# Causal effect prediction of diabetic retinopathy and glaucoma using hybrid deep learning and multi-disease fundus images

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**The present study presents a novel hybrid framework for the prediction and severity classification of diabetic retinopathy (DR) and glaucoma (GL) using synthesised fundus images. DR and GL are among the leading causes of irreversible blindness worldwide, often co-existing in ageing populations and complicating diagnosis. While DR is characterised by retinal vascular damage, GL involves optic nerve deterioration—both requiring distinct yet overlapping diagnostic features. A StarGAN v2-based generative model was employed to create hybrid retinal images containing features of both DR and GL, enhancing the diversity and complexity of the dataset. Red, green, and blue channel separation was performed to highlight disease-specific cues, with a denoising convolutional neural network applied to the green channel for enhanced vessel and lesion visibility. Two deep learning models were explored: a Hippopotamus Optimized Vision Transformer (HOViT) that captures global dependencies and a convolutional neural network (CNN) architecture augmented with a convolutional block attention module (CBAM) for focused lesion-level feature learning. The CNN-CBAM model was further optimised using Optuna's Bayesian optimisation framework, improving classification accuracy. Severity scores for DR and GL were estimated using a dual-output SoftMax layer, supported by gradient-weighted class activation mapping-based interpretability. Fusing the spatial and pathological features of both diseases into a unified model enabled simultaneous, interpretable multi-disease prediction. Experimental results demonstrate high accuracy, robust generalisation, and explainable predictions, offering a powerful tool for assisting in the clinical diagnosis of co-existing retinal diseases.**

**Keywords:** Convolutional Block Attention Module, diabetic retinopathy, glaucoma, Vision Transformer, StarGAN v2.

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DIABETIC retinopathy (DR) and glaucoma (GL) are two leading causes of irreversible vision loss globally, each arising from distinct yet complex pathophysiological mechanisms. According to the International Diabetes Federation, approximately 451 million individuals were living with diabetes globally in 2017, and this number is projected to rise to 693 million by the year 2045 (ref. 1). DR is a microvascular complication of diabetes mellitus, resulting from chronic hyperglycaemia that damages the retinal blood vessels. DR causes damage to the blood vessels in the retina, and its progression is often slow and asymptomatic, making early detection challenging. If left untreated, it can lead to vision loss. In DR, the retinal blood vessels become inflamed, and due to blood leakage or clotting, new abnormal blood vessels may form[2]. Fundus imaging plays a crucial role in detecting these changes, helping to identify both damaged vessels and the formation of new, abnormal vessels in the retina[3]. GL is characterised by progressive optic neuropathy, often associated with elevated intraocular pressure (IOP). However, GL can also occur with normal IOP, indicating the involvement of other factors such as impaired ocular blood flow, mitochondrial dysfunction, and neuro inflammation[4]. The disease leads to the loss of retinal ganglion cells and optic nerve damage, resulting in visual field defects. Fundus imaging is a noninvasive and widely accessible technique that offers critical insights into the eye and optic nerve head. It captures structural changes that are valuable indicators for detecting the presence of glaucoma[5]. Advancements in imaging technologies, such as optical coherence tomography angiography, have enhanced the early detection and monitoring of both DR and GL. Moreover, artificial intelligence (AI) and deep learning algorithms are increasingly being integrated into diagnostic processes, offering improved accuracy and efficiency in disease detection and classification[6]. Deep learning techniques have significantly advanced the early detection of DR and GL by enabling automated analysis of retinal fundus images. Deep learning (DL) can learn complex patterns and subtle abnormalities