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### Authors

Pineles, Stacy L  
Repka, Michael X  
Yu, Fei  
[et al.](#)

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## The use of atropine for treatment of amblyopia using the OptumLabs Data Warehouse

Stacy L. Pineles, MD, MS<sup>a,b</sup>, Michael X. Repka, MD, MBA<sup>c</sup>, Fei Yu, PhD<sup>a,d</sup>, Federico G. Velez, MD<sup>e,f</sup>, Claudia Perez, BS<sup>g</sup>, Danielle Sim, BS<sup>g</sup>, Anne L. Coleman, MD, PhD<sup>a,h</sup>

<sup>a</sup>Department of Ophthalmology, Stein Eye Institute, University of California, Los Angeles, California

<sup>b</sup>OptumLabs Visiting Fellow, Cambridge, Massachusetts

<sup>c</sup>Department of Ophthalmology, Wilmer Eye Institute, The Johns Hopkins University School of Medicine, Baltimore, Maryland

<sup>d</sup>Department of Biostatistics, University of California Los Angeles Fielding School of Public Health, Los Angeles, California

<sup>e</sup>Department of Ophthalmology, Doheny Eye Institute, University of California, Los Angeles, California

<sup>f</sup>Department of Ophthalmology, Duke University School of Medicine, Durham, North Carolina

<sup>g</sup>Department of Medicine Statistics Core, David Geffen School of Medicine, University of California, Los Angeles, California

<sup>h</sup>Department of Epidemiology, University of California Los Angeles Fielding School of Public Health, Los Angeles, California

### Abstract

Atropine and patching are standard treatments for amblyopia, but the prevalence of atropine therapy in the United States is unknown. This study used the OptumLabs Data Warehouse to evaluate pharmacy claims for topical atropine to evaluate the frequency of its treatment for amblyopia and to compare demographic factors in cohorts of amblyopic children who were and were not prescribed atropine. Overall, 55.2% of amblyopic children were prescribed atropine more than once. The children who were prescribed atropine had a higher likelihood of living in geographic regions in the South or Midwest.

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Amblyopia is the most common cause of decreased vision in children and is present in approximately 1%–4% of children.<sup>1,2</sup> Atropine penalization is a well-established treatment for amblyopia that is considered an alternative to occlusive patching. It has been widely studied by the Pediatric Eye Disease Investigator Group (PEDIG), and the outcomes for atropine therapy have been found to be largely similar results to those for patching in children with various age ranges and severity of amblyopia.<sup>3–6</sup> Although atropine and

patching are both considered standard amblyopia treatments, the frequency with which atropine is used throughout the United States is unknown. In 2002 a survey of PEDIG members revealed that “very few” used atropine as primary therapy for moderate amblyopia, but no investigation of its usage has been performed since then.<sup>7</sup> To explore this question, we queried the OptumLabs Data Warehouse (OLDW) claims database.

OptumLabs partners with experts across diverse fields and industries to facilitate research programs, develop data-driven applications, and innovate with new technologies to solve complex problems in health care. Partners represent the diverse health care landscape and include AARP, Johns Hopkins University, the Bloomberg School of Public Health, University of California Health System, Johns Hopkins, and the US Department of Health & Human Services. Claims data consists of the billing codes that health care providers submit to insurance companies. Most patient encounters within a medical system lead to an insurance claim, creating a standardized database of physician-recorded information.

## Methods

This study was exempt from review by the institutional review board at the University of California, Los Angeles. All research procedures adhered to the tenets of the Declaration of Helsinki. The study utilized the OLDW, which contains deidentified, longitudinal health information on enrollees and patients, representing a diverse mixture of ages, ethnicities, and geographical regions across the United States.<sup>8</sup> The claims data in OLDW includes medical and pharmacy claims, laboratory results, and enrollment records for commercial and Medicare Advantage enrollees. The database was queried to evaluate all subjects with a medical claim for diagnosis of amblyopia (ICD-9 code 368.0X, ICD-10 code H53.0X) from 2007 to 2017. The inclusion criteria included age of <19 years at the time of first amblyopia claim and a minimum follow-up of 6 months within the database. The use of atropine ophthalmic solution was identified from the pharmacy claims databases by using National Drug Code keys assigned by the Food and Drug Administration that corresponded to drug names (homatropine, atropine sulfate-0.9% NaCl, homatropine hydrobromide, atropine-1, atropine sulfate, atropine, AK-homatropine, Spectro-Atropine, Atropine-Care). Amblyopic subjects were divided into two groups: (1) those who were prescribed atropine ophthalmic solution on at least two claims during the study period and (2) those who were not prescribed atropine, including those who had a single claim for atropine. The following data were extracted and compared: age at first claim for amblyopia, sex, race, census region, education, family net worth, household income, and pharmacy coverage. The data extractions were conducted using SQL Software DBVisualizer Pro 10.0.15 (DbVis Software AB, Stockholm, Sweden), and all statistical analyses were performed using R 3.5.3 (R Foundation for Statistical Computing: <https://www.R-project.org>). Categorical variables were compared using  $\chi^2$  tests, and continuous variables were compared using *t* tests.

## Results

There were a total of 10,759,066 children <19 years of age with the minimum follow-up in the OLDW. Of these, 166,364 (1.55%) patients had a claim for the diagnosis of amblyopia. Of those, 91,818 (55.2%) were prescribed atropine on two or more occasions Table 1.

There was no difference in mean age at first claim for amblyopia patients with and without prescribed atropine ( $7.05 \pm 3.61$  vs  $7.00 \pm 3.59$  years [ $P = 0.015$ ]) (eTable 1). Patients with atropine use had slightly longer follow-up ( $4.4 \pm 3.2$  vs  $3.9 \pm 3.0$  years [ $P < 0.001$ ]). Patients with the highest familial net worth and household income both had the highest rate of atropine use, at 81.5% and 83.8%, respectively ( $P < 0.001$ ). Of note, patients living in the South had a higher rate of atropine use compared with patients in the Northeast (59.4% vs 47.1 [ $P < 0.001$ ]). Because of the large number of “unknowns” in several variables including race, parental education status, net worth, and household income, the analyses were repeated after removing patients with “unknown” status; the overall relationships were unchanged (eTable 1).

## Discussion

Our results indicate that the usage of atropine for treatment of amblyopia is widespread. Prescriptions for atropine in more than half of children is notable, especially given the relatively short time that it has been in use compared with patching and the rarity of its use prior to 2002.<sup>7</sup> In our cohort, children who were prescribed atropine were more often from families with higher income levels and in geographic regions in the South and Midwest. This finding suggests possible disparity in treatment choices and deserves further exploration. It is well known that racial and socioeconomic factors influence the diagnosis of ocular disorders as well as access to certain treatments.<sup>9,10</sup> This may be due to physician biases, cultural influences, access to healthcare, issues related to the cost of atropine or patches, or larger systemic issues. The regional differences were most striking, with atropine usage being more common in the South and least common in the Northeast. Differences across geographic groups may simply reflect the training and regional preferences of practicing physicians in various communities or perhaps skin sensitivity or problems patching in warmer climates because of perspiration.

Although the disparities demonstrated by these data are interesting, they must be understood within the context of their limitations. First, in any “big data” study, the findings are limited by the use of insurance claims data, which include the possibility of incomplete or incorrect coding, a large amount of unknown data, and a lack of generalization to certain populations (ie, uninsured patients). In addition, whether ophthalmic atropine was prescribed for a different disease, such as progressive myopia, cannot be ruled out. However, the use of atropine for myopia is unlikely to be highly common among patients with amblyopia because the most common indication for this purpose is in bilateral progressive myopia, which is not associated with amblyopia. A general strength of “big” claims data is its use for hypothesis generation; these data have provided rationale to further explore the variations in amblyopia treatment within diverse geographic, racial, and socioeconomic groups.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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**Table 1.**

Demographics of amblyopia patients with and without prescribed atropine in categories with more than 50% unknowns analyzed removing unknown category<sup>a</sup>

Variable/levels	Without atropine [n = 74,546]	With atropine [n = 91,818]	P value
Family net worth			<0.001
<\$25K	3869 (18)	12,430 (16.1)	
\$25K-\$149K	4784 (22.3)	15,910 (20.7)	
\$150K-\$249K	2767 (12.9)	8961 (11.6)	
\$250K-\$499K	4421 (20.6)	14,837 (19.3)	
\$500K+	5653 (26.3)	24,895 (32.3)	
Race			<0.001
Asian	2160 (9)	6233 (7.5)	
Black / African American	1908 (7.9)	5863 (7)	
Hispanic	2797 (11.6)	8850 (10.6)	
White	17,232 (71.5)	62,457 (74.9)	
Parental education			<0.001
<12th grade	103 (0.4)	198 (0.2)	
High school diploma	4566 (17.6)	14,546 (16)	
<Bachelor's degree	13,565 (52.2)	45,978 (50.7)	
Bachelor's degree plus	7735 (29.8)	30,033 (33.1)	
Household income			<0.001
<\$40,000	1546 (9.4)	5645 (7.8)	
\$40,000-\$74,999	2942 (17.9)	11,170 (15.5)	
\$75,000-\$124,999	4349 (26.4)	18,190 (25.2)	
\$125,000-\$199,999	3815 (23.2)	17,277 (24)	
\$200,000+	3821 (23.2)	19,760 (27.4)	

<sup>a</sup> Parenthetical values indicate percent of total or, in the case of study subgroups, percent of subtotal within a category.