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Article

SNAPSHOT INSIGHT TO MACHINE LEARNING METHODOLOGIES FOR EARLY DETECTION OF ONSET OF GLAUCOMA

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Abstract: Early identification of glaucoma is a critical demand as well as prominent concern due to its risk of irreversible blindness if left unattended. Irrespective of presence of variable advanced imaging technologies powered by analytical operation, still there is no report of any benchmarked application or technology associated with it. In past half decade, machine learning algorithms and Artificial Intelligence (AI) has been showing some promising direction towards predictive analysis resulting in precise detection of early onset of glaucoma. However, there are manifold challenges associated with AI and learning algorithms too. Hence, this paper presents a compact snapshot of existing machine learning algorithms evolved recently in research area in order to identify the scale of effectiveness towards solving issue pertaining to early detection. The paper further contributes to briefing of frequently adopted dataset, highlighted updated research trends of publication along with exclusive learning outcomes and research gap.
Keywords: Artificial Intelligence, Early Detection, Glaucoma, Machine Learning, Predictive Analysis

1. INTRODUCTION

Glaucoma is a form of an ocular disease causing maximized intraocular pressure leading to an extreme damage to optic nerve [1] . From clinical perspective, there are 5 types of glaucoma viz. open-angle glaucoma, angle-closure glaucoma, normal-tension glaucoma, congenital glaucoma, and secondary glaucoma. Various medical condition like high-blood pressure and diabetes, age, ethnicity, and family history also acts as risk attributes to glaucoma. As glaucoma leads to irreversible blindness it is essential to carry out an early detection of glaucoma. An early detection of glaucoma will assist in prevention of vision loss, effective treatment options, enhanced outcomes, identification of high-risk individuals, and monitoring disease progression. At present, there are various screening methods ranging from basic to advanced technological utilization towards detection of glaucoma. Some of the frequently adopted screening approaches in ophthalmology are tonometry, visual field testing, Optical Coherence Tomography (OCT), fundus photography, gonioscopy, pachymetry, confocal scanning laser ophthalmoscopy, electrophysiological test, and visual acuity tests. Usually, the early stages has no exhibition of noticeable symptoms while the progressive stages is characterized by blurred vision, difficulty adapting to low light, loss of peripheral vision, and halos around lights. Although, early detection is quite critical in determining the positive presence of onset of glaucoma but yet it has many potential challenges. An individual with early stage of glaucoma is found to exhibit very insignificant symptoms giving more challenges to ophthalmologist as well as patient. There are various types of screening approaches for diagnosing glaucoma which can eventually lead to variable diagnostic outcomes and thereby it can further obfuscate the clinical interpretation. Further, not all ophthalmologists are experienced nor adequately trained to identify the early onset of glaucoma leading often to outlier diagnosis. Apart from this, one basic challenges in diagnosing glaucoma is strongly related to the existing form of screening methods itself. For an example, the frequently adopted OCT screening demand specialized training in order to understand and extract logical inference of the precise outcome. Usage of automated perimetry is associated with time-consuming test administration process. Fundus imaging is another evolving technological advancement in diagnosis of glaucoma using wide-field fundus photography; however, they are also connected with fluctuating image quality as well as complex interpretation adversely affecting the diagnosis outcome. Another evolving technology is confocal scanning laser ophthalmoscopy that generates three-dimensional images related to optic nerve offering comprehensive information of internal structure of retina. However, such equipment are quite expensive while an expertise is required for interpreting the complex form of outcome. Although, there are many more evolving imaging technologies offering promising result, but they are still under the roof of research and development while assumptions towards integrating them is also associated with higher implementation cost. All the above-mentioned screening methods are found to be highly fruitful only when an individual has progressive stages of glaucoma and very few is found towards early detection. The complexity associated with lack of potential indicators to confirm diagnosis of glaucoma in early stage is still a bigger problem. In this perspective, machine learning and Artificial Intelligence (AI) has been noted with increasing adoption for diagnosis of various occlar diseases. Although, this evolving technology is capable of analyzing complex dataset and perform early prediction of glaucoma, yet such models demand image dataset with high quality, which may not be available for implementation and research. There are various works carried out towards facilitating an effective screening of glaucoma. There are various types of computerized methods utilized towards detection of glaucoma where more important yielding outcomes was noted to be arriving upon investigation from optic disc and cup from fundus (Abdullah et al. [2]). Ngo et al. [3] have presented an interesting finding by their approach towards assessing the screening complexity associated with pupil for determining glaucoma. The model has used bandpass filters and hampel filter to preprocess the pupillary signals followed by using fractal dimension, permutation entropy, and conditional entropy as a way to measure the complexity. Vente et al. [4] have presented an innovative model to showcase the productive and efficient usage of AI for screening glaucoma. This model has been experimented using 113,000 images, which is the largest till date used in research arena of diagnosing glaucoma. Further adoption of AI is also witnessed in research model presented by Aurangzeb et al. [5] . Existing system has extensively seen the evolving usage of machine learning and deep learning algorithms towards investigating the features related to disc and cup for assisting glaucoma detection as noted in study of Masot et al. [6] . According to this scheme, independent detection of optic cup and disc is subjected to segmentation and machine learning method while detection of glaucoma is confirmed by using transfer learning method. Adoption of transfer learning in multiple stage is also noted in work carried out by Yi et al. [7] where attention network is integrated with pretrained model for enhancing the feature extraction process. The work carried out by Manassakorn et al. [8] have used Convolution Neural Network (CNN) mainly meant for automating the feature extraction and classification towards diagnosing glaucoma. Adoption of CNN is also noted in work carried out by Virbukaite et al. [9] where an ensemble version of CNN is used with multiple pretrained model in order to generate multi-classification outcomes for glaucoma. The work carried out by Pham et al. [10] have discussed about utilization of deep learning models explicitly using pretrained model and Long Short-Term Memory (LSTM) for the purpose of predictive analysis of visual fields affected by glaucoma. Another contributing work presented by Shyamalee et al. [11] have addressed the explainability issues linked with usage of deep learning algorithms in medical research. The model has performed segmentation process using multiple pretrained model followed by generating heatmaps in order to accurate visualize the presence of glaucoma. Existing system has also witnessed utilization of generative adversarial network for classification of glaucoma using fundus images as noted in work of Leonaro et al. [12] . However, there are various research problems associated with the existing system of adopting AI-based diagnosis of glaucoma as follows: i) the frequently increasing usage of AI in diagnosis of glaucoma or any other occular disease calls for high-quality annotated dataset which otherwise leads to outliers or sub-optimal outcomes, ii) there is a lack of generalizability characteristic associated with existing learning-based algorithm reducing the applicability scope in real-time, iii) the models towards diagnosis of glaucoma required to be subjected for continuous learning, iv) inappropriate or unreliable detection of glaucoma will lead to permanent blindness while AI is still in its nascent stage of development and hence reliable predictive and computational performance of AI is still a bigger question in critical healthcare sector. Irrespective of various challenges and out of various effective diagnosis possibilities for glaucoma, there is no doubt that AI and machine learning has been consistently creating a ground-breaking innovation progressively at faster pace. Therefore, the main aim of this paper is to investigate the effectiveness of current machine learning methodologies of detecting glaucoma. The value-added contribution of proposed system are viz. i) to present a compact discussion highlighting the core taxonomy of machine learning based approaches towards early screening of glaucoma and exhibit their strength and limitation, ii) to furnish a snapshot of publicly available dataset used in research arena of glaucoma, iii) to present a comprehensive learning outcomes of the presented study of existing methodologies along with updated trends of publications, and iv) to highlight the identified research gap linked with existing approaches.

2. METHODS

There are different variants of machine learning algorithms that has been adopted towards diagnosing glaucoma ranging from early detection to progressive stages. There are various existing review work already elaborated about various machine learning and deep learning-based approaches [13] towards diagnosis of glaucoma; however, there is a need of more compact and updated version for simplifying the findings. Hence, the presented study has been carried out considering a simplified version of systematic review of literature as noted in Fig. 1.

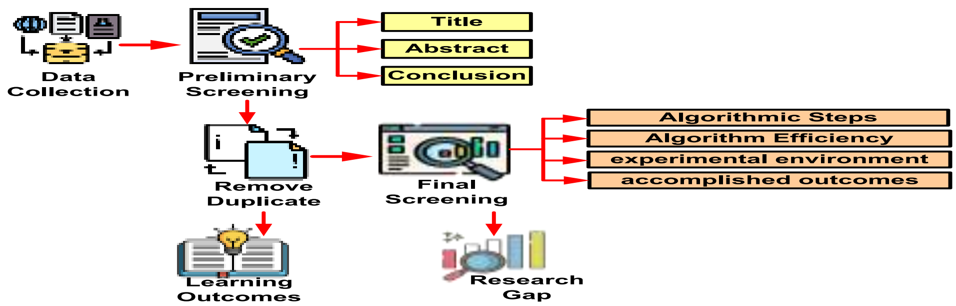

Figure 1 Considered Research Method for Systematic Review

Referring to Fig. 1, the initial step is to collect the research papers from reputed publications using permutation and combination of following keywords viz. "early detection", "glaucoma", "machine learning", "deep learning", "artificial intelligence." The collected research papers are further preliminarily screened from their Title, Abstract, and Conclusion section followed by elimination of any redundant concept or papers. The final screening is carried out by deeper review of steps involved in algorithms, studying effectivess of algorithm, experimental environment, and accomplished outcomes. In the meanwhile, a parallel investigation is also carried out to understand the trend of research papers published in IEEE, PMC Journal, Springer Journal, and MDPI Journals with respect to all the identified variants of machine learning algorithms. The inclusion criterion includes i) only journal published between 2019-2024 with reputed publishers with high impact factor, ii) research work using machine learning and deep learning, iii) research papers with complete discussion of algorithmic steps and elaborated result analysis. The exclusion criterion includes i) any research article without disclosure of source or specification of dataset, ii) any research work that doesn't significantly contribute to glaucoma diagnosis, iii) no conference or symposium or discussion papers are included in reviewing the implementation in results. The next section presents discussion of accomplished study outcomes of this review work.

3. Results

This section presents discussion of reviewed machine learning approaches towards early glaucoma detection. It was noted that there are two types of implementation categories for this purpose viz. i) implementing individual machine learning algorithm and ii) integrating multiple machine learning algorithm. There is no explicit rationale furnished for adopting above form of implementation approach which is solely dependent on strategy to address the problem.

3.1 Current Machine Learning Schemes

Current literatures have witnessed wider varieties of machine learning schemes for diagnosing glaucoma. Each schemes have been noted with beneficial features towards addressing definitive challenges. Following are the highlights of machine learning methods:

3.1.1. **Supervised Learning Methods**

These methods are noted to be generally opted by researchers when they choose to work on labelled data with very clear goal of prediction. This method is found to offer higher accuracy for classification task while its deployment is quite ideal for normal clinical settings with demand of higher preciseness in prediction. Apart from this, it is also noted that supervised approach offers much significant to the attributes when it targets to assess the impact of threat-based attributes inducing glaucoma. Current studies have explored this approach implemented using classification algorithms e.g. Support Vector Machine (SVM) [14] -[17] , Decision Tree (DT) [18] -[20] , Random Forest (RF) [21] -[23] . This method is also implemented using Linear Regression (LR) [24] -[27] and Logistic Regression (LoR) [28] -[31] .

3.1.2. **Unsupervised Learning Method**

This is another frequently adopted approach towards early diagnosis of glaucoma suitable in circumstance when there is lack of labelled data. For an example: it was noted that k-means clustering algorithm in this category can assists in identifying early signs of glaucoma without any dependency of labeled dataset [32] [33] . These methods can significantly determine the pattern in absence of labels by performing exploratory data analysis. This also significantly assists in identifying latent information, anomalies, and structures within the dataset. Supervised methods (e.g. anomaly detection) can potentially assists in determining the early signs of glaucoma by detecting the unusual patterns and outliers.

3.1.3. **Deep Learning Method**

This is one of the evolving machine learning methods that are found to tyically implemented when there is a voluminous labelled dataset with complex data structures. In contrast with conventional machine learning algorithms, existing studies shows that deep learning methods is capable of solving classification of healthy eyes from early stage of glaucoma with superior accuracy. Further, adoption of CNN [34] -[40] , Recurrent Neural Network (RNN) [41] [42] , LSTM [43] -[47] , and Autoencoder (AE) [48] -[52] is noted to be used in exploratory research work for investigating new patterns linked to glaucoma.

3.1.4. **Ensemble Learning Method**

Ensemble Learning (EL) methods are noted to be used under specific set of condition towards early diagnosis of glaucoma [53] - [55] . Various EL methods e.g., stacking [56] , boosting [57] , bagging [58] are reported to integrate the strength of existing models (e.g. neural network, SVM, DT) improving the capabilities of standalone machine learning models. EL methods are also chosen to be implemented when there is a situation of complex or non-linear relationship between glaucoma presence and considered features. Further, they are also known to offer stability and robustness towards complex decision boundaries. However, one of the common reason to apply EL method is to assess the importance of specific feature that can contribute towards predictive identification of glaucoma.

3.1.5. **Anomaly Detection Method**

This type of method is adopted towards determining the unusual patterns residing within the dataset for detection of glaucoma. However, adoption of this method is preferred for the situation characterized by scarcity of annotated dataset and risk stratification. Anomaly Detection (AD) method is also used for case studies with imbalanced dataset as well as better alternative to supervised learning methods. There are various schemes at present using AD method characterized by better form of feature engineering method supporting continuous monitoring toward indication of onset of glaucoma [59] - [61] .

3.1.6. **Transfer Learning Method**

Within the research arena of deep learning methods, Transfer Learning (TL) method is found to use various pre-trained models that are highly particular to detection of glaucoma with a target to enhance detection performance on smaller dataset. It is considered as one of the highly effective methodology when encountered with complex image data (fundus image). It can not only enhance the existing model performance but also supports adapting to evolving technologies [62] - [68] .

3.1.7. **Feature Engineering**

This is one of the common technique usually involved in all the above-mentioned methodology. Feature Engineering (FE) method is meant for extracting potential features from image dataset for enhancing accuracy of predictive diagnosis model [69] [70] .

Table 1 summarizes the scale of effectiveness of existing literatures reported of early diagnosis of glaucoma using different variants of machine learning approaches.

3.2. Datasets for Glaucoma

Retina OCT glaucoma dataset offers three dimensional tensor images with normal and open angle glaucoma providing 884 OCT scans [71] . The dataset provided by Zhai [72] has presented wider discussion of various publicly available dataset made from 223 fundus image and 421 normal images. Pachade et al. [73] have developed dataset to be used for multiple disease classification consisting of 3200 fundus images. Kovalyk et al. [74] have presented PAPILA dataset developed from 244 patients specifically designed for diagnosing early glaucoma. Al-Fahdawi et al. [75] have created OIA-ODIR dataset which consists of 8000 high-resolution images of fundus meant for diagnosing different types of occular diseases. Orlando et al. [76] have presented REFUGE dataset consisting of 1200 high-resolution annotated fundus images. Another alternative way is also to adopt EL methods which can actually enhance the performance while working on minority classes. TL methods can be also helpful by using its pretrained model (e.g. VGG or ResNet) towards better generalization. All these datasets also offer an added advantage of crossvalidating the detection outcome to be distinguished from other similar indicators of ocular diseases.

Table 1 Summary of Effectiveness of Machine Learning towards Early Detection of Glaucoma

Approach	Authors	Accuracy(%)	Contribution	Limitation
SVM	[14] -[17]	80-95	Clear classification outcome	Sensitive to overfitting & noise
DT	[18] -[20]	70-90	Demands less preprocessing	Highly sensitive to variation
RF	[21] - [23]	85-95	Minimizes overfitting, robust to noise	Computationally intensive
LR	[24] -[27]	80-90	Efficient for linearly separable variable	Low-optimal classification
LoR	[28] -[31]	70-85	Interpretable model	Poor performance for non-linear data
k-Means	[32] -[33]	80-85	Efficient data analysis	Higher possibility of outliers
CNN	[34] -[40]	90-98	Higher accuracy, optimal feature extraction	Higher dependencies of Graphic Processing Unit (GPU)
RNN	[41] -[42]	80-90	Effective for temporal analysis	Complexity in training
LSTM	[43] -[47]	80-95	Better memory management, efficient for higher dependencies in detection	Computationally intensive
AE	[48] -[52]	90-94	Easily integrateable with other model, flexible design, granular analysis	Prone to overfitting
EL	[53] -[58]	85-95	Highly diverse, reduce overfitting, better accuracy performance	Computationally intensive model
AD	[59] -[61]	85-92	Applicable for any form of unknown patterns, rare instances	Sub-optimal classification for not well-defined classes of dataset
TL	[62] -[68]	95%	Ensured and consistent accuracy performance, minimize training time	Depends on precisely selected pretrained model
FE	[69]- [70]	80-90	Offers extensive scope of extracting indicating patterns, simplified modelling	Challenging to identify potential feature, time-consuming

Table 2 highlights other publicly available dataset that are frequently reported to be involve in investigating glaucoma. Majority of the above-mentioned dataset are imbalanced and hence demands data augmentation or certain resampling approaches.

3.3. Core findings of study

At present, there are approximately 50636 research publication as tabulated in Table 3 published between 2019-2024 related to machine learning-based algorithm implementation towards diagnosing glaucoma. The numerical scores of publications in various reputed journals shows very less degree of work is carried out considering AE technique (n=292) while deep learning approaches using TL is quite high (n=5840).

Table 2 Publicly Available Dataset Adopted in Existing Studies

Dataset	**Specification**	**Resolution**	**Number of Images**	**Types**
EyePACS [77]	Glaucoma,diabetic retinopathy	2000x2000 pixel	88000 images of retinal fundus	Fundus
DRIVE (Digital Retinal Images for	Retinal vessel segmentation for glaucoma	768x584 pixels	40 images	Fundus

Vessel Extraction)[78]				
STARE (Structured Analysis of the Retina)[79]	Retinal images for different diseases	700x600 pixels	400 images	Normal and infected images of fundus
OpenEDS (Open Eye Dataset)[80]	OCT scan images	High resolution OCT images	4000+ OCT images	OCT images
RIGA (Retinal Image Geometric Analysis) [81]	Segmentatin of cup and optical disc in glaucoma	4000x3000 pixels	200 annotated images	Fundus
IDRiD (Indian Diabetic Retinopathy Image Dataset) [82]	Diabetic retinopathy, glaucoma	3000x4000 pixels	48 OCT images, 81 fundus image	Fundus and OCT scans

From the perspective of machine learning approaches, extensive work has adopted LR technique (n=12228) followed by LoR technique (n=6335). CNN technique (n=2109) is also another evolving methods towards detection of glaucoma.

Table 3 Publication Trends for Each Machine Learning Algorithm

Approach	IEEE	Springer	PMC	MDPI
SVM	18	458	1578	3
DT	3	266	1391	6
RF	3	406	1745	9
LR	2	1993	10273	20
LoR	1	1471	4822	41
k-Means	1	984	406	10
CNN	20	583	1485	21
RNN	0	78	241	0
LSTM	1	101	284	2
AE	2	60	228	2
EL	6	296	1070	6
AD	2	220	646	12
TL	15	508	5310	7
FE	83	2012	11350	75

From the publication trends in Table 3, it can be stated that there is a rising adoption of machine learning approaches (total publication of machine learning=25910) in contrast to deep learning approaches (total publication in deep learning=11206). It is also noted that there is an extensive studies exclusively emphasizing on feature engineering (n=12352) which is witnessed to be adopted in both machine learning and deep learning approach. On the basis of deeper insight of effectiveness of each approaches towards diagnosing glaucoma, following are the inference drawn towards learning outcomes of the study and identified research gap as core contribution of presented study:

3.3.1. **Learning Outcomes**

The primary learning outcome of this review work is that machine learning and its manifold variants has been evolving and progressively adopted as preferrable mode of solution towards detection and classification of glaucoma. Machine learning is one of the undeniably the best cost effective solution to address this problem but there are various issues related to its actual implementation as follows:

- There is a significant level of research problem associated with data quality and quantity as they are found to be charecterized with limited data availabilty, imbalanced dataset, and time-consuming data annotation.
- The existing method of feature extraction and representation process doesn't seem to consider the complexity of disease in its algorithm logic. Traditional FE methods cannot extract all the significant features of glaucoma and hence higher possibility of either outliers or overfitting arrives sooner.
- Existing variants of all machine learning algorithms are not found to consider the population variability and overfitting problems much. It is quite imperative that models that are trained on specific dataset is less likely to be generalize its outcome when exposed to another dataset. It is mainly because of involvement of heterogeneous healthcare practices, environment, and genetics involved in dataset building process.
- Maximum focus is given towards deploying the dataset to machine learning algorithms without much consideration of assured involvement of computational resources associated with it. Non-involvement of such facts may offer higher accuracy in research paper but may not yield similar result when deployed on real-time diagnostics.
- None of the existing reported publicly available dataset has any clues towards progression of glaucoma over a longer period of time. Hence, lack of longitudinal charecteristic considering progression of time is found in existing dataset. Hence, it complicates the process of identification of early indicators of glaucoma, which is less discussed topic in any existing research manuscript.

3.3.2. Identified Research Gap

Not all identified problems can be solved effectively towards correcting or improving the diagnosis of glaucoma. However, there are certain identified issues extracted from existing review which were left completely unaddressed. Such unaddressed issues in form of research gap acts as an impediment towards opening up new avenues of early diagnosis of glaucoma. The identified research gap are as follows:

- *Narrowed Coverage of Critical Region*: A closer look into majority of existing approaches and dataset witnesses adoption of OCT images which basically furnishes three dimensional image modalities offering better diagnostic scope. However, majority of study has been restricted to consider two-dimensional perspective of dataset. Hence, higher feasibility of identifying critical areas have been overlooked.
- *Less Emphasis towards Early Detection*: Irrespective of large number of studies, majority of the studies contributes towards either grading or detecting the stages of glaucoma. There are very less benchmarked studies towards early detection problems. Some of the notable issues not addressed are:
- *Asymptomatic Nature*: There is no significant symptoms for people in early stage of glaucoma while applying existing machine learning algorithm may lead to outliers.
- *Variability on Dataset Presentation*: Irrespective of good number of dataset availability, there is a higher feasibility of glaucoma to be manifested in manifold forms as well as progress at fluctuating rates. This patterns are challenging to be identified by existing learning algorithms.
- *Slow Progression*: Glaucoma is a gradually progressing disease where patient may suffer vision loss much before its actual detection. This itself makes teh diagnosis much more challenging. Hence, there is a need of understand more critical areas of fundus with machine learning algorithm to be more capable of predicting uncertain conditions more intelligently.
- *Limitation with Existing Dataset*: A closer look into publication trend in last 5 years shows less deep learning approaches while traditional machine learning algorithm are more preferred. One possible reason could be success of deep learning algorithms demands higher size of quality data. On the other side, existing dataset is highly imbalanced, lacks exlcusive representation of imaging devices, environment, dmeographics, etc. Although data augmentation can address this issue, but it demands clinician input in order to resist any form of outliers at the end. Moreover, there is lack of dedicated dataset exclusively for glaucoma, majority has embedded information of multiple occular diseases.
- *Unsolved Challenges with Learning Approaches*: Keeping aside the issues of high-quality dataset, deep learning approach is actually potential solution for early detection of glaucoma. However, existing approaches doesn't reports of better validation approaches of these models thereby complicating the reliable nature of diagnosis. Apart from this, existing approaches offered an evidence of higher accuracy claims without giving sufficient support of cost-effective computational efficiency, without whom, its questionable to think of its implementation in real-time.

4. CONCLUSION AND FUTURE WORK

This manuscript presents discussion of effectiveness in growing interest of adopting machine learning approaches towards early diagnosis of glaucoma. The contribution of the proposed review work are as follows: i) the study presents curated taxonomy of recently deployed machine learning algorithms towards detecting and classifying glaucoma in last 5 years, ii) the work has presented a brief snapshot of different publicly available dataset adopted in existing machine learning implementation has been discussed, iii) the review explored recent publications trends of all machine learning algorithms to find more adoption of conventional machine learning compared to deep learning approaches, iv) the trend also shows consistent emphasis towards adopting feature engineering methods in all the approaches, v) finally, the study has presented some of the exclusive learning outcomes and research gap which demands immediate attention. Apart from this, the study outcomes also reveal that not much dedicated emphasis is carried out towards modelling solution for early diagnosis as various associated secondary issues have been left unaddressed. Further, existing machine learning approaches demands significant innovations in presence of limited availability of dataset. The future work will be carried out towards addressing the identified research gap and addressing the unsolved issues related to machine learning models to increase better accuracy and effective computational efficiency for early diagnosis of glaucoma.

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