



BRIEF REPORT

Post-market Surveillance Analysis of Refractive Data in Users of Delivery Tyro[®], a Tyrosine-Releasing Contact Lens

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Received: March 31, 2025 / Accepted: June 16, 2025 / Published online: July 3, 2025
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ABSTRACT

Introduction: Myopia is a growing public health concern, particularly among young individuals. Several pharmacological and optical interventions exist to slow its progression, yet each has limitations. In January 2021, Safilens introduced the Delivery Tyro[®] daily disposable contact lens, which releases hyaluronic acid, tamarind seed polysaccharide, and tyrosine, a dopamine precursor with antioxidative and cytoprotective properties.

Methods: This study analyzed post-market surveillance data collected by 55 optometrists from 241 myopic subjects (mean age, 14.73 years; mean initial spherical equivalent (SE) refraction, – 2.72 diopters [D]) over a 12-month period of bilateral Delivery Tyro[®] lens use. The purpose of

the analysis was to compare the observed myopia progression in Delivery Tyro[®] users with expected rates based on control SE refraction data derived from meta-analyses of similar age and ethnic cohorts.

Results: Delivery Tyro[®] users experienced slower rates of myopia progression than expected. After 12 months of lens wear, the average change in SE was a – 0.04 D compared with the expected change of – 0.28 D from the reference control group ($P < 0.001$). Furthermore, 94% of eyes exhibited no significant change in SE (defined as a change of – 0.25 D or less).

Conclusions: These findings support the hypothesis that Delivery Tyro[®] may reduce myopia progression, likely attributable to the release of tyrosine during lens wear, either due to its antioxidative properties or its role as a precursor of dopamine, a key neurotransmitter in the retina involved in visual signaling, and refractive development. Given the convenience of daily disposable lenses, Delivery Tyro[®] may offer a practical solution for myopia management, particularly for young patients at elevated risk of rapid myopia progression due to genetic and environmental factors. Further confirmation of the efficacy of Delivery Tyro[®] through controlled, randomized clinical trials is warranted.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s40123-025-01195-y>.

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PLAIN LANGUAGE SUMMARY

Myopia, or nearsightedness, is becoming increasingly common, especially among young people. If left unchecked, it can lead to potentially serious vision problems later in life. While some treatments, such as specialized glasses, contact lenses, or low-dose atropine eye drops, can slow myopia progression, each has its limitations. In January 2021, Safilens introduced the Delivery Tyro[®] daily disposable contact lens, designed to release beneficial substances into the eye. These include hyaluronic acid (for moisture), tamarind seed polysaccharide (for comfort), and tyrosine with antioxidative properties and precursor of dopamine production, which plays a role in eye growth regulation. Originally designed as a post-marketing surveillance study to assess lens tolerability and the occurrence of adverse effects, this investigation utilized real-world data collected by 55 optometrists. During data analysis, researchers observed a potential slowing of myopia progression and subsequently conducted a targeted evaluation of the relevant outcomes. A total of 241 young myopic individuals (average age 14.7 years) wore the lenses for up to 12 months. The authors compared their changes in spherical equivalent (SE), equal to the sum of the sphere power plus one-half the cylindrical power, with expected SE myopia progression rates derived from a virtual control group obtained by analyzing the progression of myopia from published scientific data. The results were promising. After 12 months, those using Delivery Tyro[®] lenses experienced an 85% lower rate of myopia progression than expected. Additionally, 94% of eyes showed no significant increase in spherical equivalent. These findings suggest that Delivery Tyro[®] lenses may help slow myopia progression, potentially as a result of the controlled release of tyrosine. As daily disposable lenses are easy to use, they could be a practical solution for young people at risk of myopia progression. However, further clinical trials are needed to confirm these benefits.

Keywords: Myopia progression; Tyrosine; Dopamine; Contact lens; Myopia control

Key Summary Points

Why carry out this study?

Myopia is an increasingly prevalent condition among children and adolescents, with rising public health and socioeconomic implications because of its long-term visual consequences.

Existing interventions to slow myopia progression have limitations in terms of efficacy, safety, and user adherence, indicating an unmet need for practical, low-risk alternatives.

This study evaluated whether the Delivery Tyro[®] daily disposable contact lens, which releases tyrosine, could slow the progression of myopia in young users based on post-market surveillance data.

What has been learned from the study?

After 12 months, users of Delivery Tyro[®] lenses experienced an 85% reduction in myopia progression compared with expected rates, with 94% of eyes showing no significant progression.

These findings support the potential role of tyrosine, as precursor of dopamine, to influence eye growth, suggesting that tyrosine-releasing contact lenses may be a promising, additional system for myopia management, pending confirmation through randomized clinical trials.

INTRODUCTION

Myopia, a condition in which the elongation of the eyeball increases the distance between the crystalline lens and the retina, affects approximately one-third of the younger population [1] and is rapidly becoming a global public health issue [2, 3]. This increase is particularly evident among younger populations, as shown in various global studies [4]. Although myopia is rarely congenital, children with one or both myopic parents are at significantly higher risk

of developing the condition [5, 6]. More commonly, myopia progression during youth is linked to lifestyle factors, such as prolonged near work (e.g., reading and using smartphones or computers) and reduced time spent outdoors, often accompanied by increased sedentary behavior [7].

To manage myopia progression, both pharmacological and optical treatments are currently employed. Daily administration of 0.01% atropine eye drops has been effective in slowing myopia progression, with minimal side effects and a low rate of rebound after treatment cessation [8]. Other pharmacological options, such as 7-methylxanthine, have shown moderate success [9]. In terms of optical interventions, techniques such as orthokeratology [10, 11], bifocal glasses [12], and multifocal contact lenses designed to create myopic defocus [13, 14], along with Defocus Incorporated Multiple Segments and Highly Aspherical Lenslet Target lenses [15–17], have demonstrated varying degrees of effectiveness in slowing the progression of myopia [18]. However, orthokeratology has been associated with side effects such as corneal staining [19], and pupil size can significantly affect the performance of multifocal contact lenses [13].

In addition to these strategies, environmental factors, such as sunlight exposure, have been shown to play a crucial role in modulating myopia [20–22]. Specifically, in pre-clinical studies violet light in sunlight has been found to activate the *EGR1* gene, which suppresses myopia, and to stimulate the production of dopamine in the retina [23]. Dopamine is a key neuromodulator that helps regulate eye growth, particularly by inhibiting excessive elongation of the eyeball, a hallmark of myopia progression [24]. Reduced levels of dopamine have been linked to an increase in myopia [25]. Thus, we speculate that reduced outdoor exposure may contribute to the progression of myopia.

Despite the benefits of sunlight exposure, ultraviolet radiation can be harmful, contributing to oxidative stress and tissue damage. As a result, many individuals avoid prolonged exposure to sunlight, inadvertently missing out on its protective effects against myopia.

Tyrosine, a naturally occurring amino acid found in the tear film and aqueous humor [26, 27], acts as a precursor to dopamine. Its antioxidative and cytoprotective properties make it an attractive candidate for reducing oxidative stress [28, 29]. Given its role as a precursor for dopamine synthesis [30], we speculate that increasing tyrosine availability in the eye could potentially help regulate the visual function.

This hypothesis has inspired the development of a new approach using tyrosine-releasing contact lenses. The Delivery Tyro[®] daily disposable contact lens (Safilens S.r.l.) is designed to release tyrosine to the anterior segment of the eye throughout the day. Alongside tyrosine, the lens matrix also contains hyaluronic acid and tamarind seed polysaccharide—molecules commonly used in eye drop formulations—which enhance the pre-lens stability of the tear film and help reduce dry eye symptoms [31–33]. These components are also useful to enhance the controlled release of the active compounds [34]. This release is facilitated by factors such as body temperature, blinking, and eyelid pressure.

Measurement of tyrosine and dopamine concentrations in the tear film of healthy subjects, conducted before and after 1 and 5 h of wearing the Delivery Tyro[®] contact lens, revealed a four-fold increase in tyrosine levels after 1 h, which returned to baseline after 5 h [35]; however, the link between this observation and myopia progression remains speculative, as retinal dopamine levels should have been measured, and this cannot be done non-invasively. A prospective double-blind randomized controlled study is currently underway to assess the efficacy of Delivery Tyro[®] contact lens on the progression of myopia (Study code: TYMP; No. Eudamed: 23.06-043174; CA approval: date 10/08/2023 prot. 68275).

The present analysis concerns real-world data collected in the context of post-market surveillance (PMS) with the purpose of assessing the potential effect of Delivery Tyro[®] lenses in slowing myopia progression under conditions of routine use.

METHODS

Data Collection

These data were collected as part of a post-market clinical follow-up (PMCF) activity, designed to proactively gather clinical evidence on the performance and safety of the Delivery Tyro[®] contact lenses. The activity was conducted under the manufacturer's post-market surveillance (PMS) plan and Design and Manufacturing Records (DMR), in compliance with applicable regulatory requirements for medical devices.

Within this framework, clinical outcomes were systematically collected and evaluated to monitor the real-world use and performance of the device.

The research concerns a study in which anonymous data were collected at the source, a condition that at the time of the survey did not require Ethics Committee approval. The study was performed in accordance with the 1964 Declaration of Helsinki and its later amendments. The participants agreed that data on medical device use would be collected and transferred to Safilens as part of the post-market surveillance activity. All data were collected anonymously and individual consent for publication was not required.

Since the aim of the data collected during this PMS activity was not to evaluate a possible effect of the lens under investigation, Eye Care Practitioners (ECPs) considered only non-cycloplegic refraction. Refractive measurements were collected without a predefined schedule, as data collection was contingent upon subjects' visits to the ECP for lens acquisition. For the purpose of analysis, data from one randomly selected eye per subject were grouped according to the approximate duration from the initial lens fitting (i.e., 3, 6, 9, 12, 18 and 24 months), recognizing that the exact timing of follow-up assessments could vary depending on individual patient requirements and standard practice procedures. We report the evaluation at the 12-month time point, which includes a larger sample size than the subsequent 18 and 24-month time points, in order to reduce potential sources of bias and

enhance the robustness and interpretability of the results.

Data were recorded using a standard form provided by Safilens to contact lens retailers as part of the PMCF program and a copy is available in Appendix 1. The anonymous form included subject details such as age, contact lens history, occupation, duration of daily outdoor activity, use of digital devices, refractive data, and any adverse events or product defects related to the medical device.

In multi-staffed practices, the same ECP conducted both lens fitting and non-cycloplegic refraction evaluations (using the hyperfocal distance refraction procedure [36] for each subject at approximately a 3–6 month interval during the observation period. This interval corresponds approximately to the typical frequency at which subjects purchase lenses following the initial application.

Meta-Analysis for Reference Progression Rates

To compare the observed progression rate of myopia in Delivery Tyro[®] end-users with a reference baseline and establish a literature-based comparator, we conducted a meta-analysis of published progression rates in children of white ethnicity, stratified by age. We preferred to undertake a new review, instead of using a calculator, to provide a fresh and unbiased synthesis of the available literature, thereby enriching the current understanding of myopia development and progression. The list of studies included in the meta-analysis is reported in Appendix 2. The following electronic databases were searched for RCTs and controlled clinical trials, limited to the English language and with no restriction on publication date:

- PubMed
- International Clinical Trials Registry Platform (ICTRP)
- Excerpta Medica Database (EMBASE)
- ClinicalTrial.gov (CT)

Search terms included: myopia, distribution, age, spherical equivalent, best vision sphere,

population, segmentation, progression, stratification, rates, and Caucasian ethnicity. Reference lists of relevant studies and review articles were also screened. The search date was 8 January 2024.

We identified 821 records through database searching (301 in PubMed, 122 in ICTRP, 273 in EMBASE, and 125 in CT). After removing duplicates, 708 records were screened by title and abstract, yielding 245 articles for full-text review. Studies were excluded if they were non-randomized, based on a non-Caucasian population, lacked interim refraction values, had small sample sizes, focused on high myopia (>− 6.0 diopters [D]) or specific syndromes, were

retrospective, or used controls other than single-vision spectacles or contact lenses.

A total of 25 studies were included for data extraction and quantitative analysis (Fig. 1), encompassing 19,865 subjects.

Data from the selected studies were compiled into a single database and stratified and normalized by age and degree of ametropia. An exponential curve with a constant offset was derived using weighted cubic spline interpolation to estimate expected myopia progression (EP) based on baseline age and mean spherical equivalent (SE), with the progression rate decreasing as age increases.

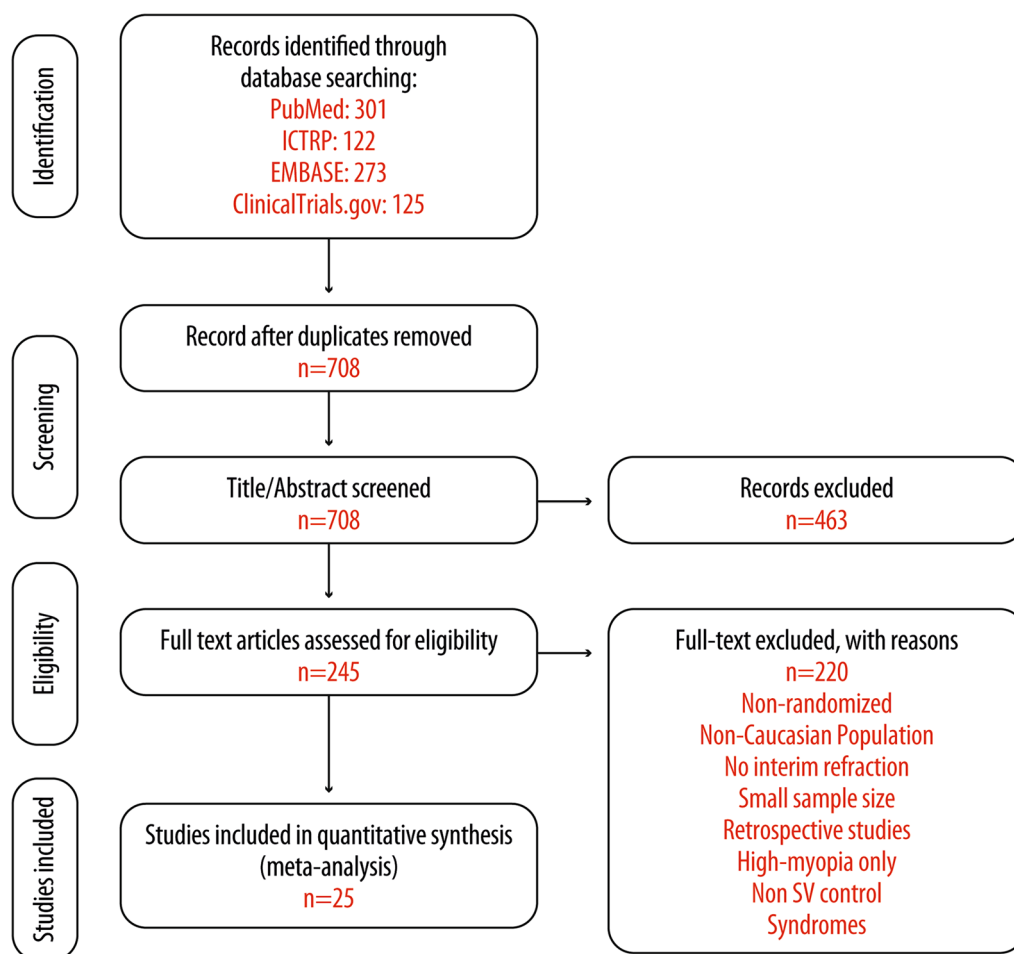


Fig. 1 PRISMA flow diagram illustrating the search strategy and database search results for literature included in the meta-analysis. *EMBASE* Excerpta Medica Database,

ICTRP International Clinical Trials Registry, *CV* Clinical-Trials.gov, *SV* single vision

Expected Myopia Progression

The EP was calculated using the following exponential formula:

$$|EP| = \left| \left(7.42e^{-0.29 \times \text{Age}(\text{years})} + 0.19 \right) \times 0.9 \right|.$$

The adoption of an exponential formula facilitates a more efficient and scalable application of the prediction tool across large datasets. This formula was validated against the Brien Holden Vision Institute (BHVI) Myopia Calculator (<https://bhvi.org/myopia-calculator-resources/>) and other peer-reviewed tools, such as mEYE™ Guide (<https://www.ocumetra.com>) and MyAppia (<https://myopia.care>), which estimate myopia progression based on age and baseline SE refraction, within a 95% confidence interval. This is consistent with the BHVI Myopia Calculator for statistical evaluation (Fig. 2), at least for the first 24 months.

Statistical analysis was performed using Student's *t* test for independent variables.

RESULTS

A total of 273 datasets were initially collected through the PMS program. Among these, 241 subjects provided sufficient longitudinal refractive data, specifically, evaluations conducted after 1 year of continuous lens wear, which allowed for inclusion in the final analysis. These 241 datasets collected by 55 participating ECPs, correspond to end-users with a mean age of 14.73 years and a mean SE refractive error of -2.72 D at the start of Delivery Tyro® use. Demographic characteristics are detailed in Table 1. Baseline refractive measurements showed a maximum astigmatism of -1.75 D and a maximum spherical power of -5.00 D.

Treatment efficacy was assessed using subjective refraction procedures, performed by the same ECP who fitted the lenses whenever possible. Subjects were under 18 years of age at the start of the observational period, and free from ocular conditions that could interfere with accurate refractive assessment.

Myopia progression in Delivery Tyro® users was evaluated against refractive expected progression values derived from an exponential curve model based on a meta-analysis of existing literature, with comparisons made at 12 months

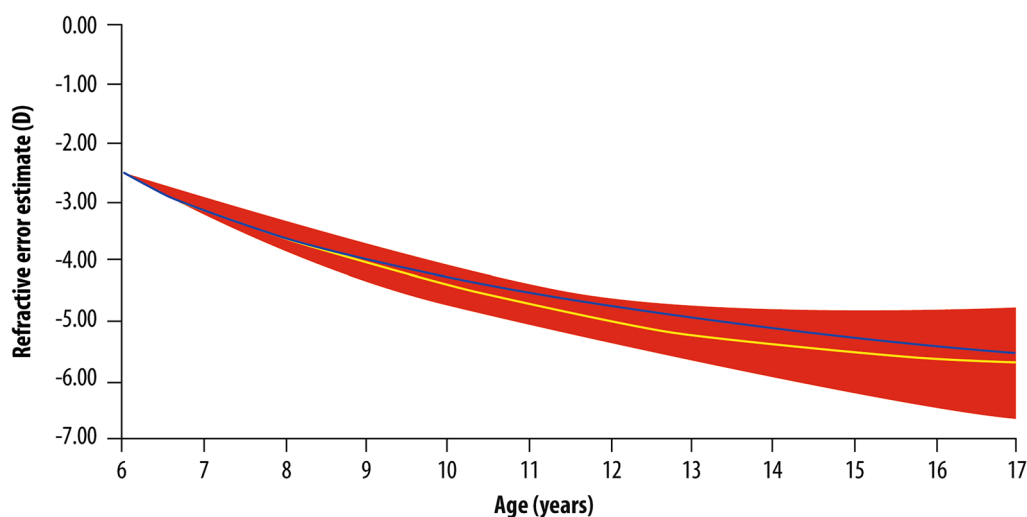


Fig. 2 Comparison between the exponential curve derived from the meta-analysis of published literature (blue line) and the prediction generated by the Brien Holden Vision

Institute (BHVI) Myopia Calculator. The simulation was performed for a subject aged 6 years with an initial spherical equivalent refraction (SER) of -2.50 diopters (D)

Table 1 Participant demographics at baseline

Parameter	Delivery Tyro [®] users (<i>n</i> = 241)
Age (years)	
Mean (SD)	14.73 ± 3.29
Median	14.25
Range	7–18
Sex	
Male (<i>n</i>)	71
Female (<i>n</i>)	170
Spherical equivalent (D)	
Mean ± SD	− 2.72 ± 1.27
Median	− 2.50
Sphere, range	− 5.00 to − 0.50
Cylinder, range	− 1.75 to − 0.25
Family history of myopia (%)	63
Previous CL use (%)	37
Mean daily use of digital devices (h)	5.0
Mean daily time spent outdoors (h)	2.8
Mean CL wear per week (days)	6.0
Mean daily CL wear (h)	8.0

CL contact lens, D diopters, SD standard deviation

(Fig. 3). At baseline Delivery Tyro[®] users had a SE of -2.72 ± 1.27 D. After 12 months the SE of Delivery Tyro[®] users was -2.76 ± 1.27 D, while that of reference population was -3 ± 1.29 D (Fig. 3). This indicates that, at the 12-month mark, Delivery Tyro[®] users exhibited an average refractive error progression of 0.24 D lower than expected (-0.28 D reference progression rates vs. -0.04 D in Delivery Tyro[®] users) (Fig. 3). By 12 months, 94.2% of eyes showed no significant change in SE refraction (defined as a change of -0.25 D or less) (Table 2).

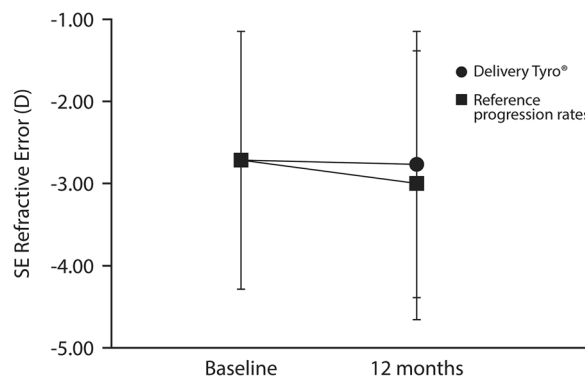


Fig. 3 Expected vs. measured mean refractive error values ± standard deviation after 12 months of Delivery Tyro[®] usage. Data are based on 241 subjects. D diopters, SE spherical equivalent

Table 2 Distribution of eyes across different categories of myopia progression (SE) over 12 months

Reported myopia progression (12 months)	Eyes	%
≤ -0.25 D	227	94.2
> -0.25 D	14	5.8

DISCUSSION

Pharmacological treatments, including atropine and pirenzepine, as well as optical methods such as multifocal soft contact lenses, or orthokeratology, have demonstrated moderate to high efficacy in slowing myopia progression through different mechanisms [37]. A recent systematic review and network meta-analysis evaluated the efficacy and safety of various interventions to slow myopia progression in children [37]. At 1-year follow-up, the most effective interventions included repeated low-intensity red light (mean difference (MD) 0.80 D; surface under the cumulative ranking curve (SUCRA) 93.8%), high-dose atropine ($\geq 0.5\%$; MD 0.90 D; SUCRA 93.3%), and medium-dose atropine (0.1 to $<0.5\%$; MD 0.55 D; SUCRA 75.5%) [37]. Other options such as low-dose atropine, peripheral plus spectacle lenses, multifocal soft contact lenses, and multifocal spectacle lenses showed smaller effects with lower certainty of evidence

[37]. At 2 years (34 studies, 3556 participants), high-dose atropine, medium-dose atropine, and peripheral plus lenses ranked highest in effectiveness [37]. However, a minority of these approaches may be associated with side effects, such as photophobia with atropine use and corneal epitheliopathy in orthokeratology [19].

The Delivery Tyro[®] contact lens offers a novel approach through the controlled release of tyrosine, which not only provides optical correction but may also modulate biochemical pathways involved in ocular growth. Unlike orthokeratology or daily pharmacologic treatment, the daily disposable format of these lenses could improve convenience and adherence among pediatric users, potentially enhancing their practicality as a myopia control option.

The results of this PMS study suggest that Delivery Tyro[®] contact lenses, designed to release tyrosine, may reduce myopia progression in young users, with up to an 85% reduction in expected progression over 12 months. The significant reduction in myopia progression observed in Delivery Tyro[®] users aligns with current understanding of the dopamine pathway in ocular growth regulation. Dopamine, a known neuromodulator in the retina, inhibits axial elongation, the primary anatomical change in myopia progression [24]. However, dopaminergic compounds are either poorly soluble or have limited intraocular penetration when applied topically [24]. Tyrosine's increased availability may augment retinal dopamine synthesis by dopaminergic amacrine cells, supporting its potential utility in myopia control [37, 38]. Additionally, tyrosine's antioxidative properties may mitigate oxidative stress [28], a factor associated with abnormal ocular development [27]. This effect may be particularly beneficial for young users who frequently engage in digital device use and near work, both of which are linked to increased myopia progression [40–42].

These findings suggest that Delivery Tyro[®] lenses may offer an effective option for managing myopia progression in pediatric patients, particularly those with lifestyle-related risk factors such as family history of myopia, reduced time spent outdoors, and frequent use of digital devices.

No incidents or undesirable side effects were reported, and the device was demonstrated to be safe and perform as intended.

Given the convenience of daily disposable lenses and the promising results observed here, Delivery Tyro[®] contact lenses may offer a practical advantage for young patients and their families.

While PMS data provide valuable insights, certain limitations must be acknowledged.

First, as a PMCF study, the data were collected in a real-world setting and the observational nature of the data precludes strict control over confounding variables, such as adherence to lens wear, outdoor time and digital device use. Notably, subgroup analyses were conducted using overall expected progression rates, as subgroup-specific expected rates were not available from the literature, and no analysis by myopia stage was performed, given the small number (32/241) of subjects with SE ≤ -4.00 D and the lack of axial length data. Additionally, measurements collected by multiple ECPs introduce potential variability due to the use of non-cycloplegic refractive assessments. However, the large sample size, while enhancing the robustness of the analysis, appears to adequately mitigate the subjectivity of different optometrists' measurements [43]. Finally, in order to avoid inter-eye correlation as a limitation of real-world PMS data analysis, only one eye per subject dataset was randomized for the statistical analysis.

However, the proactive collection and systematic evaluation of clinical outcomes within the PMCF framework provide valuable insights into the real-world performance and safety of the Delivery Tyro[®] lenses, supporting their potential role in myopia management.

While these preliminary findings are promising, the impact of Delivery Tyro[®] lenses on myopia progression needs to be confirmed through an ongoing RCT in Italy comparing Delivery Tyro[®] lenses with standard single-vision lenses.

CONCLUSIONS

The evaluation of data voluntarily provided by ECPs as part of the PMS activity conducted by

the lens manufacturer indicates a significant reduction in myopia progression among Delivery Tyro[®] contact lens users, compared with the expected refractive progression rates derived from the literature—even when accounting for the subjectivity of refractive error measurement.

The results of the PMS analysis suggest a potential role of the Delivery Tyro[®] contact lens in slowing myopia progression.

ACKNOWLEDGEMENTS

The authors thank Sergio Momini for the preliminary evaluation of PMS data and the initial contribution to this work. The authors also thank the participants of the study.

Medical Writing/Editorial Assistance. Medical writing/Editorial assistance was provided by Valeria Benedusi, Simonetta Papa, Valentina Attanasio, and Aashni Shah (Polistudium Srl, Milan, Italy). This assistance was unconditionally supported by Safilens S.r.l.

Authors' Contributions. Study conception and design: Giancarlo Montani, Daniele Bazzocchi; collection and interpretation of data: Daniele Bazzocchi; statistical analysis: Daniele Bazzocchi; manuscript drafting: Giancarlo Montani; manuscript editing: Diego Ponzin, Adriano Fasolo; approval to submit: all authors.

Funding. Editorial assistance and Rapid Service Fee for the publication of this article were unconditionally supported by Safilens S.r.l.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflicts of Interest. Diego Ponzin, Adriano Fasolo, and Giancarlo Montani served as consultants for Safilens S.r.l.; Daniele Bazzocchi is an employee of Safilens S.r.l. The authors report no other conflicts of interest in this work.

Ethics Approval. The research concerns a study in which anonymous data were collected at the source, a condition that at the time of the survey did not require Ethics Committee approval. The study was performed in accordance with the 1964 Declaration of Helsinki and its later amendments. The participants agreed that data on medical device use would be collected and transferred to Safilens as part of the post-market surveillance activity. All data were collected anonymously and individual consent for publication was not required.

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