TECHNOLOGY REVIEW (MINI-HTA)

WIDE FIELD DIGITAL EYE IMAGING SYSTEM FOR UNIVERSAL NEONATAL EYE SCREENING

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
007/2024

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EXECUTIVE SUMMARY

Background

Eye health is a critical public health concern with far-reaching implications for quality of life, overall health, and sustainable development. Vision impairment and blindness, particularly in children, undermine educational, social, and economic progress. Globally, many preventable or treatable eye conditions persist due to limited access to affordable, quality care. In Malaysia, the prevalence of blindness and visual impairment underscores the urgent need for early interventions and improved eye care services. A significant proportion of childhood visual impairments are preventable, highlighting the importance of early screening and treatment. Advanced technologies, such as Wide-Field Digital Imaging Systems (WFDI), hold great promise for universal newborn eye screening (UNES), enabling early detection and management of potentially blinding conditions. However, traditional methods like the red reflex test (RRT) have limitations, particularly in detecting posterior segment abnormalities. While WFDI offers a promising solution to these gaps, its current application in Malaysia is limited to Retinopathy of Prematurity (ROP) screening in premature infants at select hospitals. Expanding WFDI to all neonatal units for universal eye screening has the potential to significantly improve outcomes but requires a thorough evaluation of cost implications and feasibility. This technology review was initiated by the Ophthalmology Department at Hospital Kuala Lumpur to evaluate the evidence, effectiveness, safety, and economic feasibility of implementing WFDIS for universal newborn eye screening.

Objective

To evaluate the effectiveness, safety, and economic implications of WFDI system for universal neonatal eye screening.

Methods

A comprehensive search was conducted on the following databases without any restriction on publication language and publication status. The Ovid interface: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily 1946 to May 13th, 2024. Searches were also run in PubMed and Embase databases. Google was used to search for additional web-based materials and information. Additional articles were identified by reviewing the references of retrieved articles. The last search was conducted on 13th May 2024.

Results and Conclusions

Effectiveness:

WFDI system demonstrated superior diagnostic performance compared to RRT, detecting anterior and posterior segment abnormalities often missed by RRT. Detection rates ranged from 4.7% to 41.2% (detect ocular abnormalities at early stage), with percentage requiring further interventions ranging from 11.1% to 59.4% (of all abnormalities).

Safety:

WFDIS is a safe and non-invasive tool with no significant adverse events reported. It is approved as a Class II medical device by the USFDA.

Organizational Challenges:
Implementing WFDIS requires significant investments in training, infrastructure, and referral networks. WHO's postnatal guidelines emphasize early screenings, but logistical barriers, particularly in resource-limited settings, remain.

Cost Effectiveness:
Though initial costs are higher than RRT (WFDIS: RM 49.48/screening vs. RRT: RM 2.62), WFDIS offers long-term benefits, including reduced severe visual impairments. Total costs from 2026–2030 are estimated at RM 97.7M for WFDIS compared to RM 5.2M for RRT. Sensitivity analyses reveal substantial variations based on implementation scenarios.

Conclusion

A substantial fair level of retrievable evidence demonstrated that WFDI as compared to RRT and IBO is a safe and well-tolerated screening modality in UNES and effective in providing good detection rate of ocular abnormalities that usually missed by RRT. Organisational issues such as trained personel, referral mechanism, economic evaluation, feasibility and cost in implementing UNES using WFDI need to be considered judiciously.

Suggested Recommendation

Based on the above reviewed, WFDI can be used for Neonatal Eye Screening. However for it to be used for UNES programme, challenges in organizational issues such as trained personel, referral mechanism, feasibility and cost implication in implementing UNES using WFDI should be considered. Alternatively, stratified screening in healthy newborn at risk can be considered

Methods

A systematic review was conducted. Review protocol and search strategy was developed by the main author while literature search was conducted by an Information Specialist who searched for published articles related to wide field digital retinal imaging (WFDI) in universal neonatal eye screening. The following electronic databases were searched through the Ovid interface: MEDLINE (R) ALL 1946 to May 13th 2024. Parallel searches were run in PubMed, Embase US FDA and INAHTA database while additional articles were retrieved from reviewing the bibliographies of retrieved articles. The search was limited to articles on human. There was no language limitation in the search. The last search was conducted on May 13th 2024.

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ABBREVIATION

AMD	Age-Related Macular Degeneration
BW	Birth Weight
IBO	Indirect Binocular Opthalmoscope
CASP	Critical Appraisal Skills Programme
CI	Confidence interval
EDI	Enhanced Depth Imaging
FA	Fluorescein Angiography
FAF	Fundus Autofluorescence
GA	Gestational Age
ICGA	Indocyanine Green Angiography
INAHTA	International Network of Agencies for Health Technology Assessment
MaHTAS	Malaysian Health Technology Assessment Section
MOH	Ministry of Health
NICU	Neonatal Intensive Care Unit
OR	Odds ratio
OCT	Optical Coherence Tomography
PICU	Pediatric Intensive Care Unit
RCT	Randomised controlled trial
RRT	Red Reflex Test
RoB	Cochrane Risk of Bias Tool
ROBIS	National Collaborating Centre for Methods and Tools
ROP	Retinopathy of Prematurity
SD-OCT	Spectral Domain OCT
US FDA	United States Food and Drug Administration
UWFDI	Ultra Wide Field Digital Imaging
WFDI	Wide Field Digital Imaging

1.0 BACKGROUND

Eye health and vision have widespread and significants implications on many aspects of life, health, sustainable development, and the economy. Nowadays, many people, families, and populations continue to suffer the consequences of poor access to high-quality, affordable eye care, leading to vision impairment and blindness. Lancet Global Health Comission on Global Eye Health defines eye health as maximised vision, ocular health, and functional ability, thereby contributing to overall health and wellbeing, social inclusion, and quality of life. Eye health is essential in achieving Sustainable Development Goals (SDGs). Eye health is an important public health concern that improves both wealthy and underprivileged people' quality of life. [1, 2] Visual impairment in childhood has a significant impact on a child's development, academic opportunities, employment, and social life. It is also associated with a considerable lifelong burden of disability and cost on the nation's economy. [3]

About one million children suffer from blindness due to eye diseases (excluding refractive errors), and at least 25% of these cases could have been avoided if preventative measures, diagnosis, and treatment had been implemented at early stage. [4] At the start of VISION 2020 program, WHO estimated that half of all blindness cases were preventable. Additionally, they projected that 1.4 million children under 15 year old were permanently blind, with approximately 19 million people visually impaired. Most blind children are either born blind from congenital conditions or become blind before the age of five years from acquired conditions. [1] Approximately about 80 to 90% of these children are born in developing countries, and 66% of them are blind from preventable or curable aetiologies including congenital cataract, uncorrected refractive error, retinopathy of prematurity, vitamin A deficiency, tumours and congenital glaucoma. [2] Between 2011 and 2017, the prevalence of birth defects in 21 European nations was 36.2 (95% CI: 34.6 to 37.9) per 100,000 live births. Congenital cataracts is the third most common. [5] The birth prevalence in low and middle income countries is likely to be higher due to a higher incidence of intrauterine infections, and consanguinity which increases the incidence of autosomal recessive conditions, such as glaucoma and cataract. [6] The number of live births was 423,124 births in 2022, a decrease of 3.8 per cent (16,620 births) as compared to 439,744 births in 2021. The crude birth rate was 12.9 per thousand population (2022). [7]

In Malaysia, the prevalence of blindness and low vision was 0.29% and 2.44% respectively in all ages as reported by the Malaysian National Eye Survey (NES I). [8] Teoh RJ et al. (2022) conducted a cross-sectional retrospective study to determine the prevalence and causes of visual impairment among children aged 7 years and below in a tertiary eye care centre in Kuala Lumpur. In Malaysia, there are five tertiary referral centers for paediatric ophthalmology, but no data available on the prevalence of visual impairment among children attending these clinics. This study, involving 2460 children who attended the clinic in 2020, highlighted that most patients were referred by public and private healthcare providers, with minimal walk-ins. The findings aim to identify preventable causes of visual impairment and support the implementation of targeted strategies across healthcare levels to alleviate the national healthcare burden. Among these children, 549 (22.3%) were diagnosed with visual impairment. The prevalence of visual impairment in the sample population was 2.2 per thousand: 402 children (73.2%) of them presented with blindness at the time of diagnosis, 25.1% had moderate visual impairment, and 1.6% had severe visual

impairment. Majority of visually impaired children, 345 (62.8%) were under 1 year old. The leading cause of visual impairment was cerebral visual impairment, affecting 133 children (24.2%), followed by congenital cataract and retinoblastoma affecting 91 children (16.6%) and 34 children (6.2%) respectively. Additionally, 211 cases (38.4%) of visual impairment were deemed treatable, while 171 cases (31.1%) were preventable. This study emphasised the critical need for early screening and intervention programs to address and prevent childhood visual impairment in Malaysia. [3]

The causes of childhood blindness and severe visual impairment in Malaysia among 469 children under 15 years old, attending 24 schools for the blind across the country found 95.6% had blindness or severe visual impairment. The major causes of visual loss were retinal disorders, accounting for 33% of cases, with retinopathy of prematurity (ROP) being a significant factor (17.4%). Other major causes included lens-related issues like cataracts/pseudophakia/aphakia (17.2%) and conditions affecting the globe, such as microphthalmos and anophthalmos (21.7%). Perinatal factors were responsible for 20.5% of cases. The study estimated the prevalence of blindness in Malaysian children to be approximately 3 per 10,000, translating to about 2,300 blind children, nearly 2,000 of whom are of school-going age. Around 50.5% of the cases had avoidable causes, including preventable conditions like trauma and infections, as well as treatable conditions such as ROP and cataracts. The findings emphasize the need for improved neonatal care, particularly in managing ROP, and the importance of early detection and treatment of conditions like cataracts. The study suggests that about half of childhood blindness cases in Malaysia could be prevented or treated with better healthcare interventions. [9]

Universal newborn eye screening (UNES) is an emerging concept for early intervention of many eye diseases that present at birth. [10]. This screening aims to detect any eye problem present in the newborn, which, if left undetected and untreated, can lead to vision loss or other serious complication. [11] The red reflex test and torch light examination are carried out by the pediatricians and other qualified medical experts to identify ocular pathologies affecting the anterior, posterior, adnexa, and lid. [11] Red reflex test is 99.6% sensitive in detecting anterior segment pathology, however it has low sensitivity in detecting posterior segment pathology. [12] In Malaysia, currently newborn eye examination is performed to those deemed at risk. Normal healthy term newborns will undergo a general examination by pediatrician using direct opthalmoscope (RRT), and will be referred to an ophthalmologist if the basic screening test is grossly abnormal. The RRT however has limitation in the detection of posterior segment abnormalities (sensitivity 4.1%), compared to anterior segment abnormalities (sensitivity 99.6%). Wide field digital retinal imaging for paediatric patient is currently available at Hospital Tunku Azizah, Kuala Lumpur and Hospital Cyberjaya. They are used for screening of Retinopathy of Prematurity (ROP) in premature infants.

Hence, this technology review was requested by the Head of the Department, Department of Opthalmology, Hospital Kuala Lumpur to assess the evidence and feasibility of using wide field digital imaging system for universal newborn eye screening.

2.0 OBJECTIVE / AIM

The objective of this technology review was to evaluate the effectiveness, safety, organisational and cost effectiveness of using wide field digital imaging system in universal neonatal eye screening.

3.0 TECHNICAL FEATURE

Wide field digital imaging system is a retinal imaging involved in creating a two-dimensional image of the three-dimensional (3D) retinal tissue. Such retinal imaging techniques are indispensable for diagnosis and management of disease processes in ophthalmic practice. These help ophthalmic practitioners directly view retinal disease and plan treatment according to the pathology. Retinal imaging techniques are useful in diagnosis and management of ocular and systemic disorders like diabetic retinopathy, hypertensive retinopathy, age-related macular degeneration, vascular pathologies (vascular occlusions, vasculitis, etc), retinal detachments, glaucomas, systemic infections, leukemias, systemic malignancies with ocular metastasis, and other.

Retinal imaging techniques have evolved at a remarkable pace in the last two decade. [13] Carl Zeiss company developed the first fundus camera in 1926, providing a 20° and later 30° view of the posterior pole. [14] Conventional retinal imaging currently utilises a fundus camera that limits the field of view to approximately 30˚ to 50° of of retina in a single capture. These imaging modalities provide sufficient views of the optic nerve and posterior pole, but are restricted in their ability to visualise the peripheral retina because of the spherical features of the eye. [15] In the beginning of widefield imaging, it was performed using a conventional camera, fixation lamp, and mirror to capture a wider field of vision than the standard 30˚ view. [16] Recent advances in fundus imaging technology now enable physicians to capture up to 200 degrees of the retina in a single image. The goal of widefield imaging is to obtain a comprehensive pan-retinal image (from ora to ora) in a single capture, offering the highest possible detail and resolution. [17]

Nowadays, wide field digital imaging (WFDI) and ultra-wide field imaging (UWFI) are increasingly popular. Wide field digital imaging refers to imaging beyond 50 degrees field area while UWFI devices have a 200 degree imaging range. They are well capable of imaging over 80% of the retinal surface area. The peripheral retina can be photographed with small pupils in instances where dilated peripheral fundus examination may be limited due to pupil size. In addition to imaging, WFDI provides important details about other retinal abnormalities and the peripheral vasculature that might otherwise be missed with conventional imaging systems. [13]

Latest fundus imaging systems have significantly advanced, allowing for wide-angle views of the retina ranging from 100° to 200°. Notable systems include the Pomerantzeff camera, which provides a 148 degree view using separate illumination sources for the central and peripheral fields. While this camera allows imaging in a sitting position, it has limitations such as a lack of high resolution and bright artifacts at the peripheral retina due to its illumination method. Another system, the Retcam by Natus Medical Inc., Pleasanton, California, United

States, offers a maximum view of 130 degrees. This system typically images patients in a supine position, though cooperative patients can also be imaged while sitting. The Panoret-1000™ camera, produced by Medibell Medical Vision Technologies, offers a 130-degree view using a digital camera with transscleral illumination. The resolution is reasonable, with minimal peripheral retinal brightness issues; however, this system is no longer commercially available. In contrast, the Optos® camera from Optos PLC, Dunfermline, United Kingdom provides a maximum view of 200 degrees and is capable of producing pseudocolor images. This non-contact system images patients in a sitting position or, in the case of infants, in a "flying baby" position. Another advanced option is the Heidelberg Spectralis with the Staurenghi lens manufactured by Heidelberg Engineering, a company based in Heidelberg, Germany, while the Staurenghi lens, an accessory that enhances the imaging capabilities of the Spectralis, is produced by Ocular Instruments Inc., located in Bellevue, Washington, United States. These two components are often used together for advanced ophthalmic imaging, offering a non-contact 105-degree view or a 150-degree view with contact, and are also capable of producing pseudocolor images. The Clarus® 500 by Carl Zeiss Meditec, based in Germany, provides a 133-degree view in a single image or up to 200 degrees with two images. This non-contact system excels in true color imaging and offers autofluorescence modes using blue, green, and infrared light. Overall, modern retinal imaging techniques have expanded to include near-histopathological examination of the retina, non-invasive visualization of retinal vasculature, assessment of Retinal Pigment Epithelium (RPE) health, photoreceptor density quantification, and the measurement of various fundus pigments, blood flow, and oxygenation. These advancements allow for a more comprehensive and detailed analysis of retinal health and function. [13]

Previously, device-specific nomenclature was used to define UWF and WF imaging in a variety of ways depending on the retinal capture's degrees of freedom. UWF was initially defined as images with at least 100˚ view of the fundus (The Diabetic Retinopathy Clinical Research Network). In 2019, an international panel with expertise in retinal imaging had a consensus meeting aimed at defining terminology for wide field imaging across all retinal imaging methods and to provide recommendations for the nomenclature used to describe related images. Based on anatomical landmarks, the definition of these two terms were formalized by this consensus committee of retinal imaging experts. Widefield image was defined as a single-capture, fovea centered image, which captures retinal features beyond the posterior pole, but posterior to the vortex vein ampulla, in all four quadrants. UWF was defined as a single-capture, fovea centered image, which captures retinal features anterior to the vortex vein ampullae in all four quadrants (Table 1) [17]

Table 1 : Definition of WF and UWF eye imaging [17]

Region	Anatomic location	Field of view
Posterior pole	Retina just beyond disc and vascular arcades	50˚
Mid-periphery (widefield)	Retina up to posterior edge of vortex vein ampulla	60-100˚
Far-periphery (ultra-widefield)	Anterior edge of vortex vein ampulla and beyond to pars plana	110-220˚
Pan-retinal	Imaging of the entire retina	360˚

Modern digital Wide Field Imaging (WFI) and Ultra-Wide Field Imaging (UWFI) systems offer numerous advantages over traditional imaging techniques in ophthalmology. These advanced systems provide enhanced resolution, allowing for detailed visualisation of retinal

structures and abnormalities. They significantly reduce image processing time and accelerate image acquisition, leading to quicker diagnosis and treatment. Additionally, the ease of duplicating, manipulating, and electronically transmitting images enhances efficiency and facilitates remote consultations. Unlike traditional fundus cameras, UWFI systems excel in imaging patients with cataracts and are particularly beneficial for young paediatric patients who cannot tolerate dilated retinal examinations. They are also effective for individuals with very small pupils and enable simultaneous imaging of both the central and peripheral retina. This capability is crucial for evaluating peripheral retinal ischaemia in conditions such as diabetic macular oedema and other vascular complications affecting the central macula. Overall, these advancements contribute to improved diagnostic capabilities, patient management, and clinical efficiency. [13] A great advantage offered by many of the present WFI and UWFI systems is the possibility of simultaneous acquisition of fundus fluorescein angiography (FFA), indocyanine angiography (ICGA), red-free photography, fundus photography, color fundus stereo imaging, adaptics optics confocal scanning laser opthalmoscope (CSLO), hyperspectral retinal imaging and fundus autofluorescence (FAF). Currently, the available devices/platforms for WFDI include Heidelberg Spectralis, Retcam 3, and Clarus® 500. [13]

The RetCam 3 is an advanced, fully integrated system designed for superior ophthalmic visualisation, photo documentation, and ease of use. It features a new user interface and an ergonomic handpiece, enhancing user-friendliness. The system captures brilliant, full-color images of the retina and anterior chamber, which are crucial for immediate assessment. These high-quality digital images can be electronically transmitted to ophthalmologists for instant interpretation and tracked over time. The RetCam 3 is particularly valuable for capturing photographs of the paediatric retina in Neonatal Intensive Care Units (NICUs) and Paediatric Intensive Care Units (PICUs). It includes a variety of lenses tailored to different imaging needs, including the Premature Infant 130-Degree Lens, Standard Baby 120-Degree Lens, High Magnification 30-Degree Lens, High Contrast 80-Degree Lens, and Flat-Field Portrait Lens for external photographs, which enhance the system's versatility and enable detailed imaging across diverse clinical scenarios. [18]

ZEISS Clarus® 500 is an advanced ultra-widefield retinal imaging system that is designed to capture high-resolution, true-color images across the entire retina, from the macula to the far periphery. This imaging system is particularly valuable for detecting and documenting ocular diseases that may manifest in subtle ways, such as changes in the optic disc, nevi, and lesions where accurate color representation is crucial.Its' ability to produce images that closely resemble the natural coloration of the fundus as seen during clinical examination enhances the diagnostic process, giving clinicians a clear and accurate view of retinal structures. It leverages ZEISS optics to achieve a resolution down to 7 microns, enabling the detection of early indications of disease that might be missed by lower-resolution imaging systems. Additionally, Clarus® 500 features a Live Infa Red Preview, which helps technicians optimise image alignment and remove artifacts before capturing the final image, leading to fewer image captures and a more efficient process for both the patient and the practice.This system represents a significant advancement in fundus imaging, allowing for a more detailed and comprehensive evaluation of the retina, which is critical in managing and diagnosing various eye conditions. [19]

The Spectralis Optical Coherence Tomography (OCT) by Heidelberg Engineering is an advanced imaging device widely used in ophthalmology. It captures high-resolution, cross-

sectional images of the retina and other ocular structures at speeds of up to 40,000 A-scans per second, enhancing image clarity and detail for accurate diagnosis and monitoring. Key features include multimodal imaging capabilities such as Fundus Autofluorescence (FAF), Fluorescein Angiography (FA), and Indocyanine Green Angiography (ICGA), which provide comprehensive assessments of retinal and choroidal conditions. The Spectralis OCT employs Spectral Domain OCT (SD-OCT) technology for high-resolution imaging and Enhanced Depth Imaging (EDI) to visualise deeper structures like the choroid. Its advanced scanning modes, including real-time eye tracking and auto-alignment, ensure consistent and precise imaging. This OCT system is crucial for diagnosing and monitoring ocular conditions such as Age-Related Macular Degeneration (AMD), diabetic retinopathy, and glaucoma, and is valuable for preoperative and postoperative evaluations. The user-friendly interface and integrated software further streamline data analysis and patient management. [20]

The PanoCam™ LT Wide-field Digital Imaging System from Visunex Medical Systems is available and has been FDA-approved for imaging all newborn infants. This system is a compact, wireless device designed to capture high-resolution images of the retina in newborns. It is particularly valuable for detecting various vision disorders that can have long-term effects if not identified and treated early. The device is portable, making it suitable for use in different clinical settings, including neonatal intensive care units and clinics. [21]

Figure 1: RetCam 3 Wide-Field Digital Imaging System

Figure 2: ZEISS Clarus® 500 fundus imaging system

Figure 3: SPECTRALIS diagnostic imaging platform

Figure 4: PanoCam™ LT Wide-field Digital Imaging System

4.0 METHODS

A systematic review was conducted in accordance with the PRISMA statement. Search strategy was developed by the main author and reviewed by the co-author.

4.1 SEARCHING

The following electronic databases were searched through the Ovid interface:

- MEDLINE(R) In-Process and Other Non-Indexed Citations and Ovid MEDLINE (R) 1946 to present
- EBM Reviews – Cochrane Central Registered of Controlled Trials – May 2024
- EBM Reviews – Database of Abstracts of Review of Effects – 2nd Quarter 2024
- EBM Reviews – Cochrane Database of Systematic Reviews – 2005 to May 2024
- EBM Reviews – Health Technology Assessment – 2nd Quarter 2024
- EBM Reviews - NHS Economic Evaluation Database – 2nd Quarter 2024

Other databases: PubMed, Embase, US FDA, INAHTA

General databases such as Google were used to search for additional web-based materials and information. Additional articles retrieved from reviewing the bibliographies of retrieved

articles. The search was limited to articles on human. There was language limitation in the search (English). **Appendix 1** showed the detailed search strategies. The last search was conducted on 13th May 2024.

4.2 SELECTION

A reviewer screened the titles and abstracts against the inclusion and exclusion criteria. Relevant articles were then critically appraised depending on the type of the study design. Studies were graded according to *US/ Canadian Preventive Services Task Force* (**Appendix 2**). All data were extracted and summarised in evidence table as in **Appendix 3**.

The inclusion and exclusion criteria were:

Inclusion criteria:

a.	**Population**	Neonate, Newborn (Term)
b.	**Intervention**	Wide Field Digital Eye Imaging System
c.	**Comparator**	1. **Direct Opthalmoscope (RRT)** - limitation in detection posterior segment abnormalities (sensitivity 4.1%) compared to anterior segment abnormalities (sensitivity 99.6%) 2. **Conventional retinal imaging** using traditional camera, fixation lamp and mirror (a fundus camera that limits the filed of view to approximately 30 to 500 of the retina in a single capture) – limited in providing views of the peripheral retina.
d.	**Outcomes**	**Effectiveness:** accuracy, diagnostic performance, detection, processing time **Safety:** adverse event **Organisational issues:** **Economic implications:** cost effectiveness analysis, cost benefit analysis
e.	**Study design**	HTA reports, systematic review without meta-analysis, randomised controlled trial (RCT), cohort, diagnostic, case-control, economic evaluation studies
f.	Full text articles published in English	

Exclusion criteria:

a.	**Study design**	Case report, case series, animal study, laboratory study, narrative review
b.	Non-English full text articles	

5.0 RESULTS

Search results

An overview of the search is illustrated in **Figure 5**. A total of **153** records were identified through the Ovid interface, PubMed and Embase. **Fourteen** duplicates references were found; **139** potentially relevant titles were screened using the inclusion and exclusion criteria. Of these, **42** relevant abstracts were retrieved in full text. After reading, appraising and applying the inclusion and exclusion criteria to the **42** full text articles, **11** were included. **Thirty one** were excluded as those irrelevant study design and irrelevant outcome. All full text articles finally selected for this review comprised of three cohort studies, seven cross sectional studies and one budget impact analysis. The studies were conducted mainly in Asia, North America, South America and New Zealand.

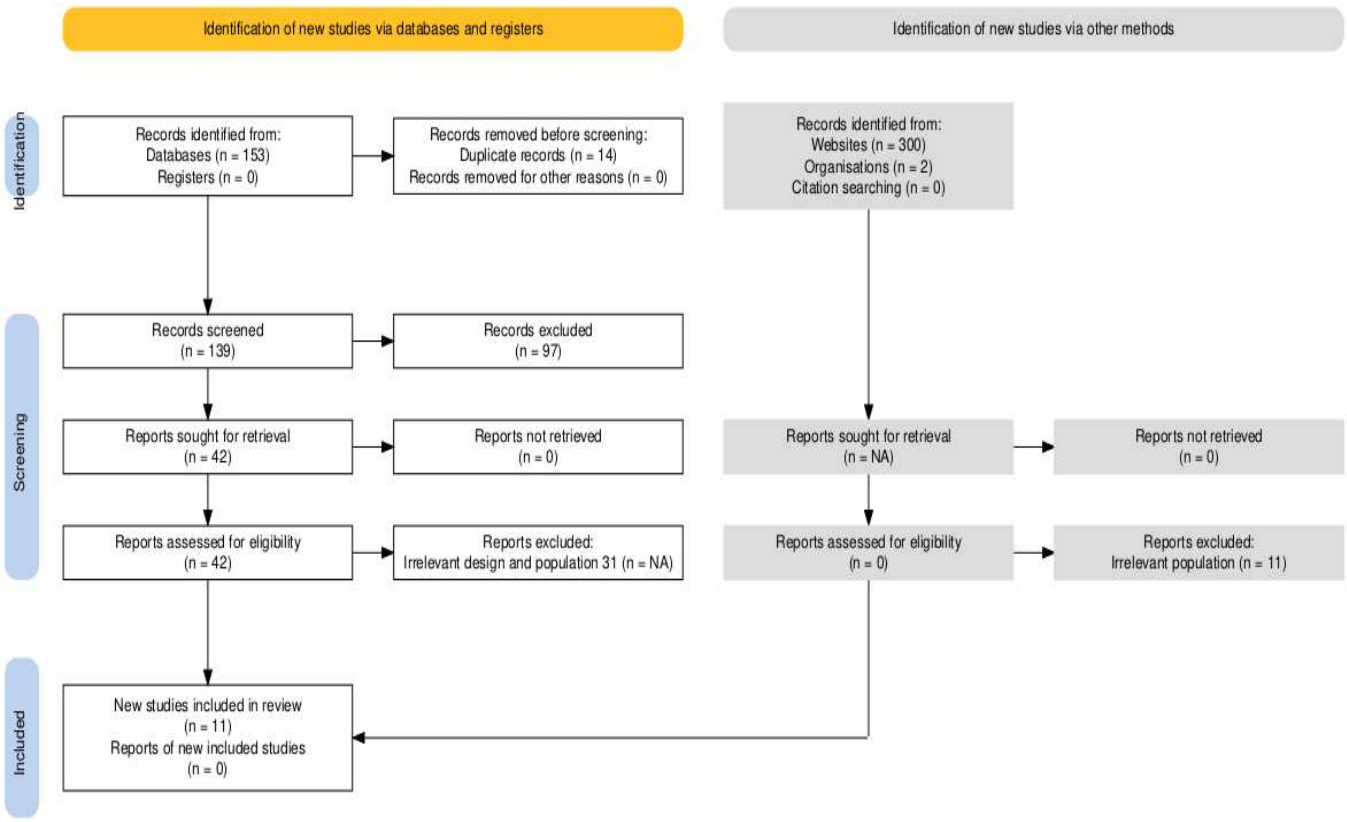

Figure 5: Flow chart of retrieval of articles used in the results

Quality assessment of the studies

The risk of bias or quality assessment (methodology quality) of all retrieved literatures was assessed depending on the type of the study design. These assessments involved answering a pre-specified question of those criteria assessed and assigning a judgement relating to the risk of bias: using the relevant checklist of National Collaborating Centre for Methods and Tools (ROBIS) for systematic review and meta-analysis, a revised Cochrane Risk of Bias Tool (RoB 2) for randomised controlled trials, Critical Appraisal Skill Programme (CASP) checklist for observational study, and The Joanna Briggs Institute (JBI) Critical Appraisal tools for Quasi-Experimental Studies (non-RCT). All full text articles were graded based on guidelines from the *U.S. / Canadian Preventive Services Task Force*.

Risk of bias assessment for included cohort using CASP

Based on the CASP checklist, the study had low risk of bias (**Table 2**).

Review	Risk of bias domains					
	D1	D2	D3	D4	D5	Overall
	Selection of cohort	Exposure accurately measures	Outcome accurately measures	Confounding factors	Follow-up and timing	
daCunha et al. 2021 [42]	+	+	+	+	?	+
Fei P et al 2020 [00]	+	+	+	+	?	+
Vinekar A et al 2015	+	+	+	+	+	+

+ low risk; - high risk ? unclear risk

Table 2: Risk of bias assessment for cohort study using CASP

Risk of bias assessment for included cross sectional studies using JBI

Seven studies were included in this assessment and were summarised in **Table 3**. All were judged to have overall low risk of bias.

Risk of bias assessment for cross sectional study using JBI (Table 3)

	CAJBI1	CAJBI2	CAJBI3	CAJBI4	CAJBI5	CAJBI6	CAJBI7	CAJBI8
Leong et al. (2021)	+	+	+	+	+	?	+	+
Sitorus RS et al. (2021)	+	+	+	+	+	?	+	+
Simkin SK et al. (2018)	+	+	+	+	+	?	+	+
Goyal P et al. (2018)	+	+	+	+	+	?	+	+
Ma Y et al. (2018)	+	+	+	+	?	?	+	+
Tang H et al. (2018)	+	+	+	+	+	?	+	+
Li LH et al. (2013)	+	+	+	+	?	?	+	+

CAJBI1 Were the criteria for inclusion in the sample clearly defined?
CAJBI2 Were the study subjects and the setting described in detail?
CAJBI3 Was the exposure measured in a valid and reliable way?
CAJBI4 Were objective, standard criteria used for measurement of the condition?
CAJBI5 Were confounding factors identified?
CAJBI6 Were strategies to deal with confounding factors stated?
CAJBI7 Were the outcomes measured in a valid and reliable way?
CAJBI8 Was appropriate statistical analysis used?

Judgment:
+ Yes
- No
? Unclear
x Not applicable

5.1 EFFICACY/ EFFECTIVENESS

DaCunha et al. (2021) have conducted a prospective cohort study to compare the effectiveness of the red reflex test (RRT) with the wide-field digital imaging (WFDI) system for universal newborn eye screening in Brazil. This study involved 380 newborns (760 eyes) in the Maternity Ward of Irmandade Santa Casa de Misericordia de Sao Paulo hospital from May to July 2014 whom underwent RRT by paediatricians and WFDI performed by the authors. Wide-field digital imaging (WFDI) images were analysed by the authors. Validity of the paediatrician's RRT was assessed by unweighted kappa statistic (k) statistic, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV). The results revealed that WFDI detected abnormalities in 130 eyes (17.1%), significantly higher than the 13 eyes (1.7%) detected by RRT. Furthermore, WFDI identified treatable retinal pathologies, such as hyphema, CMV retinitis, FEVR, and vitreous haemorrhage, which were missed by RRT. The sensitivity of RRT was found to be remarkably low at 0.77% (95% CI, 0.02% to 4.21%), while its specificity was 98.10% (95% CI, 96.70% to 99.01%). The positive predictive value (PPV) was 7.69% (95% CI, 1.08% to 38.85%), and the negative predictive value (NPV) was 82.73% (95% CI, 82.46% to 83.00%). The sensitivity and unweighted kappa statistic were similarly poor when separated into anterior segment abnormality detection (sensitivity 16.70%, 95% CI, 0.42 to 64.12%; 5% CI, · 0.10 to 0.29) and posterior segment abnormality detection (sensitivity 0.00%, 95% CI, 0.00% to 2.93%; 95% CI, 0.05 to 0.02). There was no agreement between the two screening modalities (κ = - 0.02, 95% CI, -0.05 to 0.01). Number needed to screen (NNS) to detect ocular abnormalities using WFDI was 5.9 newborns, and to detect treatable abnormalities was 76 newborns. These findings indicate that while RRT is effective at detecting gross abnormalities that preclude visulalization of the retina (i.e media opacities and very large tumours), it fails to identify subtle, treatable retinal and optic nerve pathologies that WFDI can consistently detect. With higher sensitivity than the current gold standard, WFDI allows for early detection and management of potentially blinding ophthalmic diseases missed by RRT.[2]

A cohort study conducted by Fei et al. (2020) demonstrated the efficacy of the wide-field digital retinal imaging (WFDI) system for early detection of ocular abnormalities in newborns across multiple centers in China. This study involved 64,632 newborns in nine hospitals including eight Maternal and Children's Hospitals, and one general hospitals across China over one year from July 2016 to June 2017. Ocular examinations were performed on newborns within 28 days after birth using wide field digital imaging system. The inclusion criteria for the study encompassed all live neonates born at the participating hospitals between July 2016 and June 2017, provided their parents had signed the consent form. Additionally, premature infants, as defined by the Chinese Ophthalmological Society specifically those born with a gestational age (GA) of less than 32 weeks or a birth weight (BW) of under 2000 grams were also included in the study. The exclusion criteria ruled out infants whose images or medical charts were not available for review, those with infectious conjunctivitis, and those deemed too unstable for examination. These criteria ensured that the study focused on a well-defined population while excluding cases that could not be accurately assessed. The study found 13,514 ocular abnormalities which accounted for 20.91% of all screened neonates. The most frequent abnormality was retinal haemorrhage (RH), detected in 7648 (11.83%) cases including 4553 (7.04%) cases involved bilaterally and many mild retinal haemorrhage resolve spontaneously. A total of 348 (0.54%) neonates had foveal haemorrhage which was potentially vision threatening. None of the screened neonates

had any significant adverse events during or after the examination. The abnormalities were classified into three types which are external eye and systemic abnormalities, abnormalities of the anterior segment and abnormalities of the posterior segment. Red reflex test detected 94.8% (492 out of 519 cases) of the anterior segment abnormalities. However, only 3.97% (614 cases out of 15 456) of the posterior segment abnormalities, such as persistent hyperplasia of primary vitreous (PHPV), severe RH and choroidal coloboma, were detected correctly by the red reflex test. Notably, 59.44% from the detected ocular abnormalities (accounting for 2.16% of all the screened population) required further intervention or observation. Among them, 258 patients (0.41% of all the screened population) needed immediate or timely intervention for severe conditions such as congenital cataract, retinal detachment, retinoblastoma and other ocular abnormalities. Additionally, 1098 patients (1.75% of all the screened neonates) required close follow-up and needed further diagnosis or intervention if necessary, such as retinopathy of prematurity (ROP) or ROP like retinopathy, familial exudative vitreoretinopathy (FEVR) and persistent hyperplasia of primary vitreous. A total of 5906 patients (9.4%) with minor clinical significance needed short term follow up. Wide Field Digital Imaging System demonstrated remarkable efficacy in detecting conditions that could potentially result in blindness or visual impairment as compared to standard method such as red reflex test (RRT. [22]

Vinekar et al (2015) in a cohort study "Universal ocular screening of 1021 term infants were imaged using wide-field digital imaging in a single public hospital in India aimed at assessing the feasibility of using wide-field digital imaging for universal ocular screening of neonates. This pilot study, conducted as part of the Karnataka Internet Assisted Diagnosis of Retinopathy of Prematurity (KIDROP) program, focused on infants born between September 1, 2013, and March 31, 2014. During this period, a total of 1,954 babies were delivered at the study hospital. Of these, the parents of 1,021 infants (52.3%) were present on the screening days and provided consent for their newborns to participate in the study. All enrolled infants were born at term with a birth weight exceeding 2000 grams. Screening was performed using the Retcam shuttle by technicians trained in infant eye imaging, with an average of 1,100 imaging sessions conducted monthly as part of the KIDROP program. Eligible study subjects were imaged within 72 hr of birth using Retcam shuttle (Clarity MSI, USA) to obtain anterior and dilated posterior segment images. Infants with abnormal images were examined clinically, and medical or surgical treatment was given when needed, at no cost to the family. During the study, 1,021 infants were screened, with 559 males (54.8%) and 462 females (45.2%). Remarkably, 96.9% of these deliveries were by Caesarean section, and only 3.1% were vaginal births. Ocular pathology was identified in 4.7% of the infants, with retinal haemorrhages being the most common finding, present in 2.4% of all babies screened. According to Egge's classification, the majority of these haemorrhages were classified as grade II. Additionally, a 'ROP-like ridge' was observed in 0.9% of the infants, which resolved spontaneously over eight weeks in all cases without progressing to ROP. Medical or surgical intervention of any form was required in 9 infants which accounted for 18.8% of abnormalities detected and 0.89 % of all 1021 babies screened. This percentage is primarily for conditions such as posterior uveitis and retinoblastoma. Two infants required surgical procedures one for a unilateral cataract and the other for retinoblastoma, both of which were treated successfully. The study concluded that universal eye screening using wide-field digital imaging is feasible and safe, advocating for national consideration of such screening programs to prevent undiagnosed visual morbidity. The researchers extrapolated their findings to the national scale, estimating that 226,950 infants in India would require treatment

for ocular conditions annually, highlighting the potential impact of implementing universal infant eye imaging strategies. [23]

A cross sectional study conducted by Leong et al. (2021) involving 203 healthy term newborn infants were screened for ocular abnormalities aim to evaluate the effectiveness of using wide-field digital retinal imaging system for neonatal eye screening. This study was conducted in Obstetric and Gynecology ward at Hospital Kuala Lumpur over a 6 months period (1 January to 1 June 2019). The inclusion criteria included neonate (age< 28days), born term (between 37 weeks, 0 days and 41 weeks,6 days), birth weight (≥2000g), APGAR score ≥7, any mode of delivery (e.g spontaneous vaginal delivery, assisted birth and caesarean section), stable vital signs, informed consent given by parent(s) for participation and able to comply to all requirements of the study protocol. Exclusion criteria include born pre-term, dysmorphic babies, syndromic babies, congenital diseases, complications intra and postpartum requiring intensive care and monitoring and unstable for an eye examination. Eligible study subject selected underwent an ocular examination within the first 72 hour or prior discharge. The examination list includes external eye examination, red reflex test and fundus imaging using a wide field digital retinal imaging system (Phoenix Clinical ICON Paediatric Retinal Camera) by a trained investigator. The pathologies detected were documented. They found ocular abnormalities in 34% of them, with retinal haemorrhages being the most common finding (29.6%), of which 53.3% occurred bilaterally. Other ocular abnormalities detected were subconjunctival haemorrhage, iris nevus, congenital hypertrophy of retinal pigment epithelium and vitreous haemorrhage. This study revealed spontaneous vaginal delivery (SVD) remained the greatest risk factor which has nearly 3.5 times higher risk of newborns developing retinal haemorrhage compared to Lower Segment Caesarean Section (LSCS). There was a 6% increased likelihood of developing retinal haemorrhage for every one minute increment in the duration of second stage of labour. The early detection capability of the imaging system enables timely intervention, potentially preventing long-term visual impairments. Overall, the study conclude that wide-field digital retinal imaging system is realistically possible, safe and useful in detecting posterior segment disorders. [24]

Sitorus et al (2021) conducted a cross sectional study in Indonesia aimed to identify ocular abnormalities in healthy newborns using wide field digital imaging system and to analyse factors associated with the findings. This study involved 1208 full-term newborns infant, conducted at two hospitals, Cipto Mangunkusumo National Referral Hospital and Koja Hospital in Jakarta Indonesia. The study subjects underwent fundus examinations within 48 hours of birth using RetCam Shuttle (Natus Medical Incorporated, USA). Retinal findings were documented and analysed according to obstetric and neonatal risk factors. The examination of the anterior segment revealed no abnormalities, and the infants maintained stable heart rates and oxygen saturation within 24 hours post-procedure, with no systemic complications arising from the use of topical mydriatics. Among the infants screened, 32 patients (7.3%) at CM Hospital and 118 (34.9%) at Koja Hospital were found to have ocular abnormalities. Retinal haemorrhage was the most common abnormality, observed in 6.88% of newborns at CM Hospital and 13.11% at Koja Hospital. Chorioretinitis was the second most common issue, occurring in 0.57% of infants, followed by macular haemorrhage in 0.33% of cases. Additional ocular abnormalities, including retinal exudate, maculopathy, suspected retinoblastoma, optic nerve head abnormalities, iris nodules, persistent pupillary membranes, and localised vitreous or peripapillary haemorrhage, were each found in one infant (0.08%). Among the cases of retinal haemorrhages, 64 infants (48.5%) had grade III retinal hemorrhages, 59 infants (44.7%) had grade II, and nine infants (6.8%) had grade I.

Univariate analysis showed caesarean section (C-section) (OR 0.27, 95% CI 0.18 to 0.41) was a protective factor against RH, while prolonged labor increased the risk of developing RH (OR 1.84, 95% CI 1.24 to 2.72). Further multivariate analysis showed similar protective association between C-section and risk of RH (OR 0.29, 95% CI 0.19 to 0.44), while other risk factors were not. APGAR score was not significantly associated with the incidence of retinal haemorrhages in either univariate or multivariate analysis. No significant associations were found between retinal haemorrhage and gender or instrument-assisted deliveries.[25]

Simkin SK et.al (2018) conducted a prospective observational study aimed to assess wide-field digital imaging (WFDI) for universal newborn eye screening (UNES) to determine the prevalence of neonatal ocular abnormalities in New Zealand. This study involved 350 infants born in Auckland District Healthboard (ADHB) National Women's hospital maternity ward and BirthCare, a community birth centre in Auckland, New Zealand between June 2015 and December 2016. Infants who were already enrolled in retinopathy of prematurity screening (infants born <30 weeks gestational age or <1250 g birth weight) were excluded from this study. A total of 346 infants with median age 2 days old completed screening using the RetCam (Natus Medical, San Carlos, California, USA) imaging system and images reviewed by an ophthalmologist via an established telemedicine methodology. All participating infants were clinically observed by qualified midwives, paediatricians or nurses for adverse events. To determine the prevalence of ocular abnormalities with 95% CI, and absolute precision of 5%, a minimum sample size of 323 infants was required. Therefore, the recruitment goal was 350 participating infants to account for possible cases of incomplete data, or attrition. In the UNES study, 350 newborn infants were recruited, and complete screening photos were obtained for 346 (99%) of them, with 205 being hospital-based and 141 from community settings. Over half of the infants (182/346) were delivered vaginally, with 23.6% (43/182) requiring instrumental intervention, while the rest were delivered by caesarean section. The study included 11 sets of twins, all of whom were analysed together. The prevalence of retinal haemorrhages (RH) at birth was 14.5% (50/346). Among these cases, 68% (34/50) had bilateral haemorrhages, and 32% (16/50) had unilateral haemorrhages, evenly distributed between the right and left eyes. Eight infants had RH involving both maculae. One case of dense pre-retinal haemorrhage (pre-RH) was noted. Statistical analysis revealed significant associations between RH and delivery method ($p<0.001$), induction of labor ($p<0.001$), and screening within 72 hours of birth ($p=0.014$). No significant differences were found in RH occurrence based on ethnicity ($p=0.602$) or gender ($p=0.26$). While there appeared to be a slight association between higher gestational age and RH ($p=0.042$), it was not clinically significant. Infants screened in community settings were more often screened before 72 hours, correlating with a higher prevalence of RH (25%) compared to those screened in hospitals (8.3%) ($p<0.001$). Follow-up was completed by 66% (33/50) of the infants with RH, with a median follow-up time of 50 ± 14 days and an interquartile range (IQR) of 43 to 59 days. At follow-up, 94.0% (31/33) of the infants showed complete resolution of RH. The two infants with persistent RH were initially classified as having extensive RH following ventouse delivery; their RH took an additional three months to fully resolve. Ocular abnormalities with potential visual or systemic impact were identified in five infants (1.4%). These included congenital cataract, suspected choroidal hemangioma, congenital hypertrophy of the retinal pigment epithelium (CHRPE), and two cases of suspected optic nerve hypoplasia. The study demonstrates that wide-field digital imaging is a viable method for detecting ocular abnormalities in newborns, offering potential benefits over traditional red reflex screening, which has a low sensitivity for posterior ocular abnormalities. The use of this

imaging technology in both hospital and community settings in New Zealand highlights its feasibility and effectiveness in a universal screening program. [26]

Goyal P et al. (2018) conducted a cross sectional study, aimed to evaluate the outcomes of universal newborn eye screening using a wide-field digital retinal image (WFDI) system in Eastern India. This pilot study involved a total of 1,152 apparently healthy newborn infants, all under 28 days of age, delivered either vaginally on the same or previous day or by caesarean section within the past three days. The study was conducted over 1.5 years from March 2014 to October 2015 in obstetrics and gynecology service of a civil hospital in Bhubaneswar, Eastern India. Eligible study subjects underwent external eye examinations, red reflex tests, and fundus imaging using the wide field digital retinal imaging (Retcam II, Clarity Medical System, Pleasanton, CA, USA) by a trained optometrist who took safety precautions while handling these babies, assisted by a standby nurse. The images captured were analysed by an ophthalmic resident, and images with positive findings were further reevaluated and cross-checked by a paediatric retina specialist. The pathologies detected, net monetary gain and skilled manpower saved were documented. The amount of time saved by screening on site by a photographer or ophthalmology resident and reading of the images later by a pediatric retina specialist was estimated. The study found ocular abnormalities of any kind in 172 (14.93%) infants, with retinal haemorrhage being the most common abnormality, observed in 153 babies (88.9% of all abnormal findings). It was bilateral in 118 (77.12%) babies and four babies had foveal haemorrhage. Other abnormalities included vitreous haemorrhage (n=1), congenital glaucoma (n=2), uveal coloboma (n=2), retinopathy mimicking retinopathy of prematurity (n=2) and cystic fovea (n=3). Retinal haemorrhage resolve spontaneously in all eyes. This early detection facilitated timely interventions, directly or indirectly helped seven babies, including one saved from blindness due to congenital glaucoma. None of the babies had any significant adverse events after the examination. They calculated the overall expenses for the usage of equipment, manpower, stationeries, and other accessories, which amounted to INR 845 000 (US$ 12 612 at 1 US$=INR 67.00). Considering an average life expectancy of an Indian at 70 years, the minimum average monthly per capita income at INR 3000 (US$ 45.00) and the extra living cost of maintaining life of a blind person at another INR 3000/month, the estimated loss incurred due to a child going blind at INR 5.04 million (US$ 75 224). Hence, the net monetary gain was INR4.195 million (US$ 62 612). The use of WFDI saved 319.4 hours of skilled manpower and generating a net monetary gain of INR 4.195 million (US$ 62,612). Compared to traditional methods like the red reflex test, WFDRI demonstrated a significant advantage in identifying pathologies that required immediate care or follow-up, underscoring its promise as a valuable tool in neonatal eye care. [10]

In a cross-sectional study conducted by Ma et al. (2018), which evaluated the prevalence of ocular abnormalities in infants around six weeks of age in China. A total of 481 infants around 6 weeks of age were included in the study, which took place in a public hospital in Beijing, China between April 2015 to August 2016. All patients underwent comprehensive eye examinations, including vision assessment, eye position check, external eye examination, pupillary light reflex, red reflex examination, and examination of the anterior and posterior ocular segments using a flashlight, ophthalmoscope, and wide-field digital imaging system (RetCam 3). During the study, 481 infants (52.6% male, 47.4% female) were screened, including 408 full-term (84.8%) and 73 premature (15.2%) infants. Low birth weight (less than 2500 g) was noted in 10.4% of infants, while 8.5% had macrosomia (birth weight $\geqslant$4000 g). Vaginal delivery occurred in 57.4% of cases, with Caesarean section accounting for 42.6%. Hypoxia at birth (Apgar score <8) was observed in 2.3% of infants. The 73 preterm infants

had an average birth weight of 2400.0 ± 459.5 g and a gestational age of 35.2 ± 1.4 weeks. Of the 1785 eligible newborns, 481 participated in the ocular screening, resulting in a 26.9% participation rate. The main reasons for non-participation were concerns about the necessity of the exam and potential adverse effects. Ocular abnormalities were detected in 198 infants (41.2%), with the most common being retinal white spots (42.9% of abnormalities, 17.7% of all screened infants) and retinal haemorrhages (16.2% of abnormalities, 6.7% of all screened infants). Other conditions included concomitant exotropia, retinal pigmentation, and retinopathy of prematurity (ROP). Intervention was required for 22 infants (4.6% of all screened), and 8 were referred to dermatologists for further evaluation. Most retinal white spots resolved spontaneously by 12 months, with similar outcomes for retinal and vitreous haemorrhages. ROP was detected in 9 preterm infants (18 eyes), with one case requiring photocoagulation. The RetCam system demonstrated exceptional effectiveness in the early detection of treatable conditions, such as congenital cataracts and Familial Exudative Vitreoretinopathy (FEVR), allowing for timely surgical interventions that prevent visual impairments like amblyopia and nystagmus. Based on this study, intervention of any form was required in 22 infants, which accounted for 11.1% (22/198) of abnormalities detected and 4.6% (22/481) of all screened infants. Wide-field digital imaging significantly enhanced detection sensitivity compared to traditional methods, such as the red reflex examination.[27]

In the cross-sectional study by Tang H et al. (2018), the effectiveness of fundus examination using the RetCam wide-field digital imaging system was assessed in a cohort of 199,851 newborns across eight centers in China, conducted between January 2009 and July 2017. The study aimed to implement digital imaging for ocular screening and describe abnormal findings. It compared the RetCam system to the traditional Red Reflex Test (RRT), highlighting its superiority in detecting posterior ocular abnormalities. The RetCam system successfully identified a range of conditions, from common issues like severe retinal haemorrhage to rare disorders such as familial exudative vitreoretinopathy and retinoblastoma. This study found 18,198 (9.11% of screening neonates) prevalence of ocular abnormalities, with severe retinal haemorrhage accounted for 6.41% of all screened neonates and 70.39% of all abnormal cases. Among these cases, 1279 cases involved macular haemorrhage. A study on ocular abnormalities in infants revealed that familial exudative vitreoretinopathy (FEVR) was detected in 217 infants, making up 1.19% of all abnormalities observed. Persistent hyperplasia of the primary vitreous was found in 29 infants, accounting for 0.16% of the abnormalities. Various congenital ocular defects were also identified, including choroidal coloboma in 98 infants, persistent pupillary membranes in 105 infants, and congenital cataracts in 40 infants. The most severe condition, retinoblastoma, was diagnosed in 5 newborns. Other conditions observed included retinal dysplasia (1.06%), subconjunctival hemorrhage (1.41%), abnormal fundus pigmentation (8.20%), and retinal exudative changes (6.91%). Additionally, some pathologies remained undefined, potentially caused by infectious factors, and represented 2.21% of all abnormal findings. All affected infants were referred to ophthalmology departments or specialised hospitals for early intervention to address these conditions. This study also examined the influence of delivery methods and outcomes in premature or low birth weight infants. The study also found a significant relationship between the mode of delivery and the occurrence of retinal haemorrhage (RH) in newborns. It showed that 87.4% of newborns with severe RH were delivered vaginally while only 46.7% of the normal neonates were delivered by this route ($p<0.001$). This suggests that birth trauma associated with vaginal delivery is a major contributor to RH in newborns. Additionally, the study highlighted the effectiveness of the

RetCam system in capturing detailed retinal images, providing ophthalmologists with crucial information for early diagnosis and intervention to prevent long-term visual impairments. [28]

Li HL et al. (2013) conducted a cross-sectional study to detect ocular pathology in healthy full-term newborns in China. A total of 3,573 healthy full-term infants, around 6 weeks of age, were included in the study between May 2010 and June 2011 at the Kunming Maternal and Child Healthcare Hospital in Kunming, Yunnan province, China. Eligible subjects underwent an ocular examination within 42 days after birth using a flashlight, retinoscope, handheld slit lamp microscope, and the RetCam wide-field digital imaging system (Clarity Medical Systems, Pleasanton, California, USA). The external eye, pupillary light reflex, red reflex, opacity of refractive media, and anterior and posterior segments were also examined. The study found 871 abnormal cases (24.4%), with retinal haemorrhages being the most common, occurring in 769 cases (21.53%), including 215 cases (6%) of Grade 3 retinal haemorrhage and 67 cases (1.9%) involving macular haemorrhage. Additionally, 107 infants (2.99%) had visually threatening ocular abnormalities, 28 of which were associated with retinal haemorrhage. The study also identified other significant ocular pathologies that would likely be missed on RRT alone, especially discrete abnormalities of the optic nerve or peripheral ocular pathology, such as retinal hamartoma versus retinoblastoma, familial exudative vitreoretinopathy (FEVR), and retinopathy due to infections like cytomegalovirus. The ability to capture detailed retinal images provided valuable information for early diagnosis and intervention, emphasizing the potential for wide-field digital imaging to enhance neonatal ocular healthcare by improving early detection and treatment outcomes. [29]

5.2 SAFETY

There were six evidences retrieved on the safety of WFDI as screening tool for universal neonatal eye screening.

In terms of safety, Retcam Envision was registered as **Class II medical device by USFDA** for general ophthalmic imaging including retinal, corneal and external imaging, photodocumentation of pediatric ocular diseases including retinopathy of prematurity (predicate device: Retcam 3; Retcam shuttle; Retcam Portable (K182263). [30]

The PanoCam LT (Visunex Medical System) widefield handheld system is now approved in the United States and offers a wireless, contact-based system for newborn widefield imaging (130˚). [14] According to the safety assessment, WFDI was generally safe and effective tool for neonatal eye screening, with no significant adverse events reported from the screening procedure conducted. In a cross-sectional study by Leong et al. (2021), there was no reported adverse effect from the screening procedure conducted on these healthy term newborns. Previous studies showed that systemic effect were mild and resolved spontaneously. [24] This imaging process involves non-invasive techniques and can be performed by trained technicians, reducing the need for extensive handling or invasive procedures.[23]

In a cohort study conducted by daCunha LP et al. (2021) to compare WFDI with red reflex test for universal newborn eye screening in Brazil as described earlier suggests that WFDI is safe and effective tool for newborn eye screening. Its ability to detect subtle abnormalities and its non-invasive nature make it a valuable alternative to traditional methods like red reflex

test. The rare side effects associated with pupil dilation are outweighed by the benefits of early detection and treatment of potentially serious ophthalmic conditions. Implementing WFDI in neonatal screening programs aligns with global health initiatives aimed at reducing preventable blindness in children. [2]

Simkin SK et al. (2018) reported no episodes of allergic reaction, significant bradycardia or corneal abrasions were identified at or after screening. In addition, there were no reports of adverse events to the screening team, throughout the period that screening was being undertaken.[26] Goyal et al. (2018) reported none of the babies had any significant adverse events after the examination.[10]

Studies conducted in various countries, including India, China, and New Zealand, have confirmed the safety and practicality of implementing widefield digital imaging as part of neonatal screening programs. [23, 24, 26]

5.3 ORGANISATIONAL ISSUES

In terms of organisational, WFDI procedures are primarily performed by trained ophthalmologists or specialised technicians, with some involvement of neonatal nurse technicians in certain studies. Photodocumentation by a technician with remote expert interpretation is an effective telemedicine screening tool for early detection of eye diseases like diabetic retinopathy and retinopathy of prematurity. [2, 22, 23, 10, 4, 29.]

The implementation of widefield digital imaging systems presents several organisational challenges, particularly in resource-limited settings. One of the primary concerns is the lack of trained professionals such as ophthalmologist and paediatricians to operate these advanced imaging systems effectively. In countries with resource-limited settings like India and Brazil, the lack of specialised staff limits the coverage and effectiveness of universal eye screening program. [4, 23]. The study points out that the successful deployment of WFDI requires specialised training, which can be a significant barrier for healthcare facilities that do not have access to adequately trained personnel, such as ophthalmologists and paediatricians. [2]

Hafaeli LM et al. (2022) reported that the implementation of universal WFDI worldwide remains uncertain, as many ocular abnormalities detected through universal screening are temporary and may not impact visual development. However, certain aspects of the Brazilian healthcare system may justify the implementation of universal WFDI in the country. Firstly, most deliveries occur in hospital settings, and newborns typically remain in the maternity ward for at least 48 hours before discharge, providing a valuable timeframe for screening. Secondly, similar to the situation in India, Brazil has a significant shortage of trained professionals to conduct the current screening methods (red reflex test and indirect binocular ophthalmoscopy), making it difficult to ensure comprehensive coverage for all newborns. Lastly, the referral networks in Brazil are often inefficient, leading to delays in diagnosis and treatment. Considering Brazillian scenario, universal WFDI could be a solution to improve the quality and efficiency of neonatal screening, especially because a reading centre based in a tertiary hospital may facilitate referral and consequently treatment of blinding eye disease. [4]

The feasibility of implementing WFDI on a large scale is questioned in several studies. The logistics of deploying the equipment, training staff, and ensuring consistent quality across

different locations present significant challenges. This is especially true in large, diverse countries where healthcare infrastructure varies widely. [23, 4]

Recent guidelines on universal neonatal eye screening (UNES) have emerged as a significant focus in global health, particularly highlighted by the World Health Organization (WHO). In 2022, WHO included neonatal eye screening in their updated postnatal care guidelines, marking the first time such a recommendation was made at the global level. This inclusion emphasise the importance of early detection of eye conditions, which can be critical in preventing long-term visual impairment or blindness. The WHO's guidelines advocate for eye screenings to be conducted before newborns are discharged from health facilities or during the first postnatal care visit for those born at home. This screening typically includes a red reflex test, which is essential for detecting congenital cataracts and other serious eye conditions. The WHO has also rolled out specific implementation guidance for universal newborn screening in regions like South-East Asia. This guidance supports the integration of eye screenings into existing healthcare systems and emphasise the need for capacity-building, training, and the use of appropriate, non-invasive tools. The global push for UNES reflects growing awareness of the impact early eye care can have on a child's development, aiming to ensure that every newborn has the opportunity to receive timely and potentially sight-saving treatment. [31, 32, 33]

In United Kingdom (Royal College of Ophthalmologists & the British Paediatric Association 1994) and the United States of America (American Academy of Pediatrics, Section on Ophthalmology, American Association for Pediatric Ophthalmology & Strabismus, American Academy of Ophthalmology, American Association of Certified Orthoptists 2008), the recommendation is to perform red reflex testing (RRT) at birth or thereafter. [23]

5.4 ECONOMIC IMPLICATION

There was no evidence retrieved on cost effectiveness with only one budget impact analysis retrieved, and one cost analysis study related to the economic implication of the use of wide field digital imaging (WFDI) in universal neonatal eye screening.

Haefeli LM et.al (2022) conducted a budget impact analysis study using a static model aimed to asses incremental cost and effectiveness of implementing portable WFDI for screening neonatal visual impairment causes in Brazil. A budget impact analysis was performed comparing WFDI against existing screening methods, namely red reflex test (RRT) and indirect binocular ophthalmoscopy (IBO), considering all babies born in government maternity wards from 2020 to 2024. A total of 24 maternity wards were identified, with 92% having implemented a retinopathy of prematurity (ROP) screening program. The study population was divided into three hypothetical screening strategies: RRT for all newborns except those needing ROP screening, IBO specifically for ROP screening, and WFDI for all newborns. This study found WFDI offers higher sensitivity in detecting eye conditions compared to traditional methods like the red reflex test, which has low sensitivity and insufficient coverage due to a lack of trained professionals. Additionally, the study highlighted that WFDI could improve screening accuracy and accessibility while remaining cost-effective, given the potential to reduce the incidence of blindness and improve child development outcomes. They assessed financial impact of integrating WFDI into government maternity wards in Rio De Janeiro focusing on conditions like retinopathy of prematurity (ROP), cataracts, and glaucoma, which

are major contributors to childhood blindness and visual impairment. The primary outcome was the direct cost of indirect binocular ophthalmoscopy, red reflex test and portable WFDI screening comprising all babies born in Rio de Janeiro's government maternity wards. The secondary outcome was the budget impact of implementing portable WFDI screening in Rio de Janeiro, Brazil. This cost analysis included human resources, capital, consumables, and transportation, estimating the total cost per examination at US$34.36 for IBO, US$0.75 for RRT, and US$14.19 for WFDI. The study highlighted efficiency gains through WFDI training, reducing examination time by nearly 50%. They projected a total budget impact of US$3,820,706.04 ranging from US$3,139,844.34 to US$6,099,510.35 between 2020 and 2024 considering 100% coverage of maternity wards. The incremental cost would be US$3,124,457.28, ranging from US$2,714,492.26 to US$4,880,608.63. The study's finding can assist decision-makers in assessing the feasibility of implementing this strategy within their municipalities. Further economic evaluations was suggested to confirm the affordability of this screening strategy in the Brazilian setting. [4]

In the study conducted by Goyal P et. al (2018) cost analysis conducted highlighted the benefits of universal eye screening, including savings in skilled manpower amounting to 319.4 hours or 35.5 working days, resulting in a net monetary gain of INR 4.195 million (US$ 62,612). The results indicate that screening with WFDRI is promising, as it detected pathologies needing immediate care or regular follow-up, ultimately saving skilled manpower with significant financial benefits.

Wittenborn et al. (2013) estimated the total economic burden of eye disorders in children younger than 18 years old in United State was $5.9 billion per year. This includes $2.6 billion in direct costs, which cover medical expenses for diagnosed eye disorders, costs of vision aids like glasses and contact lenses, special education services, and school vision screening programs. Indirect costs amounted to $3.3 billion, primarily due to productivity losses from caregivers needing to take time off work to care for affected children and the value of unpaid informal care. This study estimated that vision disorders in children result in a loss of approximately 81,000 quality-adjusted life years (QALYs) annually. This metric reflects both the reduced quality and quantity of life experienced by children with vision impairments. A benchmark of $50,000 commonly is cited for societal willingness to pay per QALY gained by health care. Based on this benchmark, the study calculates the quality-of-life losses from vision impairment and blindness for children to be $4.1 billion. [34]

In Peru, Dave HB et al. in a study reported that the lifetime burden of raising visually impaired children due to ROP is significant, with a calculated cost of $123,806 per child. This burden includes both the lost productivity of the individual and the costs of informal care provided by family members. Additionally, the national lifetime burden of raising all visually impaired children following retinopathy of prematurity was estimated to be $516 million. [35] According to paediatric ophthalmologist, a unit of widefield digital retinal imaging is estimated to cost around RM550,000, and there will be additional cost for telemedicine programme software.

5.5 PARTIAL ECONOMIC EVALUATION

Method

This partial economic evaluation was conducted using local context to compare the costs and outcomes of Wide Field Digital Eye Imaging (WFDI) versus the conventional Red Reflex Test (RRT) for universal neonatal eye screening in Malaysia.

Study designs and population

The number of newborns eligible for universal neonatal eye screening in Malaysia was estimated for 2026–2030 using autoregressive integrated moving average (the ARIMA model) based on a 15-year time live birth series (2008–2022) as per table below.

Year	Number of newborns
2008	493,203
2009	501,644
2010	491,239
2011	511,594
2012	526,012
2013	503,914
2014	528,612
2015	521,136
2016	508,203
2017	508,685
2018	501,945
2019	489,863
2020	471,504
2021	439,744
2022	423,124

Table 4: Prevalence of preterm babies and average life expectancy

Parameter	Value	Reference
Prevalence of preterm babies	6.63%	Ravichandran J & Shamala DK (2022)

Table 5: Cost analysis based on a static model

Clinical pathway study model was conceptualized based on population parameters, diseases burden, equipment accuracy tests, costs associated with the screening models. The cost of adoption of WFDI was compared with a reference scenario based on RRT.

Clinical pathway

The clinical pathway for implementing Wide-Field Digital Eye Imaging (WFDI) in universal ocular screening for newborn babies in Malaysia, as depicted in the Figure 1, illustrates a bifurcated approach based on the presence or absence of Retinopathy of Prematurity (ROP) risks. All newborns are initially evaluated for ROP risks. Those identified with ROP risks—such as infants with a birth weight of less than 1750 grams, gestational age below 34 weeks, or an unstable clinical course—will directly undergo Binocular Indirect Ophthalmoscopy (BIO), the conventional gold standard performed by an ophthalmologist.

For newborns without ROP risks, two potential screening methods are considered. The current practice involves the Red Reflex Test (RRT), conducted by paediatricians or paediatric medical officers. If the RRT identifies any abnormalities, the newborns are then referred for full screening via BIO. However, should WFDI be implemented, it would replace RRT for these babies. WFDI, performed by two trained nurses, would capture digital images of the infant's eyes, which are subsequently sent to an ophthalmologist for interpretation according to the latest Clinical Practice Guidelines (CPG) 2023.

The sensitivity of WFDI, at 77%, is significantly higher than RRT, which has a sensitivity of only 0.77%. This improved sensitivity suggests that WFDI would identify a larger number of true positives, ensuring more accurate detection of ocular abnormalities. Newborns who test positive for any ocular abnormalities through WFDI would then undergo further evaluation using BIO. Conversely, any negative results from WFDI could still miss some cases, leading to false negatives, similar to the RRT. This pathway highlights the potential for WFDI to enhance the early detection of ocular issues among newborns, although it also introduces additional steps and costs that would need to be considered in a comprehensive budget impact analysis.

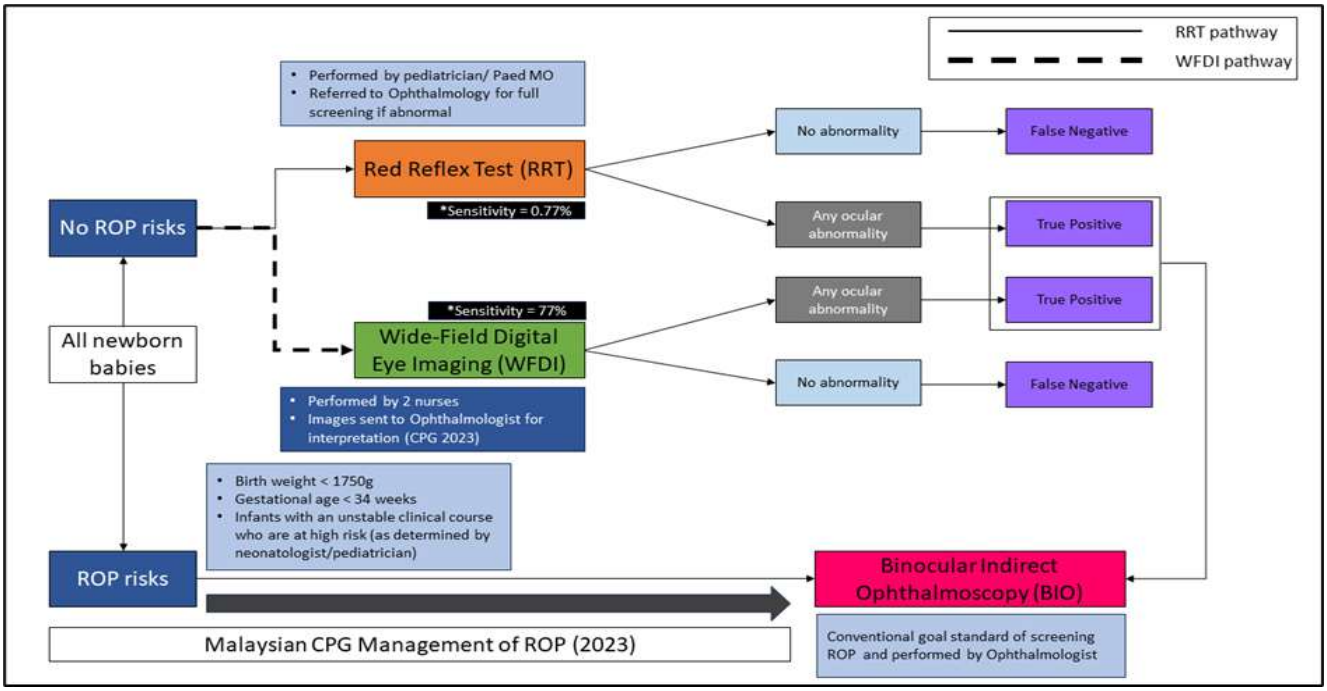

Figure 6: The clinical pathway for hypothetical universal ocular screening in Malaysia

Step-by-Step Calculation

To derive the final results for the cost impact analysis of implementing Wide-Field Digital Eye Imaging (WFDI) for universal ocular screening of newborns in Malaysia, the following steps were undertaken:

Step 1: Estimating the number of newborns eligible for screening

The number of newborns eligible for screening was projected for the years 2026–2030 using an Autoregressive Integrated Moving Average (ARIMA) model, based on historical data from 2008–2022. The ARIMA model estimated the total number of newborns over the five years as shown below:

Step 2: Determine the Prevalence of ROP Risks

It was determined that 6.63% of all newborns would be at risk for Retinopathy of Prematurity (ROP) for being born in prematurity (Ravichandran J & Shamala DK 2022). These newborns would be directly screened using BIO, the gold-standard method for diagnosis ROP. The total number of newborns with ROP risks was calculated as:

-Total Newborns with ROP Risks (2026–2030) x 6.63/100

Step 3: Calculating the number of babies screened using WFDI or RRT

Newborns without ROP risks would be screened using either WFDI or RRT. The number of such screenings was calculated by subtracting the number of ROP risk babies from the total newborns each year:

-Total Newborns without ROP Risks (2026–2030): Total newborns – total newborns with ROP risks

Step 4: Estimating the cost of Screenings (WFDI, RRT, BIO)

The cost of screening for each method was calculated based on per-screening costs. These cost estimates comprehensively include essential components such as human resources, capital expenditures, consumables, and transportation. The figures were derived from existing literature and have been adjusted and converted as necessary for the current analysis. This ensures that the estimates accurately reflect the actual operational demands of the screening process. These costs were multiplied by the number of screenings to estimate the total screening costs.

Screening Cost	Cost	Reference
Cost WFDI per screening*	RM 49.48	Haefeli et al (2022); CCEMG–EPPI Centre Cost Converter
Cost BIO per screening*	RM 119.82	Haefeli et al (2022); CCEMG–EPPI Centre Cost Converter
Cost RRT per screening*	RM2.62	Haefeli et al (2022); CCEMG–EPPI Centre Cost Converter

Table 6: *Converted into MYR from reference article and adjusted for 2024. The price is assumed as indices to *unit cost of human resources, capitals, consumables and transportation.*

Step 5: Apply sensitivity and calculate TP and FN for WFDI and RRT

Accuracy parameters	Sensitivity	Reference
Sensitivity of Red Reflex Test (RRT)	0.77% (0.02–4.21)	Kenneth TKL et al. 2021
Sensitivity of Wide Field Eye Digital Imaging	77% (0.69–0.84)	Wang et al. 2021

True Positives (TP) and False Negatives (FN) were calculated using the sensitivity and the total number of abnormalities detected by each method.

TP and FN for WFDI:

True Positives = Total number of abnormalities detected x 0.77
False Negatives = Total number of abnormalities detected x (1 - 0.77)

TP and FN for RRT:

True Positives = Total number of abnormalities detected x 0.0077
False Negatives = Total number of abnormalities detected x (1 - 0.0077)

RESULTS

The estimated newborn babies based on ARIMA year 2008-2022 are projected for 2026 to 2030 as per ***Table 4.***

Year	Number of newborns	CI Lower	CI Upper
2026	423,072	366,045	480,098
2027	423,065	360,712	485,419
2028	423,061	356,034	490,088
2029	423,058	351,848	494,269
2030	423,055	348,029	498,082
	2,115,311	1,782,668	2,447,956

Table 7: The estimated number of newborn and their confidence intervals for 2026 to 2030 (forecasted)

Year	Total screened by WFDI or RRT	Total screened for ROP	WFDI followed by BIO	RRT followed by BIO
2026	395022	28,050	131,467	29084
2027	395016	28,049	131,464	29083
2028	395012	28,049	131,463	29083
2029	395009	28,049	131,462	29083
2030	395006	28,049	131,461	29083
	1,975,066	**140,245**	**657,317**	**145,416**

Table 8: Number of babies screened by respective techniques (RRT vs WFDI vs BIO)

	WFDI screening cost	RRT screening cost	BIO screening cost	
			+ WFDI abnormalities	+ RRT abnormalities
2026	RM19,545,704.71	RM1,034,958.50	RM15,752,318.26	RM3,484,825.95
2027	RM19,545,381.31	RM1,034,941.37	RM15,752,057.63	RM3,484,768.30
2028	RM19,545,196.52	RM1,034,931.59	RM15,751,908.70	RM3,484,735.35
2029	RM19,545,057.92	RM1,034,924.25	RM15,751,797.00	RM3,484,710.64
2030	RM19,544,919.32	RM1,034,916.91	RM15,751,685.30	RM3,484,685.93
	RM97,726,259.78	**RM5,174,672.61**	**RM78,759,766.90**	**RM17,423,726.16**

Table 9: The cost estimation for WFDI vs RRT vs BIO

Table 10 presents a cost estimation analysis for implementing a screening program, showing the projected costs under different scenarios: maximum case, base case, and minimum case, across varying levels of coverage (100%, 75%, and 50%). In the base-case scenario, based on average parameters over five years, the estimated cost is RM 19,545,251.96 for 100%

coverage. This cost decreases to RM 14,658,938.97 at 75% coverage and RM9,772,625.98 at 50% coverage.

In the maximum-case scenario, which assumes the highest number of newborns and a 50% increase in screening costs, the total cost at 100% coverage is estimated to be RM 36,337,458.86. At 75% coverage, the cost decreases to RM 27,253,094.15, and further drops to RM 18,168,729.43 at 50% coverage. Meanwhile, in the minimum-case scenario, where the lowest number of newborns and a 50% reduction in screening costs are considered, the cost is estimated at RM 8,820,641.26 for full (100%) coverage. The cost drops to RM 6,615,480.95 at 75% coverage and RM 4,410,320.63 at 50% coverage.

Scenario by	100% coverage	75% coverage	50% coverage
Maximum case**	RM36,337,458.86	RM27,253,094.15	RM18,168,729.43
Base case*	RM19,545,251.96	RM14,658,938.97	RM9,772,625.98
Minimum Case***	RM8,820,641.26	RM6,615,480.95	RM4,410,320.63

** Average of the parameter by five years course*

***Increases considered by upper CI of newborns and screening cost by 50%*

****Reduction considered by lower CI of newborns and screening cost by 50%*

Table 10: Cost estimation by worst, base and best-case scenario according its coverage

DISCUSSION

The analysis conducted on the potential implementation of Wide Field Digital Eye Imaging (WFDI) as a universal ocular screening tool for newborns in Malaysia presents significant insights, particularly when compared to the current standard practice of the Red Reflex Test (RRT). This discussion aims to critically evaluate the findings, highlighting the cost implications, the practicality of implementation, and considerations for policymakers.

The cost analysis reveals a substantial difference between the implementation costs of WFDI and RRT. WFDI, with a per-screening cost of RM 49.48, incurs significantly higher expenses compared to RRT, which costs only RM 2.62 per screening. Over the projected period from 2026 to 2030, the total cost of implementing WFDI screening is estimated at RM 97,726,259.78, while RRT screening is projected to cost RM 5,174,672.61. This disparity in costs is largely driven by the higher sensitivity of WFDI (77%), which allows for the detection of a greater number of true positive cases, leading to a more comprehensive screening process.

The sensitivity analysis further explores the financial implications under different scenarios of newborn coverage and cost variability. In the base-case scenario, which assumes average parameters over the five-year course, the total cost of WFDI at 100% coverage is RM 19,545,251.96. However, in the worst-case scenario, where both the number of newborns and screening costs are increased by 50%, the cost rises sharply to RM 36,337,458.86. Conversely, in the best-case scenario, which considers a 50% reduction in both parameters, the cost drops to RM 8,820,641.26. These variations underscore the potential financial burden of adopting WFDI, depending on the specific circumstances of implementation. While the superior sensitivity of WFDI presents clear clinical benefits in terms of early detection, the associated costs present a significant challenge. The current analysis focuses solely on the

costs of screening, deliberately excluding treatment costs to avoid the potential bias of overestimating the financial burden based on assumptions about the necessity of interventions following the detection of ocular abnormalities. This focus on screening costs is methodologically sound, as it provides a clear and unbiased comparison of the financial implications of adopting WFDI versus continuing with RRT.

However, the high cost of WFDI raises questions about its practicality. Well considerations are warranted whether the increased costs associated with WFDI can be justified by the potential long-term benefits of improved early detection. The sensitivity analysis highlights that even under more favourable cost conditions (as in the best-case scenario), the financial outlay remains substantial. Moreover, while the sensitivity and specificity of WFDI are relatively high, no diagnostic test is infallible. False positives can lead to unnecessary anxiety and additional diagnostic procedures, while false negatives could result in missed diagnoses and delayed treatment. Therefore, the operational efficiency and accuracy of the screening program must be continuously monitored and evaluated. Given the high cost of implementing a universal screening program using WFDI and the scarcity of local data, several strategies could be considered to optimize the cost-effectiveness and feasibility of neonatal ocular screening:

***1. Targeted screening for high-risk groups*:** Rather than implementing universal screening, focusing on high-risk groups could be more cost-effective. High-risk groups may include newborns with a family history of ocular diseases, premature infants, or those with other risk factors identified through prenatal and perinatal assessments.

2. Pilot programs and phased implementation: Implementing pilot programs in selected hospitals or regions can provide valuable data on the feasibility, cost, and effectiveness of the screening program. A phased approach allows for adjustments based on initial findings and can help manage costs and logistics more effectively.

***3. Cost-effectiveness analysis of alternative screening methods*:** Conducting comparative studies on the cost and effectiveness of different screening methods, such as RRT and WFDI, can help identify the most efficient strategy. However, more detailed data in terms of cost and effectiveness are required for a robust analysis. Combining methods may also enhance overall screening accuracy and coverage.

These findings should be interpreted with caution. The scarcity of local data, the high cost of WFDI implementation, and the inherent limitations of diagnostic tests must be carefully weighed. Future research should aim to generate more robust local data, explore cost-effective screening strategies, and evaluate the long-term sustainability of such programs. Only with a comprehensive and balanced approach can we ensure that the cost-effectiveness of neonatal screening for ocular abnormalities are fully realized in the Malaysian healthcare context.

5.6 LIMITATIONS

We acknowledge some important limitations in our review and these should be considered when interpreting the results. The selection of the studies and appraisal was done by a

reviewer. Although there was no restriction in language during the search, only the full text articles in English published in peer-reviewed journals were included in the report, which may have excluded some relevant articles and further limited our study numbers. Most of the follow-up in these studies was relatively short, limited to approximately one year, which does not allow drawing any conclusions for a longer period of time.

Based on evidences from this study, the outcome measured is scarce and lack of long term outcome. Furthermore, diagnostic accuracy is not quantified and not being compared to gold standard. Heterogeneity was also observed among the studies geographical location, which can be attributed mainly due to different level of healthcare infrastructure. The studies are conducted in different countries, including Brazil, India, China, and others, each with varying levels of healthcare infrastructure. The availability of trained professionals such as ophthalmologists and nurse technicians varies greatly across the studies. In some countries, like Brazil and India, there is a notable shortage of trained personnel, which complicates the implementation of WFDI systems. In contrast, other studies may have been conducted in regions with better access to trained professionals.

6.0 CONCLUSIONS

A substantial fair level of retrievable evidence demonstrated that WFDI as compared to RRT and IBO is a safe and well-tolerated screening modality in UNES and effective in providing good detection rate of ocular abnormalities that usually missed by RRT. Organisational issues such as trained personel, referral mechanism, economic evaluation, feasibility and cost in implementing UNES using WFDI need to be considered judiciously.

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8.0 APPENDIX

APPENDIX 1: LITERATURE SEARCH STRATEGY

OVID MEDLINE® ALL <1946 to May 13th 2024>

Search Strategy:

1 INFANT, NEWBORN/ (680053)
2 neonate*.tw. (109268)
3 newborn*.tw. (186679)
4 (newborn* adj1 infant*).tw. (27853)
5 VISION SCREENING/ (2493)
6 (vision adj1 screen*).tw. (1564)
7 (newborn adj2 eye screen*).tw. (17)
8 or/1-7 (785801)
9 IMAGE PROCESSING, COMPUTER-ASSISTED/ (142091)
10 (biomedical adj2 image proces*).tw. (76)
11 (medical adj2 image proces*).tw. (774)
12 (digital adj2 image proces*).tw. (1652)
13 ((biomedical or medical or digital) adj2 image proces*).tw. (2489)
14 (image adj1 reconstruct*).tw. (11847)
15 ((computer-assisted or computer assisted) adj3 image process*).tw. (130)
16 (medical adj2 image process*).tw. (774)
17 OPTICAL IMAGING/ (15454)
18 (fluorescence adj1 image*).tw. (3076)
19 (autofluorescence adj 1 image*).tw. (0)
20 (optical adj1 image*).tw. (1970)
21 ((fluorescence or autofluoresce) adj1 image*).tw. (3076)
22 (fundus adj2 autofluorescence image*).tw. (149)
23 wide field digital.tw. (73)
24 17 or 18 or 19 or 20 or 21 or 22 or 23 (20297)
25 8 and 24 (106)

Other Databases

PubMed
INAHTA
US FDA

} Same MeSH and keywords as per MEDLINE search

APPENDIX 2: HIERARCHY OF EVIDENCE FOR EFFECTIVENESS

DESIGNATION OF LEVELS OF EVIDENCE

I	Evidence obtained from at least one properly designed randomized controlled trial.
II-I	Evidence obtained from well-designed controlled trials without randomization.
II-2	Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one centre or research group.
II-3	Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s) could also be regarded as this type of evidence.
III	Opinions or respected authorities, based on clinical experience; descriptive studies and case reports; or reports of expert committees.

SOURCE: US/CANADIAN PREVENTIVE SERVICES TASK FORCE (Harris 2001)

APPENDIX 3: EVIDENCE TABLE

Evidence Table : Effectiveness/ safety/ economic implication
Question : What is the effectiveness, safety, and cost-effectiveness of wide field digital eye imaging for universal newborn eye screening

Bibliographic Citation	Study Type/ Methods	LE	Number of Patients & Patient Characteristic	Intervention	Comparison	Length of Follow-up (if applicable)	Outcome Measures/ Effect Size	General Comments
1. DaCunha LP, Costa MAAC, deMiranda HA et al. Comparison between wide-field digital imaging system and the red reflex test for universal newborn eye screening in Brazil. Acta Opthalmol.2021; 99;e1198-e1205	**Cohort Study** This prospective cohort study investigated all mothers of infants born from April to June 2014 in maternity ward of Irmandade Santa Casa de Misericordia de Sao Paulo Hospital (ISCMSP). Patients underwent red reflex test (RRT) by paediatrician and wide-field digital imaging system (WFDI) performed by authors. Validity of the paediatrician's RRT was assessed by unweighted kappa (k) statistic, sensitivity, specificity, positive preduictive value (PPV) and negative predictive value (NPV) At the end of each examination, the parents were informed of any abnormalities detected. If no abnormalities were found, the newborn was discharged according to hospital protocol.	II-2	All newborns who were in the rooming-in programme in the maternity ward with the total number of 380, 760 eyes. Newborn were excluded if they required intensive care, had additional health conditions which barred their participation in the study or if their parent declined participation. Only two patients were excluded from the study : one born with bilateral anophtalmia and one whose parent declines participation.	Wide-field Digital Imaging System	RRT with direct opthalmoscope	April-June 2014	WFDI has higher sensitivity that the current gold standard (RRT), hence it consistently detects subtle treatable retina and optic nerve pathology. Universal WFDI allows for early detection and management of potentially blinding ophthalmic disease missed by RRT. Key Findings **Detection Rates:** WFDI detected abnormalities in 130 eyes (17.1%), while RRT detected abnormalities in only 13 eyes (1.7%). **Pathology detected:** hyphema, CMV retinitis, FEVR, and vitreous hemorrhage (missed by RRT) **Number Needed to Screen (NNS):** To detect ocular abnormalities using WFDI: 5.9 newborns To detect treatable abnormalities: 76 newborns Agreement between RRT and WFDI: No agreement (κ = -0.02, 95% CI, -0.05 to 0.01)	

Evidence Table : Effectiveness/ safety/ organisational/ economic implication
Question : What is the effectiveness, safety, and cost-effectiveness of wide field digital eye imaging for universal newborn eye screening

Bibliographic Citation	Study Type/ Methods	LE	Number of Patients & Patient Characteristic	Intervention	Comparison	Length of Follow-up (if applicable)	Outcome Measures/ Effect Size	General Comments
2. Fei.P, Liu Z, He L et al. Early detection of ocular abnormalities in a Chinese multicentre neonatal eye screening programme-1 year result.Acta Ophthalmol. 2021 May;99(3):e415-e422. doi: 10.1111/aos.14586. Epub 2020 Sep 15. PMID: 32930484; PMCID: PMC8246721.	**Cohort study** **A multicentric collaborative prospective study** Aim: aimed to assess the 1-year result of multicentric prospective neonatal eye examination programme with wide-field digital imaging system in China. A multicentric collaborative prospective study group for neonatal eye screening was established in nine hospitals, including eight Maternal and Children's Hospitals, and one general hospital across Chiona from July 2016 to June 2017. Ocular examinations were performed on newborns within 28 days after birth using a wide-field digital imaging system. Data were reviewed and analysed. The primary outcome was the prevalence of ocular abnormalities in neonates.	II-2	A total of 64 632 newborns born at the nine Maternal and Children hospitals , and one general hospital involved in this study. These hospitals are all qualified for neonatal eye screening before joining this study group. All the hospitals located in seven different provinces of China. Collectively, they covered North, South, East, West and Centre China. The study sample represented subjects whose parents and paediatricians consented to the study and the infant completed the screening procedure. Inclusion criteria were all live neonates at all these hospitals whose parents had signed the consent form from July 2016 to June 2017. Premature infants as defined by Chinese Opthalmological Society were included (infant born <32 weeks gestational age (GA) or <2000g BW For the exclusion criteria were infants whose image or medical charts were not available for review, patient with infectious conjunctivitis and patient too unstable for examinations	Wide-field digital retinal imaging system		1 year (July 2016 to Jun 2017)	The study is conducted across multiple centers, which increases the generalizability of the findings as it includes a diverse population from various regions. From this prospective multicentre study of newborn ocular examinations showed a relatively high prevalence of ocular abnormalities. The primary outcome was the prevalence of ocular abnormalities, while secondary outcomes included the proportion of abnormalities requiring intervention or follow-up. **Detection rate:** 20.91% (13,514 cases) of 64,632 newborns had abnormalities. Retinal hemorrhage (RH) is most common and occurred in 11.83% of newborns, with most mild cases resolving spontaneously. **Percentage require Observation/Intervention:** 59.44% of detected abnormalities (11.56% of all screened newborns)	

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3. Vinekar A, Govindaraj I, Jayadev C et al. Universal ocular screening of 1021 term infants using wide-field digital imaging in a single public hospital in I ndia—a pilot study. Acta ophthalmologica. 2015 Aug;93(5):e372-6.	**A Cohort study** A pilot study was conducted in a public general hospital within Bangalore Metropolitan city, India. This hospital already included in Karnataka Internet Assisted Diagnosis of Retinopathy of Prematurity (KIDROP). Between 1st September 2013 and 31st March 2013, 1954 babies were born in the study hospital. A total of 1021 study subjects (about 52.3 % of total babies's) were recruited based on availability of their parents on the day of screening and the parent consented for enrolment.	II-2	Between 1st September 2013 and 31st March 2013, 1954 babies were born in the study hospital. Of these, parent of 1021 (52.3%) babies were present on the days of screening and consented for enrolment. The researcher team visited study centre three times a week. Infants born on the day of the visit or between two visits are still included in this study. No attempt was made to call back infants who were discharged from hospital during the interval between each of the team's visit. All eligible patients were born at term and had birth weight more than 2000g. Exc Criteria: Premature BW <2kg babies not present on the days of screening not consented for enrolment	Retcam shuttle (Clarity MDSI Pleasanton, CA, USA) Screening was performed by trained technicians specialized in infant eye imaging using Retcam shuttle (Clarity MSI, Pleasanton, CA, USA). On an average, they perform over 1100 imaging sessions in a month in the KIDROP programme.		Study duration is between 1 September 2012 and 31 March 2013 about 6 months and	This study established that wide field, portable ocular digital imaging is safe and effective in screening all live births in India scenario. This pilot study shows that approximately 0.9% of so called normal infants were detected with treatment requiring conditions that resulted in early and effective management that altered the course of their ocular and systemic disease. **Detection Rate** : 4.7% (48 babies) Retinal Hge : 25/48 babies (52.1% abnormalities detected & 2.4% of all screened babies) **Percentage require intervention:** 18.8% of abnormalities detected and 0.89 % of all 1021 babies screened **Pathology detected:** ROP-like ridge, Posterior uveitis, retinoblastoma	A detailed cost-impact study is needed to evaluate the economic and work force feasibility of implementation and possible expansion of this programme to other centres

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4. Leong KT, Abu Kassim SNA, Sidhu JK et.al. Neonatal eye screening for 203 healthy term new-borns using a wide-field digital retinal imaging system. BMC Ophthalmol. 2021 Mar 9;21(1):128. doi: 10.1186/s12886-021-01882-x. PMID: 33750348; PMCID: PMC7941744.	**Cross-sectional study** This cross sectional study, neonatal eye screening was performed to 203 healthy term newborns using a wide-field digital retinal imaging system in Obstetrics and Gynaecology ward at Hospital Kuala Lumpur. This study is aimed at determining the proportion and types of ocular abnormalities detected in purportedly healthy term new-borns. Inclusions criteria included neonate (age <28days), born term (between 37 weeks, 0 day and 41 weeks,6 days), birth weight (≥2000g), APGAR score≥7,any mode of delivery (e.g spontaneous vaginal delivery, assisted birth and caesarean section), stable vital signs, given informed consents by parent for participation and able to comply to all requirement of the study protocol.	III	203 healthy term infant delivered in the Obstetrics & Gynaecology Labour Room, Hospital Kuala Lumpur (HKL) in Malaysia underwent an ocular examination within the first 72h or prior to discharge. Exclusion criteria include born pre-term, dysmorphic babies, syndromic babies, congenital diseases, complications intra and postpartum requiring intensive care and monitoring and unstable for an eye examination.	Wide-field digital retinal imaging system (Phoenix Clinical ICON Paediatric Retinal Camera, Phoenix Technology Group Company, CA, USA)		6 months	**Detection rate:** 34% (69 newborns had ocular abnormalities) The most common finding was retinal haemorrhage in 29.6% of the infants, of which 53.3% occurred bilaterally **Pathology detected**: subconjunctival haemorrhage, iris nevus, congenital hypertrophy of retinal pigment epithelium and vitreous haemorrhage Spontaneous vaginal delivery (SVD) remained the greatest risk factor which has nearly 3.5 times higher risk of new-borns developing retinal haemorrhage compared to Lower Segment Caesarean Section (LSCS). There was a 6% increased likelihood of developing retinal haemorrhage for every 1-min increment in the duration of 2nd stage of labour.	Relatively small sample size reduce probability of detecting rarer ocular abnormalities

Evidence Table : Effectiveness/ safety/ organisational/ economic implication
Question : What is the effectiveness, safety, and cost-effectiveness of extracorporeal shock wave therapy for the treatment of erectile dysfunction?

Bibliographic Citation	Study Type/ Methods	LE	Number of Patients & Patient Characteristic	Intervention	Comparison	Length of Follow-up (if applicable)	Outcome Measures/ Effect Size	General Comments
5. Sitorus RS, Pambudy IM, Rohsiswatmo R et al. Retinal abnormalities in universal eye screening of healthy, full-term newborn infants in Jakarta. The incidence and its risk factors: a pilot study. *Int J Retin Vitr.* 2021 Dec;7:1-7	**Cross- sectional study** This cross-sectional study involving 1208 full term newborn infants at a tertiary eye hospital (Cipto Mangunkusumo National Referral Hospital) and a district hospital in Jakarta (Koja Hospital), Indonesia. Aim: to investigate a therapeutic protocol for ED based on the combination of LI-ESWT, tadalafil, and L-arginine. Recruited patients (all eligible newborn) underwent fundus examination within 48 h after birth using the RetCam shuttle (Natus Medical Incorporated, USA)	III	A total of 1208 full term newborn infants from two public hospitals in Jakarta were enrolled in the study. Inclusion criteria were healthy, full term and newborn infants aged <48 hour Exclusion criteria were those with red eyes prior to the examination, or whose parents declined to participate in this study. Written informed consent was given by each parent prior to the examination of their infant. This study is in accordance with Declaration of Herlsinki and received ethical clearance from the Ethics Committee of Faculty of Medicine, Universitas Indonesia, Cipto Mangunkusumo Hospital.	RetCam shuttle (Natus Medical Incorporated, USA)			Results: Among the infants examined, 32 (7.3%) infants in CM Hospital and 118 (32.9%) infants in Koja hospital had ocular abnormalities . Retinal haemorrhage was the most common ocular abnormality observed, found in 6.88% and 13.11% newborns in CM Hospital and Koja Hospital respectively. Choreoretinitis was the second most common ocular abnormality found (0.57%) followed by macular haemorrhage (0.33%) **Detection rate**: 34.9% **Pathology detected:** retinal exudate, maculopathy, intraocular tumor (suspected retinoblastoma) ,optic nerve head abnormality, iris nodule, persistent pupillary membrance, and localized blood in vitreous/peripapillary Hge	

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6. Simkin SK, Misra SL, Battin M et al. Prospective observational study of universal newborn eye screening in a hospital and community setting in New Zealand. BMJ Paediatrics Open. 2019;3:e000376.doi:10.1136/ bmjpo-2028-000376	**Observational study** This prospective observational study investigated 346 infants (median age 2 days) in a public hospital maternity ward and a community birth centre in Auckland, New Zealand. Patients underwent Wide-field digital images of the external eye and retina captured using Retcam (Natus Medical, San Carlos, California, USA), reviewed by an ophthalmologist via an established telemedicine methodology	III	All infants born between June 2015 and December 2026 were recruited for universal newborn eye screening (UNES) with a total of 350 Exclusion Criteria: BW ＜1250g Gestational age ＜30W	Wide-field Digital Imaging System Retcam (Natus Medical, San Carlos, California, USA)	No comparator	Between 6 weeks to 3 months (Median follow up time of 50±14 days	Ocular abnormalities were detected by UNES including congenital cataract and optic nerve hypoplasia. 50 cases (14.5%) of retinal haemorrhage out of 346 cases were detected, two cases exhibited persistent retinal haemorrhages at 6 weeks follow up. Retinal haemorrhage significantly associated with delivery modality, were the most common abnormality detected. **Detection Rate :** 14.5% (50 cases of Retinal Hge only) 1.4% ocular abnormalities with potential visual/systemic impact (as below) **Pathology detected:** Congenital cataract, suspected choroidal hemangioma, congenital hypertrophy of the retinal pigment epithelium (CHRPE) and suspected optic nerve hypoplasia	No comparator Short duration of follow-up time

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7. Goyal P, Padhi TR, Das T et al. Outcome of universal newborn eye screening with wide-field digital retinal image acquisition system: a pilot study. Eye.2018 32; 67-73	**A Pilot study** Aim: This cross sectional study is aim to evaluate the outcome of universal newborn eye screening with wide field digital retinal image system in obstetrics and gynecology service of the civil hospital in Bhubaneswar, Eastern India All the eligible study subjects underwent external eye examination, red reflex test and fundus imaging using Wide Field Digital Retinal Imaging (Retcam II, Clarity medical system, Pleasanton, CA, USA) by a trained optometrist that aware of safety precautions while handling these babies. The babies were monitored by a stadby nurse. The captured images were analysed by an ophthalmic resident. Images of babies with positive finding were reevaluated and crosschecked by a paediatric retina specialist.	III	A total of 1152 apparently healthy newborn infants (within first 28 days of life) was examined. The study subjects on the day of screening were from the ones delivered vaginally on the same day or day earlier and babies delivered by caesarean section in previous 3 days. Exc. criteria: • Babies older than 4w old • Too sick to undergo the screening examination (purely on the discretion of paediatrician)	fundus imaging by Wide Field Digital Retinal Imaging (RetCam ii, Clarity medical system, Plesanton, CA, USA)	External Eye Examionation, red reflex test	1.5 years The study duration was from March 2014 to October 2015 (1.5 years)	**Detection rate:** 14.93% 172 babies (Retinal Hge most common 153 babies 13.28%/ (88.9% of all abnormal findings) **Pathology detected:** vitreous hemorrhage (n=1), congenital glaucoma (n=2), uveal coloboma (n=2), retinopathy mimicking retinopathy of prematurity (n=2) and cystic fovea (n=3). Early disease detection has helped seven babies either directly or indirectly, and one baby with congenital glaucoma was saved from blindness. The benefits included savings in skilled manpower by 319.4 hour or 35.5 working days, with a net monetary gain of INR 4.195 million (US$ 62,612) The universal eye screening using WFDRI detected pathologies that needed immediate care or regular follow up; saved skilled manpower with a net monetary gain .	Screening with WFDRI is promising

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8. Ma Y, Deng G, Ma J et al. Universal ocular screening of 481 infants using wide-field digital imaging system. BMC ophthalmology. 2018 Dec;18:1-8.	**A cross sectional study** In this pilot study, 481 infants underwent vision assesment, eye position examination, external eye check, pupillary light reflex, red reflex examination, anterior and posterior ocular segments were examined using flashlight, opthalmoscope, and wide-field digital imaging system.	III	A total of 481 infants aged 6 weeks around were consecutively enrolled in a public hospital between April 2015 till August 2016. Exclusion criteria: • Infants unable to tolerate the eye screening examination conducted by the pediatrician • Infant whose guardians refused to consent All participants were screened according to the Declaration of Helsinki document on human research ethics and underwent both verbal and written informed consent by their guardians for participation and data publication	Wide-angle digital camera (Retcam 3, clarity Medical System, CA, USA) and 130-degree lens were used to acquire anterior and posterior images from one eye to the other eye	Red reflex examination	Duration of study is 17 months between April 2015 and August 2016)	**Detection rate:** 41.2% (198/481 infants) **Percentage require intervention**: 4.6% (22/481 screened infants) **Pathology detected:** concomitant exotropia, retinal pigmentation, and retinopathy of prematurity (ROP), congenital cataract and Familial Exudative Vitreoretinopathy (FEVR)- Familial Exudative Vitreoretinopathy (FEVR) presentation and severity of the disease could be different even in the same family. The severe and progressive forms of the diseases are including neovascularization, retinal exudates, retinal haemlorrhage, preretinal membranes, retinal folds and retinal detachment. In this study, two cases of FEVR managed to be detected from this universal ocular screening using RetCam and allow timely surgical intervention to avoid visual impairment consequences. Furthermore, universal ocular eye screening using RetCam able to detect some treatable diseases leading to childhood visual disability if not diagnosed earlier in life. Universal ocular screening is effective to screen congenital cataract at an early stage, thus surgical intervention could be performed earlier to avoid amblyopia and nystagmus. In infants suffering from congenital cataracts especially posterior, perinuclear, nucleus and total cataracts, the crucial time for surgery is within the first 3 months of life.	

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9. Tang. H, Li N, Li Z et al. Fundus examination of 199851 newborns by digital imaging in China: a multicentre cross-sectional study. *Br J Opthalmol* .2018 0; 1-5	**Cross-sectional study** This cross-sectional study involving 199851 newborns (within 42 days after birth) in eight centres in China underwent fundus examination using Retcam wide-filed digital imaging. This study is aimed to report the implementation of digital imaging in ocular screening of all newborns in multiple centres in China and to describe abnormal findings of fundus examination.	III	A total of 199851 newborns within 42 days after births from eights centres across China (from January 2009 to July 2017) were enrolled and examined in the study. These centres located in Liuzhou City, Zhuhai City and Kunming City in South China, Maanshan City in the middle of China, Urumqi in northwest China, Huhhot City, Linyi City in north China and Changchun in Northest China. **Inclusion criteria :** 1-Parental consent 2-Newborn Age: The study included newborns who underwent fundus examinations within 42 days after birth. This time frame was chosen to capture early ocular abnormalities that could be present from birth. Parental Consent: 3-Geographic and Institutional Scope: The study was conducted across eight maternal and children's hospitals in various regions of China. This geographic diversity aimed to ensure that the sample represented a broad cross-section of the population. Use of RetCam Digital Imaging: 4-The average gestational age was 38.9±1.8 weeks and the average birth weight was 3260±517g.	RetCam wide-field digital imaging system (Clarity Medical System, Pleasanton, California, USA)	Red Reflex Test (RRT)	Duration of the study from January 2009 to July 2017	Prevalence of Ocular Abnormalities: The primary outcome measured was the prevalence of ocular abnormalities in newborns as detected by the RetCam wide-field digital imaging system. The most common abnormalities noted in this study was Retinal Haemorrhage (RH) including grades of severity which were found in 12 810 cases. Accounting for 6.41% of all screened newborns and 70.39% of all ocular abnormalities. **Detection Rate** : 9.11% 18,198 of screened neonate 14.96% of premature newborn with gestational age ≤34w or ≤ 2Kg (560/3743 premature infants) The most prevalent abnormality was RH, which accounted for 70.39% of all abnormal cases. **Pathology detected:** Choroidal coloboma, persistent pupillary membrane, congenital cataract, retinoblastoma Comparison by Delivery Method: The study examined the prevalence of severe retinal hemorrhage in relation to the method of delivery (vaginal vs. Caesarean). This study found a high percentage of vaginal delivery in severe RH cases while less than half of the neonates without any ocular abnormalities were born by vaginal delivery, supporting the conclusion that birth trauma is the main cause of RH. This may also explain the low abnormality percentage (4.1%) in Vinekar's study, in which the majority of infants were born by Caesarean delivery, with only a few newborns diagnosed with RHs	The study showed advanced digital imaging system such as the RetCam was convenient, quick and safe.

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10. Li LH, Li N, Zhao JY et al. Findings of perinatal ocular examination performed on 3573, healthy full-term newborns. *Br J Opthalmol* 2013;97: 588-591	**Cross Sectional study** This cross-sectional study involving 3573 healthy full-term newborns underwent retinal fundus examination using Retcam wide-filed digital imaging system (Clarity Medical Systems, Pleasanton, California, USA) in Kunming Maternal and Child Healthcare Hospital, China. This study is aimed to detect ocular pathologies in healthy full-term newborn. In this study,inclusion criteria is normal newborn with gestational age ≥ 37weeks and weighing ≥2500g, patient with no evidence of systemic disease, patiengt with apgar score ≥7	III	A total of 3573 healthy full-term newborns were enrolled and examined in the programme. The exclusion criteria were infants whose mothers had known transmitted diseases like STDs, hepatitis B and HIV positive. Premature infant or infants who were examined after discharge at 42 days of birth with other follow up were excluded in this study. Exc. criteria: • Infants whose mothers had known transmitted diseases like STDs, hepatitis B and HIV positive. • Premature infant • Infants examined after discharge at 42 days of birth with other follow up	A Retcam Retcam wide-filed digital imaging system (Clarity Medical Systems, Pleasanton, California, USA)		1 year duration (May 2010 till June 2011)	Primary outcome measure is the prevalence of ocular abnormalities among healthy full-term newborns. The most common abnormality identified was retinal hemorrhage, present in 769 newborns, accounting for 21.52% of the total population. **Detection rate:** 24.4% 871 abnormal cases (Retinal Hge most common 769 cases = 21.52%) **Pathology detected:** Retinal hamartoma vs retinoblastoma, FEVR, retinopathy due to infection like CMV The effect sizes reported provide important insights into the potential need for routine ocular screenings in this population.	

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11. Haefeli LM, Neves LM, Zin A et al. Portable wide-field digital imaging for screening of neonatal visual impairment causes in Rio de Janeiro, Brazil: a budget impact analysis. BMJ Open 2022; 12:e056498.doi:10.1136/bmjopen-2021-056498	**Budget impact analysis (Static Model)** This budget impact analysis using a static model and cost calculator developed in Excel aimed to estimate the budget impact of WFDI incorporation on screening neonatal causes of childhood blindness and visual impairment in Rio de Janeiro, Brazil. The study compared WFDI method against reference scenario using red reflex test (RRT) and indirect binocular ophthalmoscopy (IBO). The analysis estimated the number of newborns eligible for screening in government maternity wards from 2020 to 2024 The study utilized the ARIMA model based on live birth data from 2008 to 2018 and conducted a survey of 24 government maternity wards in Rio de Janeiro.		All babies born in Rio de Janeiro's government maternity wards This study identified 24 government maternity wards, 23 with neonatal intensive care units, in the city of Rio de Janeiro. An ROP screening programme was implemented in 92% of the maternity wards (22 of 24). All these maternity wards admitted almost 60% (54,000) of all live births in the city in year 2018. The study population was stratified into three hypothetical screening strategies: RRT of all newborns except those requiring ROP screening, IBO for ROP screening and WFDI for both populations of newborns. RRT was performed on full term and premature newborns with no indication for ROP screening, executed by a paediatrician using a direct opthalmoscope, before hospital discharge. Infants born with BW <1.5Kg and/or GA<32W underwent IBO by a skilled ophthalmologist. WFDI was performed on all newborns by two nurse technician and the images sent to ophthalmologist before hospital discharge.	Budget impact of implementing portable wide-field digital image screening	Direct cost of indirect binocular ophthalmoscopy, red reflex test and portable wide-field digital image screening	6 months	Cost Items: The analysis included costs for human resources, capital, consumables, and transportation. The total cost per examination was estimated at US$34.36 for IBO, US$0.75 for RRT, and US$14.19 for WFDI. Efficiency Gains: The study highlighted efficiency gains in WFDI through training, reducing examination time by almost 50%. Budget Impact: The total budget impact of WFDI for 100% coverage was estimated at US$3,820,706.04 over five years, with an incremental impact of US$3,124,457.28 compared to reference scenarios. The study concluded that the cost of universal digital imaging screening corresponds to less than 1% of the government health budget of Rio de Janeiro, suggesting feasibility for implementation. This study suggests that incorporating WFDI into government maternity hospitals in Rio de Janeiro could improve the identification of causes of childhood visual impairment at a relatively low budget impact. The study recommends further health economic evaluations to verify the affordability and feasibility of this strategy in Brazil. Considering 100% coverage of maternity wards, the total budget impact between 2020 and 2024 would be US$3 820 706.04, ranging from US$3 139 844.34 to US$6 099 510.35. The additional cost would be US$3 124 457.28, ranging from US$2 714 492.26 to US$4 880 608.63.	

TECHNOLOGY REVIEW (MINI-HTA) WIDE FIELD DIGITAL EYE IMAGING SYSTEM FOR UNIVERSAL NEONATAL EYE SCREENING

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