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Commentary

From Development to Application: Bridging the Translational Gap of Artificial Intelligence-based Diagnostics for Childhood Cataract

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Every minute, a child somewhere in the world either becomes, or is born blind [1]. Despite its rarity, with an approximate global incidence of 1 per 3000, childhood cataract is one of the most important causes of preventable childhood blindness [2]. Unoperated cataract blinds children and adults. Affected babies and infants can also be irreversibly blinded by delayed treatment, due to the absence of stimuli during early-life development of the visual system (deprivational amblyopia). Blindness impacts negatively not only on the child and their family, but also on their surrounding society, due to the lifelong support related-, and lost workforce costs [1].

Globally, we face a shortage of eye specialists with the training necessary to diagnose and treat childhood cataract [3]. This shortage is particularly acute in lower income countries, but is also a concern in settings such as the UK [4]. Fast, accurate AI-based diagnosis would improve accessibility to specialist care and effective use of scarce clinical resource. It would also support the training of future specialists, through standardisation of practice and access to datasets of rare disease images.

In this issue of EclinicalMedicine, Lin and colleagues report the results of a randomised controlled trial, using an AI-based diagnostic intervention [5]. The Congenital Cataract-Cruiser (CC-Cruiser) was created using a multi-layered artificial network inspired by the

'convolutional' organisation of the biological visual system [6]. Using a training dataset of over 400 disease images acquired through biomicroscopic ('slit lamp') eye imaging at the time of surgery, and almost 500 normal images, CC-Cruiser was taught to identify, stratify, and stratigise treatment for images of childhood cataract [6]. This was a relatively small learning dataset, but childhood cataract is a relatively rare disease. In the study presented in this issue, following slit lamp image acquisition, children were randomised to routine diagnostic clinical examination by a senior consultant ('attending') ophthalmologist, or image uploaded to the cloud-based CC-Cruiser [5]. Children then underwent 'gold standard' diagnostic examination by an expert panel who reached a consensus on diagnosis and treatment. In comparison to a senior consultant, the CC-Cruiser had a lower diagnostic accuracy, but had comparable patient experience scores and required less time to reach a diagnosis [5].

AI networks trained on hundreds of thousands of clinical images can outperform experienced clinicians in the image-based diagnosis of skin or retinal disorders [7,8], but we have yet to understand how we best assess the impact of AI-based diagnostics in real-world clinical practice. A traditional randomised controlled trial of a diagnostic 'intervention' (D-RCT) would randomise participants to different tests, then compare the final clinical outcomes for both groups following the treatment indicated by that test. AI-based diagnosis, however, represents a significant 'paradigm shift' in clinical care, complicating the design and processes of D-RCTs. We have no consensus on the proof-of-concept required to permit ethical recruitment to a D-RCT where patients may receive treatment based on the findings of an AI-based tool. Where there is sufficient proof, is it ethical to withhold that technology from affected individuals? Moore's Law (that every year sees a doubling of computer processing power) suggests that the technology used within a D-RCT may be obsolete by the time study findings are reported. Lin and colleagues have selected a pragmatic methodology able to add insights to the acceptability and utility of AI diagnosis of childhood cataract, although one which is still unable to provide a true assessment of the 'real-world use' of AI diagnostic algorithms.

In the real world, children with congenital lens opacities are identified by a health care professional as part of a screening programme, or based on concerns regarding visual behaviour. Identification is followed by initial assessment by a community-based health care professional.

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Those with abnormal findings are referred to a specialist unit for prompt diagnosis and intervention by a specialist team in order to return good vision. Eye professionals do not use 2-D clinical images in isolation to stratify or strategise treatment for childhood cataract [3,9]. Thus, the utility of CC-Cruiser for decisions downstream of cataract detection is unclear. Unlike 'live' biomicroscopic examination performed on the awake child, biomicroscopic image acquisition for infants and babies necessitates sedation [5]. Thus, an automated diagnostic pathway for young children, who constitute the most important population at risk, would still involve medical input in order to capture images for analysis by the AI. The growing uptake of smartphone use and evolving imaging capabilities will change how we 'see' the eye [10]. Macroscopic images acquired at community level or by parents may generate a dataset for deep learning algorithms to support truly automated disease screening. The 'democratisation of expertise' offered by AI-based diagnosis is an attractive promise for a rare disabling disease which requires urgent diagnosis and treatment from a stretched workforce. The methodological lessons learnt through this paper from Lin and colleagues, such as the success with a limited training dataset, the innovative use of a cloud based diagnostic platform, and a consensus-based gold standard diagnosis, should provide important foundations for future work.

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