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Eyecare-Cloud enabling 21 years of real world pediatric ophthalmology practice and paperless healthcare

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Eyecare-Cloud Enabling 21 Years of Real World Pediatric Ophthalmology Practice and Paperless Healthcare

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Abstract

Global child health initiatives increasingly recognize the importance of eye care, with retinopathy of prematurity (ROP) remaining the leading preventable cause of childhood blindness. We introduce Eyecare-Cloud, a WeChat-integrated digital platform that unifies clinical workflows, telemedicine, and research to enhance pediatric eye care, with movie presentations illustrating its real-world implementation. In this retrospective study with prospective follow-up from 2004 to 2024, data from 47,372 infants across 32 provinces in China were analyzed to evaluate 21-year trends in ROP incidence, associated risk factors, diagnostic thresholds, and cost-effectiveness. Among 26,258 preterm infants, the incidence was 17.83% (95% CI, 17.37 – 18.29%) for any ROP and 5.74% (95% CI, 5.46 – 6.02%) for treatment-requiring ROP (TR-ROP), with both rates showing a steady decline and stabilization over time. Lower gestational age (GA), lower birth weight (BW), male gender, and vaginal delivery were significantly associated with ROP and TR-ROP (all $p < 0.001$). Receiver operating characteristic (ROC) analysis identified optimal thresholds for predicting TR-ROP as GA < 31.5 weeks (sensitivity 90.5%, specificity 54.4%), BW < 1598 g (90.0%, 46.8%), and GA < 31.5 weeks or BW < 1598 g (95.5%, 38.3%). Over the past decade, Eyecare-Cloud has achieved an estimated USD 925,608 in patient cost savings. By integrating real-world data, telemedicine, and clinical decision support, Eyecare-Cloud establishes a scalable digital health infrastructure for pediatric eye care, reducing healthcare costs and offering a replicable model for preventing childhood blindness globally.

Keywords: Eyecare-Cloud, pediatric, retinopathy of prematurity.

Introduction

Children's health has garnered global attention,[1] with universal health coverage (UHC) becoming an increasingly important focus in eye health.[2,3] Eye conditions affect all stages of life, with young children and adolescents being particularly vulnerable.[2] To achieve UHC in eye, countries must prioritize strengthening services for young children. Children with vision loss generally experience poorer educational outcomes, reduced mobility, and increased risk of mental health issues, dementia, falls, traffic accidents, and social isolation, collectively contributing to higher mortality rates.[2]

Retinopathy of prematurity (ROP) is the leading cause of childhood vision loss, primarily affecting premature and low-birth-weight infants.[2,4] As a lifelong condition, ROP requires ongoing preventive measures, evolving treatment modalities,[5] and long-term follow-up care to monitor eye health and quality of life across their lifespan.[6] The global burden of vision loss underscores the incidence of ROP,[7] highlighting the urgent need for attention among healthcare professionals, ophthalmologists, and parents worldwide. Understanding its incidence, trends, risk factors, and the need of longitudinal follow-up is crucial for developing targeted strategies to prevent vision loss in premature infants.

The incidence and severity of ROP vary significantly across regions and populations.[8] In China, where neonatal care has advanced rapidly over the past two decades, analyzing the epidemiology of ROP is particularly valuable.[9,10] However, collecting two decades of multi-center data remains challenging due to fragmentation and difficulties in large-scale data collection. Additionally, the large volumes of data generated in clinical settings increase workload and complicate research efforts. Therefore, establishing a platform for systematic big data collection and analysis is crucial for effectively tracking of ROP incidence trends and risk factors. Globally, electronic health technologies have demonstrated significant improvements in healthcare and research efficiency,[11] offering new insights into structured data management for pediatric eye care. However, a dedicated platform specifically tailored to pediatric ophthalmology is still lacking.

This study introduces Eyecare-Cloud, a WeChat-integrated platform designed to alleviate the workload of eye doctors and facilitate multi-center research. WeChat,

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China's leading social media and communication platform with over one billion users, is widely integrated into daily life and healthcare services across China.[12] We used movies to demonstrate the platform's multifunctionality, including its integration with WeChat to streamline clinical workflows, enable telemedicine, and manage large-scale research data, paving the way for a paperless, data-driven healthcare era. Leveraging data from Eyecare-Cloud, we present a comprehensive analysis of the ROP epidemiology in China.

Results

Overview of Eyecare-Cloud

Eyecare-Cloud, a previously described cloud platform that covering a significant portion of the premature infant population in Southern China,[13] hosts over 20 years of multimodal clinical data related to pediatric fundus diseases. It was developed by Dr. Guoming Zhang in collaboration with a professional information technology team. A dedicated technician updates system functions and manages data for clinical and research use, while ensuring data confidentiality. Operating on the hospital's high-capacity servers, Eyecare-Cloud ensures unlimited data storage and security. It supports an integrated workflow for multiple users. Infant families submit baseline information and medical history via WeChat. Nurses review the data, while doctors use the validated data and multimodal datasets for clinical decision and research (Fig.1).

Eyecare-Cloud data analysis

From January 1, 2004, to December 31, 2024, Eyecare-Cloud has recorded a total of 47,372 infants from more than 60 hospitals in 32 provinces and regions across China (Fig. 2a). Guangdong Province accounts for the largest share, with Shenzhen having the highest proportion within the province (Fig. 2b). Preterm infants constitute the majority of cases (Fig. 2c), and the distribution of different diseases is detailed in Fig. 2d. The majority of preterm infants did not develop ROP (non-ROP), followed by untreated ROP, and then treatment-requiring ROP (TR-ROP), while other fundus diseases accounted for a smaller proportion.

Of 47,372 infants, 1,132 with incomplete or erroneous data and 19,982 who did not

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meet the ROP screening criteria were excluded, leaving 26,258 preterm infants included in the analysis. Among them, 21,576 were diagnosed without ROP, while 4,682 were diagnosed with ROP. Among the ROP cases, 3,176 did not require treatment, whereas 1,506 required treatment, including laser therapy (1,112), anti-vascular endothelial growth factor (VEGF) injections (359), cryotherapy (31), and vitrectomy (4). Proportions are shown in Fig. 3.

ROP related clinical data analysis

The analysis included infants with non-ROP, untreated ROP, and TR-ROP. Increasing ROP severity was associated with male gender, the vaginal delivery, lower birth weight (BW) and gestational age (GA) (all $p < 0.001$). Singleton birth rates were comparable among the three groups (Table 1).

Table 1. Baseline characteristics of infants among the three groups.

	Non-ROP	Untreated ROP	TR-ROP	p
Participants, n	21,576	3,176	1,506	
Male, n (%)	11,757 (54.51)	1,895 (59.65)	955 (63.33)	＜0.001
Singleton, n (%)	14,717 (68.24)	2,179 (68.59)	1,039 (68.90)	0.97
Vaginal, n (%)	7376 (35.02)	1,486 (46.77)	940 (62.33)	＜0.001
GA, Mean ± SD	32±2.36	29.46±2.44	28.23±2.47	＜0.001
BW, Mean ± SD	1555±330.4	1243±346.6	1109±355.6	＜0.001

Note: *BW=birth weight, GA=gestational age, ROP=retinopathy of prematurity, TR-ROP=treatment requiring ROP.*

Using data from Eyecare-Cloud, we evaluated the 21-year trend in ROP incidence and follow-up patterns. Fig. 4a shows the annual ROP incidence. Since 2004, ROP and TR-ROP incidence has generally declined. ROP incidence began rising slightly after 2016, whereas TR-ROP has remained stable since 2010. The number of premature infants increased gradually since 2004, surged in 2016, then declined before rising again in 2021. The overall incidence rates of ROP and TR-ROP were 17.83% (95% confidence interval, 17.37%-18.29%) and 5.74% (5.46%-6.02%), respectively (Supplementary Table 1). Fig. 4b displays the male proportion across different groups, revealing a consistently higher

male proportion compared to females in TR-ROP. Figs. 4c and 4d show the distribution of TR-ROP cases across four treatment modalities. Laser therapy remained the main intervention, anti-VEGF therapy, introduced after 2009, gradually increased, vitrectomy was used infrequently, and cryotherapy was rarely used after 2005. These patterns reflect the evolving clinical practices and treatment strategies for TR-ROP. Fig. 4e presents a scatterplot of GA and BW across the four treatment modalities. Anti-VEGF therapy were more commonly used in infants with lower GA and BW, whereas laser therapy was applied across a broader range of GA and BW. Fig. 4f displays the age-specific changes in mean spherical equivalent (SE) across different groups. SE remained stable until age seven and then shifted toward myopia, most prominently in the TR-ROP group.

Risk factors for incidence of ROP and TR-ROP

Both univariable and multivariable logistic regression analyses consistently identified younger GA, lower BW, male gender, and vaginal delivery as significant risk factors for ROP (Fig. 5a, b, Supplementary Table 2, Supplementary Fig. 1) and TR-ROP (Fig. 5c, d, Supplementary Table 2, Supplementary Fig. 2). Additionally, multivariable analysis indicated that multiparity was also a significant risk factor for ROP (Supplementary Table 2).

Optimal thresholds for predicting TR-ROP

We performed receiver operating characteristic (ROC) curve analyses to identify the optimal GA and BW threshold for TR-ROP incidence. Supplementary Fig. 3a shows AUC values for predicting TR-ROP using GA (0.836), BW (0.801), and their combination (0.840). Mann-Whitney test shows that GA and BW are significantly lower in the TR-ROP group compared to the control group (untreated and non-ROP infants). GA and BW among TR-ROP infants have significantly declined over the past 21 years ($p < 0.05$) (Supplementary Fig. 4), highlighting the need to reassess and possibly refine current ROP screening thresholds. The optimal cutoff points were determined based on the sensitivity at least 90% for detecting TR-ROP. The optimal thresholds for TR-ROP were GA < 31.50 weeks (sensitivity 90.50%, specificity 54.44%) or BW < 1598g (90.00%, 46.84%). Using the combination of GA < 31.50 weeks or BW < 1598g, the sensitivity and specificity were

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95.48% and 38.28%, respectively. Sensitivity and specificity were also evaluated at other threshold values with higher sensitivity but lower specificity (Supplementary Table 3, Supplementary Fig. 3). Using combination of GA⩽29 weeks or BW⩽1600 g yielded sensitivity of 93.5% with specificity of 42.2%.

Economic evaluations of Eyecare-Cloud

Since 2021, most examination fees for children included in the platform who underwent post-treatment follow-up for ROP have been waived. On average, each child receives a fee waiver of $140 (USD) per visit. To date, around 707 infants have benefited from 1,209 visits, resulting in total fee waivers amounting to $169,260.

Societal costs from tele-image review primarily cover accommodation and transportation. For infants who remain in the neonatal intensive care unit (NICU), this approach also eliminates referral-related costs. Since 2021, approximately 4,007 infants have benefited from 5,460 screening examinations. For in-province cases, mainly from Shenzhen, the estimated taxi fare per hospital visit is approximately $26.63. For out-of-province cases, approximately 202 infants from Sichuan underwent 268 screening sessions. The estimated round-trip travel cost is around $226.37 per person, involving at least two accompanying family members. The total estimated societal costs are approximately $318,279 (Supplementary Table 4).

The Shenzhen Welfare Lottery Charitable Fund, with a 30-year history of promoting social welfare under the mission of “supporting the elderly, assisting the disabled, helping orphans, and aiding those in need,” has made notable contributions to social development. We applied for its support to assist ROP patients enrolled in Eyecare-Cloud from disadvantaged families since 2014. By 2024, the fund has provided timely treatment assistance to 374 infants with blinding eye diseases, totaling approximately $438,069 in financial aid.

Overall, Eyecare-Cloud has generated substantial socioeconomic benefits through hospital fee waivers, telemedicine services, and government support, reducing the economic burden on families by approximately $925,068 over the past decade.

Artificial intelligence-assisted ROP screening

Currently, the artificial intelligence (AI) software integrated within Eyecare-Cloud primarily serves as an annotation tool, enabling the storage of annotated data on the platform for research. The annotation tool, named “LabelR” (labeling tool for ROP), has been described in a previous study.[14] Based on this foundation, Eyecare-Cloud is expected to evolve into a multifunctional platform capable of supporting intelligent ROP screening and diagnosis.

Discussion

Eyecare-Cloud promotes a paperless healthcare system through the integration of multimodal and longitudinal data, real-time synchronization, telemedicine, patient management, and research support. This advancement is expected to significantly improve the quality and efficiency of pediatric ophthalmic services, contributing to the prevention of vision loss in infants and children. Promoting paperless healthcare is a growing priority globally. Although the transition can be initially challenging,[15] Eyecare-Cloud has effectively supported this shift, substantially alleviating clinical workload and enhancing workflow efficiency.

Eyecare-Cloud streamlines real-world clinical workflows by reducing repetitive tasks and data entry. Unlike traditional paper-based electronic health systems that rely heavily on manual input by clinicians,[16] it integrates with WeChat, enabling families to upload patient information via QR code scanning. This allows eye doctors to focus more on meaningful clinical care. The platform also supports a paperless medical experience, offering easy report access through WeChat, improving follow-up efficiency and gaining popularity among young parents. Additionally, the platform synchronizes with hospital information systems (HIS) and picture archiving and communication systems (PACS), facilitating data sharing and supporting evidence-based decision-making.[17] Given the challenges many hospitals face in achieving full digitalization, Eyecare-Cloud offers a practical for advancing efficient and streamlined healthcare.[18]

Eyecare-Cloud also plays a vital role in advancing scientific research. It provides multimodal data, including multimodal images, clinical records, genetic data, and metabolite data, supporting the development of AI-driven technologies. Researchers can utilize the platform for structured data analysis, significantly reducing time on the data

collection and management. For example, using imaging data, we have successfully implemented AI-assisted diagnosis for ROP[19-22] and various pediatric fundus diseases.[23] Furthermore, some ROP data have been publicly released, providing valuable resources for global AI research.[24] All future studies utilizing data from Eyecare-Cloud will be named the Shenzhen Prematurity Eye Study (SPES), emphasizing its long-term commitment to advancing research in pediatric eye health.

In addition, Eyecare-Cloud facilitates real-time telemedicine, promoting medical homogenization by expanding access to high-quality eye care and reducing long-term eye complications. By minimizing unnecessary remote hospital visits, it alleviates transportation, accommodation, and referral costs.[25] Only infants requiring urgent treatment are transferred, significantly reducing the need for doctor travel. Doctors can access patient data from remote hospitals anytime through Eyecare-Cloud, enabling timely diagnosis and treatment. This makes pediatric eye care location-independent, supports remote follow-ups, and fosters cross-regional medical collaboration.

In this study, the incidence of ROP significantly declined following the implementation of the ROP prevention and treatment guidelines of China in 2004. However, it has begun to rise after 2016, possibly due to improved survival rates of premature infants resulting from advancements in NICU care, along with the addition of more centers to our ROP screening alliance. We further evaluated the ROP incidence across existing studies worldwide, finding the United States reporting the lowest rates (ranging from 4.4% to 8.8%),[4,26] Vienna having the highest reported incidence (40.9%),[27] while Italy, Portugal, Sweden, and South Korea having relatively high rates (Supplementary Table 5, Supplementary References).[28-31] In China, most reported ROP incidences are below 20%, except for Taiwan.[9,10,32-36] The findings of current study are generally consistent with existing literature, with higher incidence in Taiwan possibly resulting from different ROP screening policies. These differences highlight the impact of healthcare policies, neonatal care quality, socioeconomic factors, ethnicity, public health strategies, and data collection and reporting on global ROP incidence.

Although multiple ROP risk factors exist, younger GA and lower BW remain the most significant risk factors.[37] Male infants were at a higher risk,[32] potentially due to higher maternal levels of proinflammatory cytokines and VEGF.[37] Multiparity was significantly

associated with an increased risk of ROP, potentially due to higher rates of preterm birth. Infants born via caesarean section had a lower risk of ROP and TR-ROP, possibly due to emergency caesarean sections preventing hypoxic-ischemic injury. These findings further highlight the need for early screening for high-risk infants, particularly those with younger GA, lower BW, male gender, vaginal delivery, and multiparity.

Given the strong association of lower GA and BW with the ROP incidence, and our findings of decreasing BW and GA in infants with TR-ROP in past 20 years, it is critical to assess GA and BW thresholds for risk stratification and targeted screening strategies. Building on our previous work, which established laser therapy thresholds using fluorescein angiography images,[38] we applied a similar approach to determine GA and BW thresholds predicting TR-ROP. Infants with GA＜31.50 weeks or BW＜1598 g are at high risk of developing TR-ROP. Using these combined cutoff points, data analysis yielded a sensitivity of 95.48% and a specificity of 38.28% for identifying TR-ROP. This method supports precision medicine by improving outcomes, minimizing unnecessary resource waste, and enhancing overall healthcare efficiency.

Although the costs of screening and treating ROP impose a significant burden on healthcare systems, they are minimal compared to the long-term societal costs of blindness.[39] We used the big data from Eyecare-Cloud to estimate the economic support to ROP families through cohort follow-up, telemedicine, and social policies. AI-based ROP screening shows potential cost-effectiveness,[40] with previous studies demonstrating improved screening outcomes.[41] Thus, AI-powered Eyecare-Cloud represents our next step forward. As Eyecare-Cloud continues to expand across multiple centers, ensuring data security and patient privacy will become increasingly important. Future research will focus on developing privacy-preserving AI approaches, such as federated learning, to facilitate multicenter collaboration and model training without sharing raw patient data, thereby protecting sensitive patient information.

When interpreting this study, several limitations should be considered. First, Eyecare-Cloud is integrated with WeChat, which is not widely used globally and may limit international applicability. However, it provides a replicable model for developing similar platforms in other regions. Second, we analyzed 21 years of multicenter data on ROP incidence, risk factors, and TR-ROP prediction thresholds, without including data from

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other countries. External validation is needed to confirm global generalizability. Third, despite follow-up reminders, some patients were lost to follow-up due to the large cohort size, which may affect the future longitudinal analyses. Fourth, although AI models are incorporated, their functions remain limited. Future work will integrate more advanced AI models to better support clinical decision-making and reduce clinicians' workload. Finally, while a preliminary economic analysis was conducted, a full cost-effectiveness evaluation was not performed and will be addressed in future work.

In conclusion, Eyecare-Cloud is a platform designed to support the diagnosis, treatment, and research of pediatric fundus diseases, particularly ROP. By supporting clinical practice, integrating multimodal data, and advancing paperless healthcare, it provides a practical framework to enhance data management and collaboration in pediatric eye care.

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Methods

This is a retrospective hospital-based cohort study with a prospective ophthalmologic examination of infants (since 2004) in China. The study was approved by the Institutional Review Board of Shenzhen Eye Hospital (IRB No. 2025KYPJ098) and conducted in accordance with the principles of the Declaration of Helsinki and the Declaration of Taipei. Written consent was obtained from the parents or family members of infants before ROP screening and eye examination. All personal and confidential information was anonymized before analysis and securely stored within the Eyecare-Cloud. Here, we mainly describe three components of the platform.

Three components of Eyecare-Cloud

Component 1 describes clinical workflow. Eyecare-Cloud optimizes the clinical workflow for managing pediatric eye diseases by automating key steps. Families begin by scanning a QR code with WeChat to input baseline information for the infant, such as GA and BW, with the platform automatically calculating postmenstrual age (PMA) to minimize calculating errors. For follow-up visits, previously recorded data can be easily retrieved and updated. Certified nurses verify the information, which is then synchronized with both Eyecare-Cloud and the imaging devices. During fundus photography, patient information is retrieved automatically, avoiding the error of manual data entry. Then,

captured images are automatically uploaded to Eyecare-Cloud in real time, where doctors can review the images, generate electronic reports, and make clinical decisions. For some infants examined only with a binocular indirect ophthalmoscope, no images were uploaded, and doctors generated electronic reports without images.

Families can conveniently access the reports through WeChat, facilitating timely communication and reducing the need for in-person visits. This digital approach also eliminates the need for doctors to manually print paper reports and examination images to patients. Detailed operational steps are provided in Movie 1 and Supplementary Note 1.

Component 2 describes the tele-image review workflow implemented in Eyecare-Cloud. The process enables remote hospitals within the alliance to upload images and request review. Reviewing doctors log into Eyecare-Cloud, select the requesting hospital, and access the patient information provided. By inputting the patient's ID and navigating to the "Medical Record" section, they can review uploaded images. The doctor selects standard images, records the diagnosis (e.g., ROP zone, stage, plus disease), provides treatment suggestions, and submits the report. The requesting hospital can access the report through the platform, while the patient's family can conveniently access report via WeChat. Currently, more than 60 hospitals have joined the ROP screening alliance (Supplementary Table 6). Detailed operational steps are provided in Movie 2 and Supplementary Note 2.

Component 3 describes multimodal data management, which is facilitated by the patient management module of Eyecare-Cloud. Administrators can log in and search for patient information by name or ID to access patient's visit records, including examination results and treatment histories. The platform integrates multimodal data, including refraction data, image evaluation results, corneal topography reports, IOL master data, visual acuity, et cetera. All data can be accessed and downloaded as needed. Advanced search function enable batch data retrieval or export based on specific criteria. For example, administrators can export data for ROP patients by navigating to the "Outpatient Report" section, selecting ROP as the diagnosis, and using the batch export function. This generates a comprehensive Excel file with patient baseline information, visit records, and images organized by examination date.

Eyecare-Cloud also offers additional functionalities to support clinical practice and research (Supplementary Table 7, Supplementary References). It includes automated follow-up reminders based on electronic report schedules, with increased frequency for abnormal cases or post-treatment cases and flags for missed appointments. Eyecare-Cloud supports cohort studies and manages biological sample data, including blood, tears, and aqueous humor. A variety of auxiliary tools, including hospital directories, device inventories, and system settings, helps streamline workflows and enhance clinical efficiency. Detailed operational steps are provided in Movie 3 and Supplementary Note 3.

Thresholds analysis for predicting TR-ROP

Using comprehensive baseline and ROP diagnostic data recorded in Eyecare-Cloud, we analyzed TR-ROP incidence and performed ROC curve analysis to identify the optimal GA and BW thresholds for predicting TR-ROP occurrence.

Economic evaluations of Eyecare-Cloud in clinical settings

Using this platform, we estimated economic evaluations, including discounted follow-up policies, tele-image review, and special financial assistance for ROP patients. Fee waivers for cohort follow-ups ensure that economic barriers do not affect long-term patient adherence. Tele-image reviews help reduce patient's costs by eliminating the need for costly referrals, particularly for infants still in the NICU, where transfer expenses and associated risks are high. We evaluate the cost-effectiveness of the platform by conducting a comparative analysis of standard versus remote medical workflows to identify potential cost savings. Additionally, special financial assistance for patients with TR-ROP helps prevent blindness due to financial constraints.

Statistical analysis

Continuous measures were compared using analysis of variance (ANOVA) or Mann-Whitney test, while categorical measures were compared using the Chi-square test. Univariable and multivariable logistic regression models were employed to assess the association between risk factors and the incidence of ROP and TR-ROP. Statistical analyses were conducted using GraphPad Prism (version 10.0.0) and R (version 4.1.1).

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Two-sided $p < 0.05$ was considered statistical significance.

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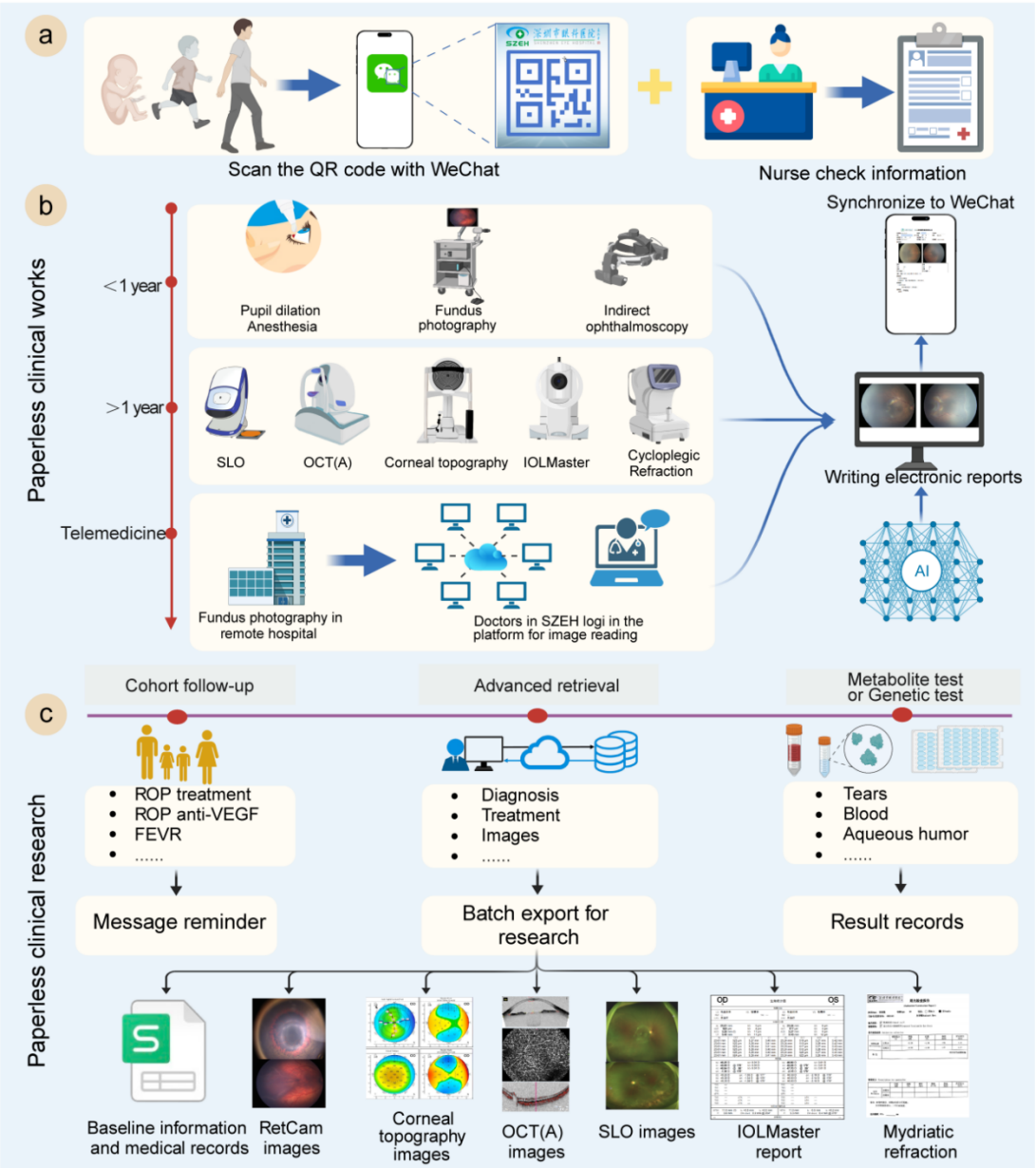


Fig.1. Eyecare-Cloud workflow for paperless clinical work and research. (a) Parents register by scanning a QR code with WeChat, enabling nurses to check the information. (b) Clinical workflows differ by age: infants＜1 year undergo fundus photography or indirect ophthalmoscopy, while older children various multimodal examinations as needed. Remote hospitals can upload images for teleconsultation, and doctors at SZEH review the images and generate reports. (c) The research component supports follow-up reminders, data retrieval, and integration with genetic and metabolic testing. FEVR=familial exudative vitreoretinopathy, ROP=retinopathy of prematurity,

OCT(A)=optical coherence tomography (angiography), QR=quick response, SLO=scanning laser ophthalmoscope.

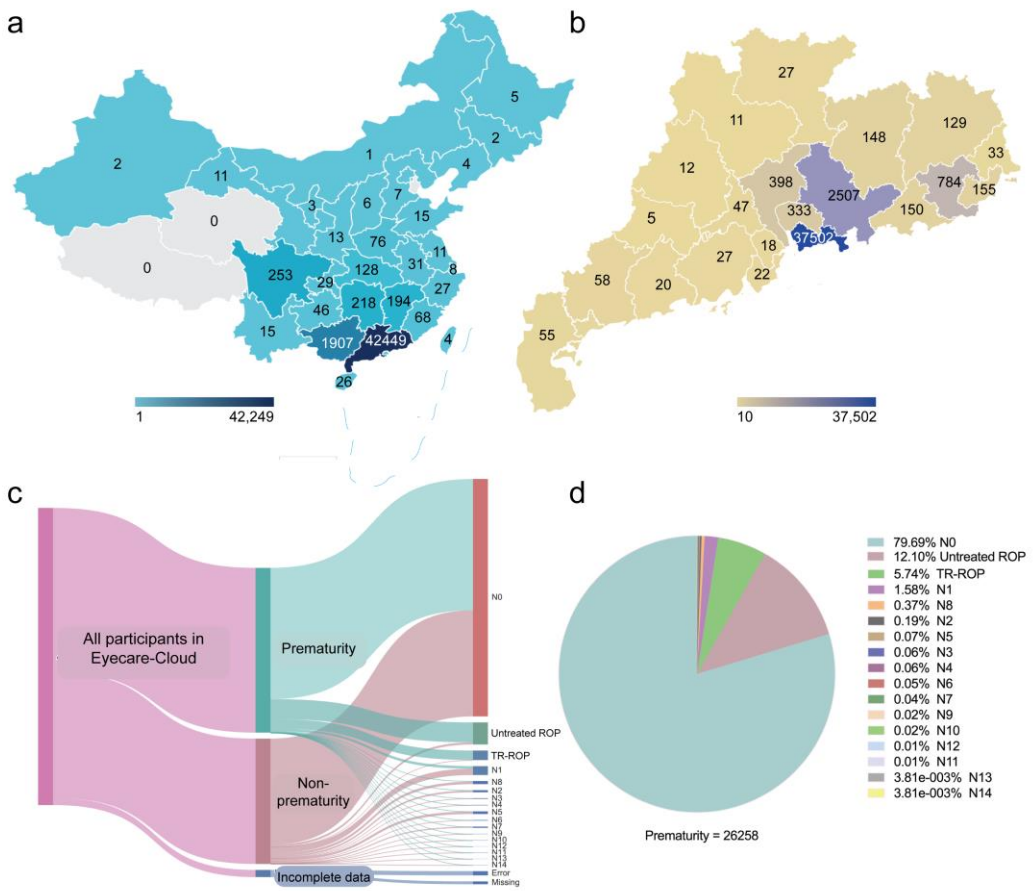


Fig. 2. Geographic distribution, demographics, and disease composition of infants in Eyecare-Cloud. N0-N14 represent different eye conditions: non-ROP (N0), other conditions (N1), cataracts and anterior segment diseases (N2), congenital optic disc abnormalities (N3), macular pathology (N4), FEVR/PFV (N5), strabismus (N6), retinoblastoma (N7), choroidal coloboma/retinoschisis/retinitis pigmentosa/subretinal exudation (N8), microphthalmia (N9), Stargardt disease/Stickler syndrome/Terson syndrome (N10), Coats' disease (N11), Norrie disease/phthisis bulbi (N12), incontinentia pigmenti (N13), and glaucoma (N14). FEVR=familial exudative vitreoretinopathy, ROP=retinopathy of prematurity, TR-ROP=treatment requiring ROP, PFV=persistent fetal vasculature.

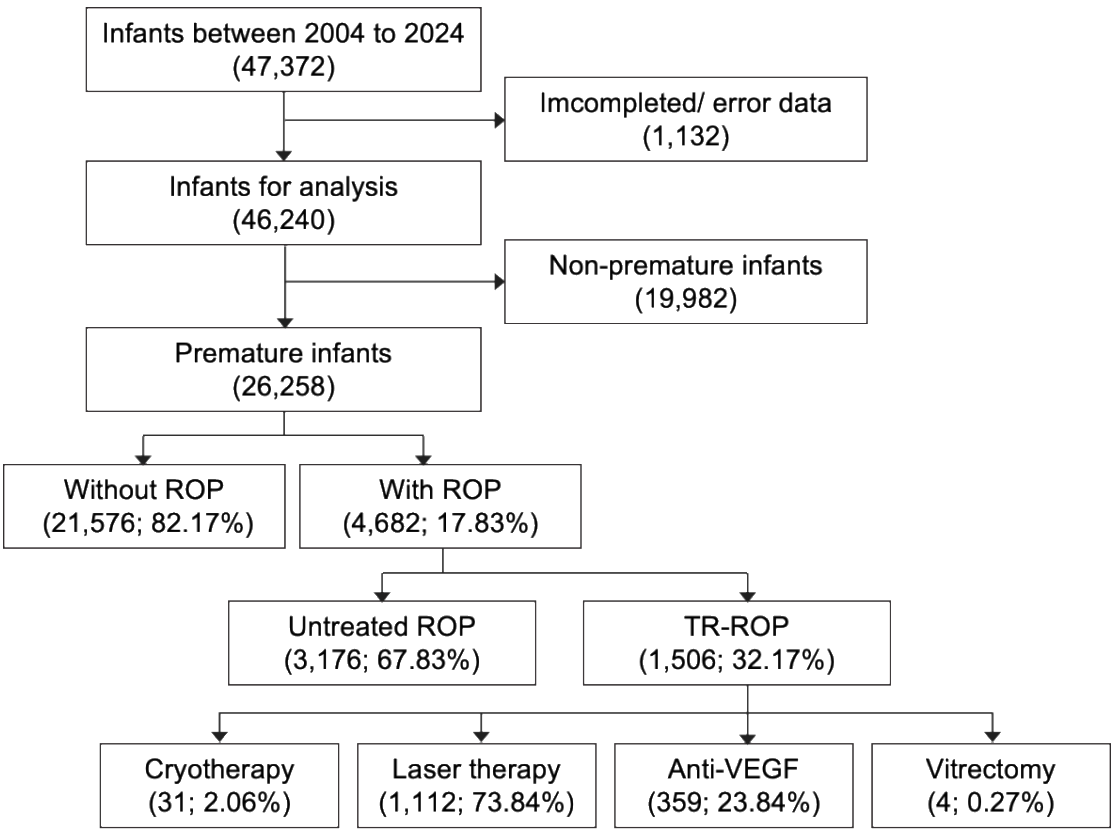


Fig. 3. Over 21 years of big data summary analysis. ROP=retinopathy of prematurity, TR-ROP=treatment requiring ROP, VEGF=vascular endothelial growth factor.

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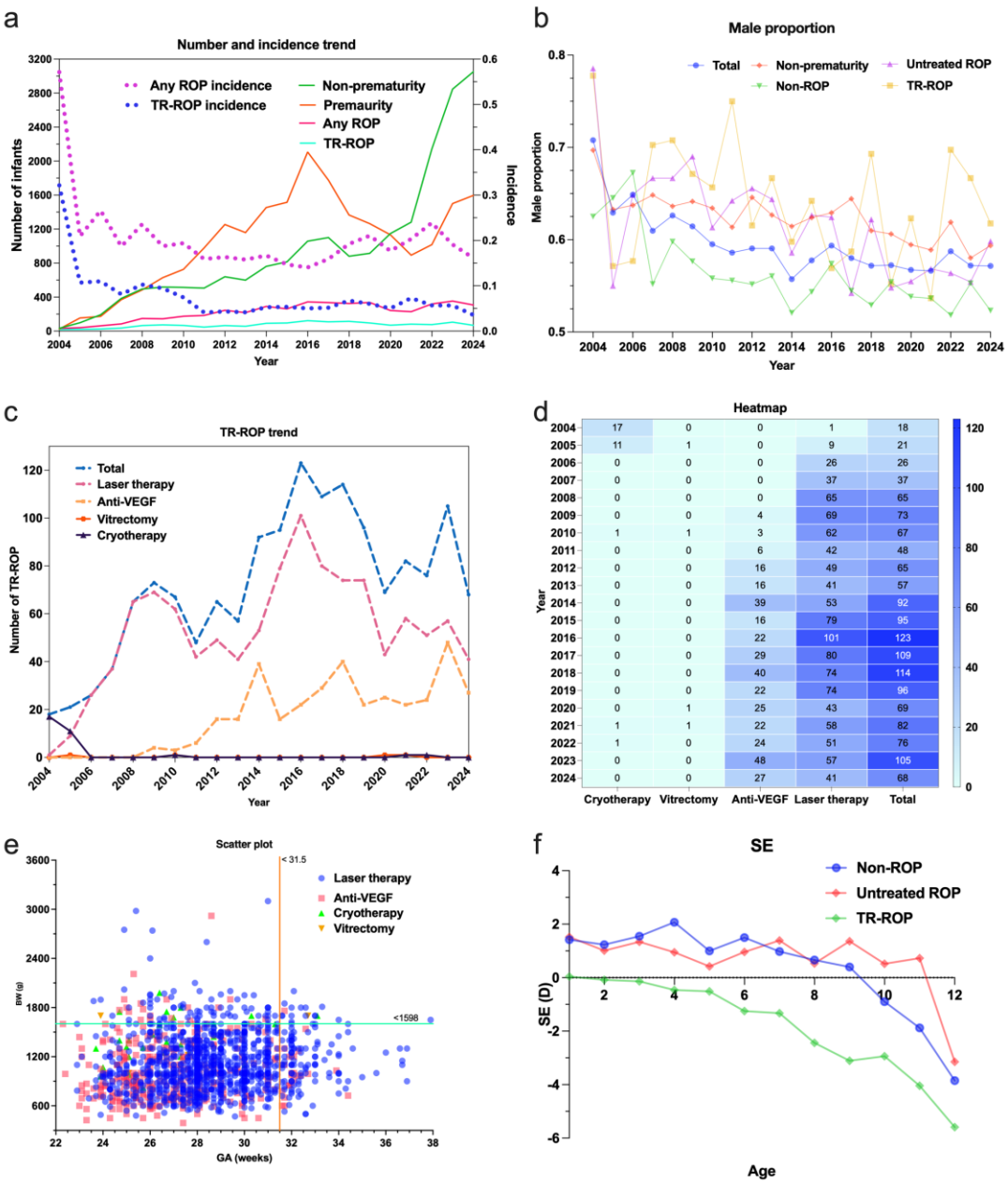


Fig. 4. Twenty-one-year trends in ROP incidence, demographics, treatment modalities, and myopic severity. (a) ROP incidence and case numbers; (b) gender proportion; (c, d) TR-ROP cases by treatment modality; (e) distributions of GA and BW ; (f) age-specific changes in SE. Abbreviations: ROP=retinopathy of prematurity, TR-ROP=treatment-requiring ROP, GA=gestational age, BW= birth weight, SE=spherical equivalent.

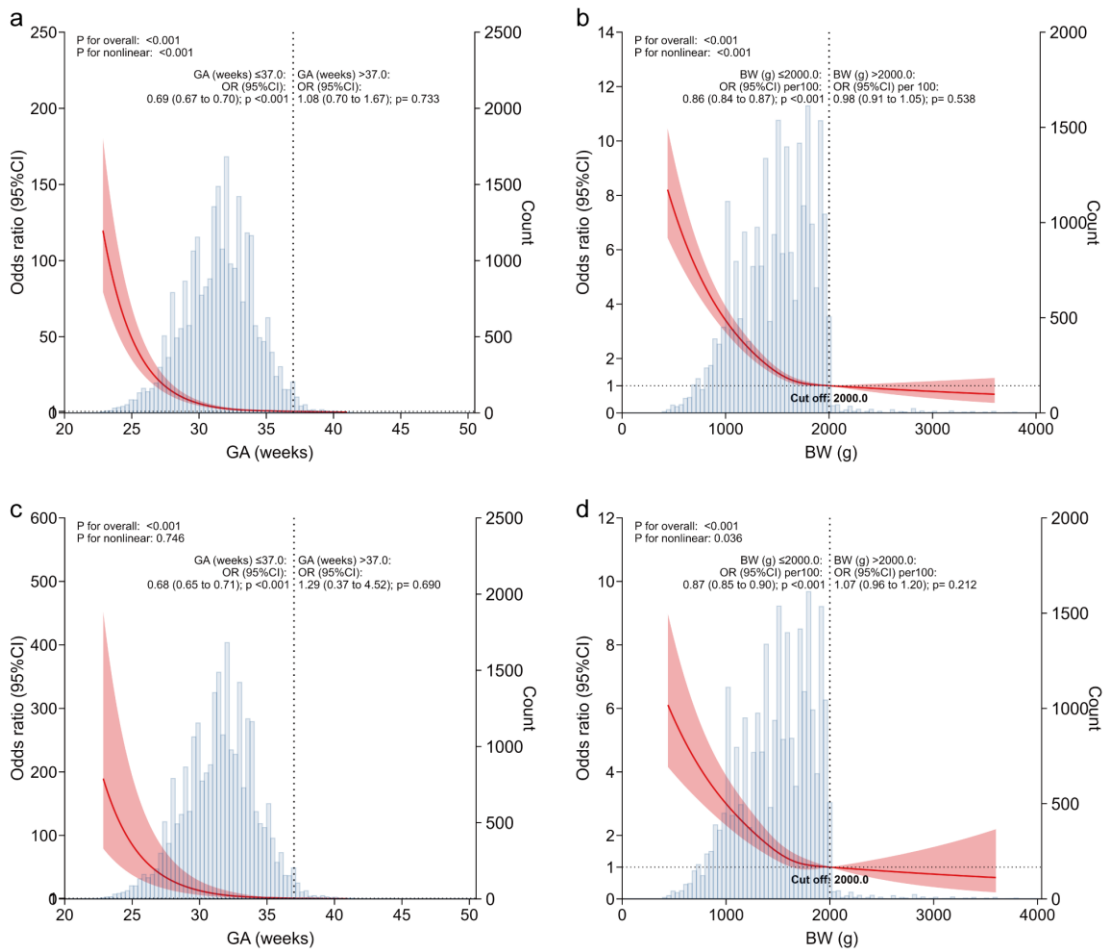


Fig. 5. Association of GA and BW with incident ROP and TR-ROP. Panels illustrate the associations between GA and ROP (a), BW and ROP (b), GA and TR-ROP (c), and BW and TR-ROP (d). Solid lines represent multivariable-adjusted odds ratio, with the area showing 95% CIs derived from restricted cubic spline regressions with four knots. The dashed line denotes a reference for no association (odds ratio = 1.0). CI=confidence interval.

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Conflict of interest The authors declare no competing interests.

Data availability The data supporting this study are obtained from the Eyecare-Cloud platform, a secure clinical big data system at Shenzhen Eye Hospital. Due to patient privacy and institutional data protection policies, the datasets are not publicly available. De-identified data used for analysis may be available from the corresponding author upon reasonable request (zhang-guoming@163.com).

Author Contributions: Xinyu Zhao, Guoming Zhang, and Zhenquan Wu contributed to all aspects of the study, including conceptualization, study design, data analysis, manuscript drafting and revision. Kaixuan Cui, Zhen Yu, Yaling Liu, Yarou Hu, Duo Yuan, Mengrui Zhang, Shaojuan Peng, Xiayuan Luo, and Mianying Zheng were responsible for data collection, supervision, initial data analysis, and manuscript revision. Yaxing Wang, Tien Yin Wong, Ruiheng Zhang, Li Dong, Wenbin Wei, Wai-ching Lam, and Peiquan Zhao contributed to manuscript drafting and review. Guishuang Ying provided statistical guidance and manuscript revision. All authors reviewed and approved the final version of the manuscript.

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