 2018;90(2):102–108.
13. Henry J. Kaiser Family Foundation. Payments for cost sharing increasing rapidly over time. 2017. Available at: https://www.kff.org/health-costs/issue-brief/payments-for-cost-sharing-increasing-rapidly-over-time/. Accessed 19 April 2019.
14. Baicker K, Goldman D. Patient cost-sharing and healthcare spending growth. *J Econ Perspect.* 2011;25(2):47–68.
15. Chambers JD, Kim DD, Pope EF, Graff JS, Wilkinson CL, Neumann PJ. Specialty drug coverage varies across commercial health plans in the US. *Health Aff (Millwood).* 2018;37(7):1041–1047.
16. Mullins CD, Lavallee DC, Pradel FG, DeVries AR, Caputo N. Health plans’ strategies for managing outpatient specialty pharmaceuticals. *Health Aff (Millwood).* 2006;25(5):1332–1339.
17. Grisham S. Medscape endocrinologist lifestyle report 2018: personal happiness vs work burnout. *Medscape.* Available at: https://www.medscape.com/slideshow/2018-lifestyle-endocrinologist-6009222. Accessed 5 April 2019.
18. Scheepers RA, Boerebach BC, Arah OA, Heineman MJ, Lombarts KM. A systematic review of the impact of physicians’ occupational well-being on the quality of patient care. *Int J Behav Med.* 2015;22(6):683–698.
19. Herkert D, Vijayakumar P, Luo J, Schwartz JI, Rabin TL, DeFilippo E, Lipska KJ. Cost-related insulin underuse among patients with diabetes. *JAMA Intern Med.* 2019;179(1):112–114.