

# Utilization of Gonadotropin-Releasing Hormone Agonist Products in Adolescents

Corinne Woods,<sup>1</sup> Amy Ho<sup>1</sup>, Rebecca Hawrusik<sup>2</sup>, Ryan Schoepfle<sup>2</sup>, Sarah K. Dutcher<sup>1</sup>, Adebola Ajao<sup>1</sup>, David Moeny<sup>1</sup>, Ting-Ying Huang<sup>2</sup>

<sup>1</sup> Office of Surveillance and Epidemiology, Center for Drug Evaluation and Research, U.S. Food and Drug Administration, Silver Spring, MD, USA  
<sup>2</sup> Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, USA

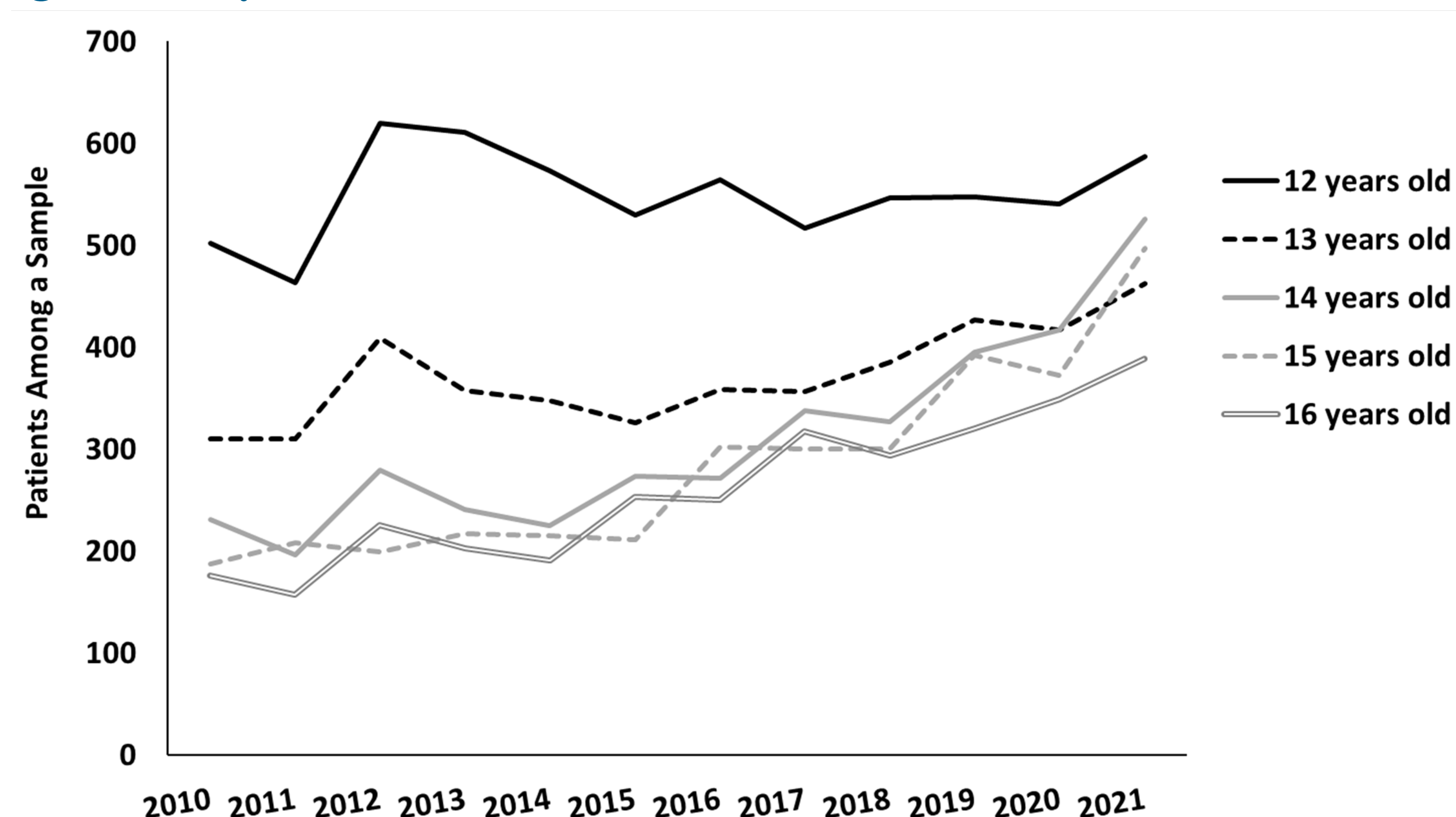
## BACKGROUND AND OBJECTIVES

Gonadotropin-releasing hormone (GnRH) agonist products are indicated for a variety of conditions, such as central precocious puberty, breast cancer, prostate cancer, and endometriosis. The utilization of GnRH agonist products among U.S. adolescents is not well-characterized in the current literature. The objectives of this analysis were to assess GnRH agonist product use in adolescents and to identify possible diagnoses associated with their use.

## RESULTS

In Integrated Dataverse<sup>®</sup>, we identified 113,792,651 patients 12-16 years old with prescription activity between 2010 and 2021, of whom 17,286 (0.02%) had GnRH agonist use (**Figure 1**). Annually, use increased during the study period from 1,407 patients in 2010 to 2,462 patients in 2021. GnRH agonists were more commonly used in patients 12 years old (587 patients in 2021) compared to the other ages studied.

**Figure 1. Sample of patients 12-16 years old with gonadotropin-releasing hormone agonist use\*, stratified by age, annually 2010-2021.**



Source: Symphony Health's Integrated Dataverse<sup>®</sup>. Study period 2010-2021, data extracted September 2022. Sample size 17,286 unique patients. Gonadotropin-releasing hormone agonist products included goserelin, histrelin, leuprolide (not in combination with norethindrone), nafarelin, and triptorelin. Patient counts may not be summed across years or age groups because patients may have received therapy over multiple years and may have changed age groups during therapy.

\* Use defined as either a dispensed prescription from U.S. retail, mail-order, specialty, long-term care, or non-retail pharmacies, captured using National Drug Codes, or an administration by a health care provider on a medical claim, captured using Healthcare Common Procedure Coding System codes.

In TreatmentAnswers<sup>™</sup>, we identified approximately 50,000 health care practitioner office visits between 2010 and 2021 where GnRH agonist use was mentioned with patients 12-16 years old (**Table 1**). The most common diagnoses reported in association with these treatment discussions were disorders of puberty (35% of office visits) and congenital malformations of the uterus and cervix (24% of office visits). This data source did not report any GnRH agonist treatment mentions associated with gender dysphoria in patients 12-16 years old.

**Table 1. Diagnosis codes associated with use mentions\* of gonadotropin-releasing hormone agonist treatment with patients 12-16 years old as reported on U.S. office-based practitioner surveys, 2010 through 2021 aggregated.**

	Use Mentions* (% share)
<b>Total Use Mentions among patients 12-16 years old</b>	<b>50,000 (100%)</b>
E30 Disorders of puberty, not elsewhere classified	17,000 (35.2%)
E30.1 Precocious puberty	11,000 (61.7%)
E30.0 Delayed puberty	7,000 (38.3%)
Q51 Congenital malformations of uterus and cervix	12,000 (23.6%)
R10 Abdominal and pelvic pain	7,000 (14.2%)
E00 Congenital iodine-deficiency syndrome	7,000 (13.5%)
N80 Endometriosis	7,000 (13.5%)

Source: Synecos Health Research & Insights, LLC, TreatmentAnswers<sup>™</sup>. Study period 2010-2021, data extracted September 2022. Diagnosis codes used International Classification of Diseases, 10<sup>th</sup> revision (ICD-10), Clinical Modification. These survey data are from a sample of U.S. office-based practitioners and do not robustly capture less common use of drugs. These results indicate very low use and are not representative of national prescribing patterns. Use mentions are rounded to thousands in its original output from the data source, Synecos Health TreatmentAnswers<sup>™</sup>. For presentation purposes this data is displayed as whole numbers and therefore "000s" are included.

\* Use mentions refer to mentions of a drug in association with a diagnosis during a patient visit to an office-based practitioner and do not necessarily result in a patient receiving a prescription for or administration of a drug.

## METHODS

We assessed GnRH agonist use in adolescents using two data sources: Symphony Health's Integrated Dataverse<sup>®</sup>, aggregated healthcare data, and Merative<sup>™</sup> MarketScan Research Databases<sup>®</sup>, an administrative claims database. Use was identified by National Drug Codes on prescription claims or Healthcare Common Procedure Coding System codes on medical claims. To determine possible conditions associated with use, we evaluated claims with proximal diagnoses of interest (the day of or 90 days prior to GnRH agonist use, MarketScan<sup>®</sup>) or diagnoses associated with treatment discussions during an office visit (Synecos Health's TreatmentAnswers<sup>™</sup>, a healthcare practitioner survey database).

In MarketScan<sup>®</sup>, we identified 5,174,410 eligible members 12-16 years old between October 1, 2015 and June 30, 2021, of whom 1,028 (0.02%) received a GnRH agonist (**Table 2**). Sixty percent of these patients were reported as female. The mean duration of GnRH agonist therapy was 251 days (median 160 days, interquartile range [IQR] 28-365 days).

The most common diagnoses of interest occurring proximal to GnRH agonist use were related to gender dysphoria, present for 580 patients, of whom 329 (57%) were reported as female. Of note, gender dysphoria is not an approved use, and these drugs have not been evaluated for efficacy and safety for this indication. Other diagnoses of interest included endocrine disorder (130 patients, 13%) and short stature (110 patients, 11%). The mean duration of GnRH agonist therapy among patients with both GnRH agonist use and a diagnosis suggesting gender dysphoria was 309 days (median 241 days, IQR 77-394 days).

**Table 2. Duration of gonadotropin-releasing hormone (GnRH) agonist therapy among patients 12-16 years old in the Merative<sup>™</sup> MarketScan<sup>®</sup> Research Databases, October 2015 to June 2021.**

	N (%)	Mean Duration of Therapy*	Median Duration of Therapy*	Interquartile Range for Therapy*
<b>Patients with any GnRH Agonist Use</b>	1,028	251 days	160 days	28-365 days
<b>Female Patients</b>	612 (60%)	–	–	–
<b>Male Patients</b>	416 (40%)	–	–	–
<b>Patients with both GnRH Agonist Use and a Gender Dysphoria Diagnosis</b>	580	309 days	241 days	77-394 days
<b>Female Patients</b>	329 (57%)	–	–	–
<b>Male Patients</b>	251 (43%)	–	–	–

Source: Merative<sup>™</sup> MarketScan<sup>®</sup> Research Databases, via Sentinel Initiative. Study period October 1, 2015 to June 30, 2021. Analysis performed October 2022. '–' indicates no data. Duration of therapy is approximate and was measured using the time between individuals' first and last GnRH agonist claims, including any gaps in therapy. Days' supply was derived from dispensed prescription claims or using approximated values on medication administration claims. Of note, gender dysphoria is not an approved use, and these drugs have not been evaluated for efficacy and safety for this indication.

## DISCUSSION AND CONCLUSIONS

Our analysis is not without limitations. Utilization data from the three separate datasets may include some overlap of patients. Practitioner survey data is from a small sample and does not robustly capture uncommon use of drugs or drug classes. The analysis of duration of therapy included possible gaps in therapy and does not necessarily imply continuous treatment.

Our analysis of GnRH agonist use among adolescents in two data sources showed relatively low use over time (less than 1%) but a small increase in recent years. Possible diagnoses associated with GnRH agonist use included puberty disorders and gender dysphoria, although the practitioner survey data did not report any gender dysphoria diagnoses – possibly due to the rarity of drug therapy mentioned during office visits for this drug class or condition. Adolescents typically were on GnRH agonist therapy for less than a year, with somewhat longer durations of therapy among patients who also had a diagnosis of gender dysphoria.

## ACKNOWLEDGEMENTS/DISCLOSURES

Presented at the 39th International Conference on Pharmacoepidemiology & Therapeutic Risk Management, August 2023, Halifax, Nova Scotia, Canada. This project was supported by Master Agreement 75F40119D10037 from the U.S. Food and Drug Administration. Many thanks are due to Drs. Michael Weiss, Jing Xu, and Sonal Goyal for their assistance with the research or poster. The authors have no relationships to disclose. The views expressed in this poster represent those of the authors and do not necessarily represent the official views of the U.S. Food and Drug Administration or Harvard Pilgrim.