PERSONALIZED ONE-SHOT LOCAL ADAPTATION FEDERATED LEARNING FOR MORTALITY PREDICTION IN MULTI-CENTER INTENSIVE CARE UNIT

By

DENG TING

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

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The increasing volumes of electronic healthcare records (EHR) encourage the development of the application and research of machine learning (ML) in digital health. Promoting ML in healthcare based on EHR can enhance health management for increased intelligence, safety, and efficiency. Unlike traditional data-centralized ML methods, federated learning (FL) provides a novel and promising distributed learning scheme to promote ML in multiple healthcare institutions while preserving data privacy. Nevertheless, the EHR datasets preserved by independent institutions differ considerably in both quantity and characteristics, making the overall data non-independently and identically distributed (non-IID). Coupled with effect of its skewness, this non-IID data can cause a significant reduction in model performance, especially prediction accuracy, rendering FL devoid of practical significance.

This study explored the problem with an in-hospital mortality prediction task under an actual multi-center Intensive Care Unit (ICU) EHR database that preserves the original non-IID data distributions. It argues that, the mechanism of generating a unified sharing model for all participants in conventional FL is no longer feasible. Instead, Personalized federated learning (PFL) focusing on generating a tailored model for each client is applicable. However, current PFL techniques still face limitations in enhancing model predictive accuracy, including the inadequate performance of the global model as a basis for personalized models, the challenge of integrating global data knowledge into highly personalized models, and the difficulty of generating optimal highly personalized models for all independent clients.

Accordingly, this study proposes a PFL method, Personalized One-shot Local Adaptation (POLA), to tackle these problems progressively through a three-step optimization. Step 1 involves obtaining a well-performing global model as a teacher by modifying the baseline FL with a selection criterion and a data estimation strategy. Step 2 enables highly personalized models as students to rebalance global and local data knowledge through knowledge distillation optimizations. Step 3 automatically evolves the best-fitting parameters for the highly personalized model at each center using an adapted genetic algorithm. Ultimately, this typical "FL training + local adaptation" PFL method can enhance model predictive accuracy by automatically generating a highly personalized model for each ICU center, guided by the FL sharing model.

To demonstrate its effectiveness, this study experimentally evaluated POLA in diverse multi-center ICU scenarios with varying non-IID skewness. After conducting stepwise experiments and comparing with three benchmark methods - a baseline FL method and two PFL approaches in similar optimization scheme - the results shows that POLA not only systematically optimizes its internal outputs but also outperforms the comparison methods.

Overall, it showcases notable outcomes, attaining 8.32% and 0.94% enhancements in ROC AUC accuracy at the 10th and 100th training rounds in slightly non-IID data, and 8.41% and 1.04% improvements in highly non-IID data, compared to the top-performing benchmark method. Individually, it obtains performance gains for the maximum number of independent centers, benefiting 100% of them when compared to baseline FL. As these expected results show, POLA is a promising option for promoting FL in the multi-center ICU scenario.

Keywords: electronic healthcare records, mortality prediction, federated learning, non-IID data

SDG: GOAL 3: Good Health and Well-Being

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Doktor Falsafah

PEMBELAJARAN BERSEKUTU ADAPTASI SETEMPAT SATU SYOT DIPERIBADIKAN UNTUK RAMALAN KEMATIAN DI MULTIPUSAT ICU

Oleh

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Peningkatan jumlah rekod kesihatan elektronik (EHR) mendorong perkembangan aplikasi dan penyelidikan pembelajaran mesin (ML) dalam kesihatan digital. Mempromosikan ML dalam kesihatan berdasarkan EHR boleh meningkatkan pengurusan kesihatan untuk peningkatan kecerdasan, keselamatan, dan kecekapan. Berbeza dengan kaedah ML yang terpusat data tradisional, pembelajaran bersekutu (FL) menyediakan skema pembelajaran yang berpusat distribusi yang baru dan menjanjikan untuk mempromosikan ML dalam pelbagai institusi kesihatan sambil mengekalkan privasi data. Namun begitu, set data EHR yang disimpan oleh institusi-institusi bebas berbeza secara ketara dari segi kuantiti dan ciri-ciri, menjadikan data secara keseluruhan tidak bersifat bebas dan identik (non-IID). Bersamaan dengan kesan skewnessnya, data non-IID ini boleh menyebabkan penurunan yang ketara dalam prestasi model, terutamanya dalam ketepatan ramalan, menjadikan FL tidak lagi penting secara praktikal.

Kajian ini menyelidiki masalah dengan tugas ramalan kematian di hospital di bawah pangkalan data EHR Unit Rawatan Rapi (ICU) multipusat sebenar yang menyimpan distribusi data asli non-IID. Ia berpendapat bahawa, mekanisme menghasilkan model perkongsian bersatu untuk semua peserta dalam FL konvensional tidak lagi praktikal. Sebaliknya, pembelajaran bersekutu peribadi (PFL) yang memberi tumpuan kepada menghasilkan model yang disesuaikan untuk setiap pelanggan boleh digunakan. Walau bagaimanapun, teknik PFL semasa masih menghadapi kekangan dalam meningkatkan ketepatan ramalan model, termasuk prestasi model global yang tidak mencukupi sebagai asas untuk model yang diperibadikan, cabaran untuk mengintegrasikan pengetahuan data global ke dalam model yang sangat diperibadikan, dan kesukaran menghasilkan model yang sangat diperibadikan secara optimum untuk semua pelanggan bebas.

Oleh itu, kajian ini mencadangkan satu kaedah PFL, adaptasi setempat satu syot diperibadikan (POLA), untuk menangani masalah ini secara berperingkat melalui tiga langkah pengoptimuman. Langkah 1 melibatkan mendapatkan model global yang berprestasi baik sebagai guru dengan memodifikasi FL asas dengan kriteria pemilihan dan strategi penilaian data. Langkah 2 membolehkan model yang sangat diperibadikan sebagai pelajar untuk menyeimbangkan pengetahuan data global dan tempatan melalui pengoptimuman penyebaran pengetahuan. Langkah 3 secara automatik membangunkan parameter yang paling sesuai untuk model yang sangat diperibadikan di setiap pusat menggunakan algoritma genetik yang disesuaikan. Akhirnya, kaedah PFL jenis "latihan FL + adaptasi setempat" ini

boleh meningkatkan ketepatan ramalan model dengan menghasilkan secara automatik model yang sangat diperibadikan untuk setiap pusat ICU, dipandu oleh model perkongsian FL.

Untuk menunjukkan keberkesanannya, kajian ini secara eksperimen menilai POLA dalam senario pelbagai pusat ICU yang berbeza dengan keseragaman data non-IID yang berbeza. Selepas menjalankan eksperimen secara berperingkat dan membandingkan dengan tiga kaedah perbandingan - kaedah FL asas dan dua pendekatan PFL dalam skema pengoptimuman yang sama - hasilnya menunjukkan bahawa POLA bukan sahaja secara sistematik mengoptimumkan output dalaman tetapi ianya juga mengatasi kaedah perbandingan.

Secara keseluruhan, ia menunjukkan hasil yang ketara, mencapai peningkatan ketepatan ROC AUC sebanyak 8.32% dan 0.94% pada pusingan latihan ke-10 dan ke-100 dalam data non-IID sedikit, dan peningkatan sebanyak 8.41% dan 1.04% dalam data non-IID yang tinggi, berbanding dengan kaedah penanda aras yang terbaik. Secara individu, ia dapat peningkatan prestasi untuk jumlah maksimum pusat bebas, memberi manfaat kepada 100% daripadanya berbanding dengan FL asas. Seperti yang ditunjukkan oleh hasil yang dijangka ini, POLA adalah pilihan yang menjanjikan untuk mempromosikan FL dalam scenario multipusat ICU.

Kata Kunci: rekod penjagaan kesihatan elektronik, ramalan kematian, pembelajaran bersekutu, data bukan IID

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LIST OF ABBREVIATIONS

EHR	Electronic Health Records
ML	Machine Learning
ICU	Intensive Care Units
GDPR	General Data Protection Regulation
FL	Federated Learning
IID	Independently and Identically Distributed
non-IID	Non-Independently and Identically Distributed
PFL	Personalized Federated Learning
FMTL	Federated Multi-Task Learning
FKD	Federated Knowledge Distillation
SVM	Support Vector Machines
CPSO	Chaos Particle Swarm Optimization
LR	Logistic Regression
ANN	Artificial Neural Network
MLP	Multi-Layer Perceptron
CNN	Convolutional Neural Networks
RNN	Recurrent Neural Networks
DNN	Deep Neural Networks
IoT	Internet of Things
SGD	Stochastic Gradient Descent
MAML	Model Agnostic Meta Learning
FTL	Federated Transfer Learning
KD	Knowledge Distillation
MTL	Multi-task Learning
FMTL	Federated Multi-Task Learning

CFL	Clustering Federated Learning
IDE	Integrated Development Environment
MLlib	Machine learning Lib
GPU	Graphics Processing Unit
MIMIC	Multi-parameter Intelligent Monitoring in Intensive Care
ANZICS APD	Australian and New Zealand Intensive Care Society Adult Patient Database
ICNARC	Intensive Care National Audit and Research Centre
LCP	Laboratory for Computational Physiology
OHE	One-Hot Encoding
LSTM	Long Short-Term Memory
AUC	Area Under the Curves
ROC	Receiver Operating Characteristics
PR	Precision-Recall
TPR	True Positive Rate
FTR	False Positive Rate
ECDF	Empirical Cumulative Distribution Function
MES	Mean Squared Error
GA	Genetic Algorithm
AGA	Adaptive GA
NAS	Neural Architecture Search
ReLU	Rectified Linear Units

CHAPTER 1

INTRODUCTION

1.1 Background

With the development of computer and information technology in medical applications and the gradual improvement of hospital digitization, electronic health records (EHR), which contain extensive patient health data comprising demographics, diagnoses, medications, laboratory records, and radiological images, have experienced a substantial rise in both scale and amount (Shickel et al., 2018). Although the primary aim of the EHR is to promote healthcare efficiency from an operational point of view, the cumulative EHR data can also be applied for secondary analysis to enhance patients' health management and drive personalized healthcare (Lokhandwala & Rush, 2016). One of the hottest techniques for secondary analysis of EHR is machine learning (ML), as the rich data resources and valuable implicit information in EHR have provided it a natural implementation foundation (Wu, Roy, & Stewart, 2010).

At present, extensive applications of ML in EHR have been made for medical decision support. For instance, some widely-used ML methods, like k-Nearest-Neighbors, Support Vector Machine, Naïve Bayes, Random Forest, Decision Tree and Logistic Regression have been applied to identify type 2 diabetes mellitus based on EHR (Zheng et al., 2017). A logistic regression ML model is implemented to identify lupus patients using available EHR (Jorge et al., 2019). A ML-based algorithm, XGBoost, is presented to detect the elders at greater risk of falling (Ye et al., 2020). Moreover, as deep learning becomes more widely applied in EHR, the accuracy of healthcare prediction models has significantly enhanced, enabling the implementation of more complex tasks (Shickel et al., 2018).

Although ML is popular in EHR research nowadays, its implementation in practical applications is arduous, due to these ML approaches generally require a central data repository that gathered from different medical institutions to achieve the desired results (Nair, Hsu, & Celi, 2016). This is hard to generalize in practical applications, since the dispersed EHR datasets that produced and maintained by various healthcare facilities are difficult to be transferred and aggregated. Moreover, these EHR data is more sensitive and harder to be gathered than regular data due to its patient privacy implications (Price & Cohen, 2019). Therefore, centralizing or disclosing these data presents technical as well as legal, ethical, and regulatory obstacles pertaining to privacy and data protection (Van Panhuis et al., 2014), such as those imposed by the Health Insurance Portability and Accountability Act (HIPAA) (Annas, 2003) and the General Data Protection Regulation (GDPR) (Voigt & von dem Bussche, 2017).

While there are certain methods available to prevent these limitations, such as redacting sensitive patient information to anonymize the data or implementing privacy-preserving algorithms during data transmission to avoid unauthorized access (Gkoulalas-Divanis, Loukides, & Sun, 2014), the underlying problem of data migration remains unresolved. In addition, the process of gathering, organizing, and preserving a dataset of exceptional quality requires significant effort, time, and financial resources (Rieke et al., 2020).

Federated Learning (FL) offers a brand new mechanism to solve this problem (Konečný et al., 2016; Brendan et al., 2017). It emerges as a paradigm to apply ML models to private distributed data silos, offering great potential for advancing ML in the digital healthcare domain. Specifically, FL enables ML implementation in independent healthcare organizations without sharing or collecting any raw data, allowing pertinent information from the dispersed data to be communicated among the independent institutions while maintaining patient privacy and sensitive data security (Brisimi et al., 2018).

Currently, the applications of FL in EHR have permeated various aspects of digital healthcare. For example, FL can facilitate the identification of patients with similar clinical characteristics across various institutions (Lee et al., 2018), contribute to the development of a decentralized framework for predicting hospitalization due to cardiac events (Brisimi et al., 2018), and forecast mortality rates and length of stay in the Intensive Care Unit (ICU) (Huang et al., 2019), including those related to COVID-19 (Vaid et al., 2021).

Although FL is practicable in EHR applications, its effectiveness could be significantly decreased by the non-independently and identically distributed (non-IID) data nature of these distributed EHR datasets (Brendan et al., 2017; Zhu, H. et al., 2021). Hence, addressing challenge of enhancing the performance of FL with the non-IID data issue resulting from the independently distributed EHR datasets has emerged as a prevalent research focus in the current FL research (Li, Sahu, Talwalkar, et al., 2020).

In this context, this study applies FL into an actual multi-center ICU scenario with an in-hospital mortality prediction task to explore the problem. ICU that generates a substantial amount of EHR data daily can fully support ML applications (Xu et al., 2017), and its distributed multi-center setting provides a natural application scenario for FL. Coupled with the significant importance of predicting in-hospital mortality (Xu et al., 2017; Liu et al., 2018), exploring and promoting the implementation of FL in this context is thus feasible and meaningful.

1.2 Problem Statement

In conventional ML research on EHR, raw data is gathered from disparate medical institutions into a single data center, with the assumption that the data is independently and identically distributed (IID). This idealized data context can ensure the accuracy and convergence rate of the ML algorithm (Courtiol et al., 2019; Ye et al., 2020). However, in the FL setting, the IID assumption no longer holds since the distributed datasets that are generated independently and maintained privately can vary significantly in both feature and amount (Cao, 2022). Consequently, in FL applications, the overall data distribution is naturally non-IID (Kairouz et al., 2019). This data distribution nature has a significant negative impact on the effectiveness of FL, leading to a pervasive and fundamental issue for model accuracy degradation in the FL training process (Zhao et al., 2018; Nilsson et al., 2018; Hsieh et al., 2020).

Furthermore, the data distributions in diverse FL application scenarios vary significantly in terms of its skewness towards non-IID (Zhu, H. et al., 2021), which is also a crucial consideration when it comes to the effectiveness of FL (Kairouz et al., 2019). Compared to training with centralized or IID data, the prediction accuracy of FL in non-IID data significantly decreases as the skewness increases (Hsu, Qi, & Brown, 2019; Zhu, H. et al., 2021). In extremely skewed cases, FL training may even fail to benefit most of its participants (Hsieh et al., 2020).

In summary, the inevitable non-IID data in the independently distributed EHR data scenario, especially that with high skewness, can significantly decrease the model effectiveness of FL, thus weakening or even removing the main incentive for independent healthcare centers to participate in FL training.

This study argues that the main reason for this problem is the indiscriminate treatment of all participants by FL. In conventional FL, the ultimate working model for all participants is unified, which could be unbefitting for non-IID data, especially that with high skewness (Hsu, Qi, & Brown, 2019; Hsieh et al., 2020; Zhu, H. et al., 2021). Conventional FL aims to generate a unified sharing model with global data knowledge to benefit all or most independent clients. However, as non-IID data skewness increases or reaches a certain degree, the global model can only benefit a small portion of client models, and for the most FL-trained models, their performance is not even as good as what could be expected from independent training.

Accordingly, the conventional FL scheme, which focuses on generating a globally uniform shared model while ignoring the data characteristics of each independent client, is not advisable in this non-IID data environment. This study shifts the focus of FL from generating a unified sharing model to customizing local models for individual ICU centers, thereby alleviating the non-IID data problem through a personalized solution. As with the conception of personalized federated learning (PFL) techniques (Kulkarni et al., 2020; Tan et al., 2022), this study will generate a unique personalized model for each independent ICU center based on its data characteristics while gaining global data experience in FL. Specifically, it will personalize FL in a typical "FL training + local adaptation" solution, which is to generate personalized models for ICU centers by locally adapting the global model in FL training.

Currently, most existing PFL methods implemented in a similar scheme directly perform local adaptations on the global model to achieve personalization (Kulkarni et al., 2020; Tan et al., 2022). After observing their shortcomings, the specific research problems of this study are presented as follows:

I. As stated above, the global FL model can be adversely impacted by non-IID data, showing instability in performance during the training process (Li, X., et al., 2020). Executing local adaptation directly on the vulnerable global model will result in the subsequent personalized models being hard to escape the negative impact of non-IID data.

   For example, two representative PFL methods, FL fine-tuning (Wang, K. et al., 2019) and FedDistill (federated-distillation) (Jiang, Shan, & Zhang, 2020) have exposed the problem. FL fine-tuning involves locally retraining several hyperparameters for the obtained global model to achieve model personalization. FedDistill utilizes knowledge distillation (KD) (Hinton et al., 2015) to locally retrain the global model to get personalization under the guidance of a local teacher model on each client. While showcasing the effectiveness in specific data environments, their results of model personalization also reveal a significant reliance on the global model. When the global model performs well in slightly skewed non-IID data, the results are correspondingly better. However, if the increase in the skewness of non-IID data leads to a decrease in the performance of the global model, the outcome will also decline.

Evidently, a stable-performing global model is indispensable for local adaptation to personalize FL. Therefore, the first research question to address in this study is how to mitigate the negative effects of non-IID data with varying skewness to ensure the stable performance of the global sharing model in FL.

II. The personalized models produced by directly adapting the global model can only be in the same structure as the global model. This results in the structure of the model being unable to be personalized, accompanying the drawback of limiting the model's performance across non-IID data with various skewness (Li, Sahu, Zaheer, et al., 2020). For instance, an algorithm for personalized FL (pFedMe) using Moreau envelopes, proposed by Dinh et al., (2020), typically involves directly fine-tuning the global model locally to produce personalized models for each client. These resulting personalized models differ from the global model only in terms of model parameters, while other settings, including the structure, remain consistent with the global model.

Furthermore, although there are KD-based methods that allow the model's structures to be personalized independently of the global model, the ensuing problem is that these personalized models cannot acquire sufficient collective data knowledge, thereby leading to a decrease in prediction accuracy. Two typical KD-based methods are Federated Distillation (FD) (Jeong et al., 2018) and Hybrid Federated Distillation (HFD) (Ahn et al., 2019). They exchange distillated model knowledge, such as prediction scores, to replace the entire global model during FL training. The distilled knowledge is then used to guide the learning of local models, enabling the resulting personalized models to have structural diversity different from the global model. However, due to insufficient collective data information of the distilled knowledge and a lack of further exploration of structure personalization, despite reducing communication costs in FL, their model prediction accuracy falls significantly short of the baseline FL.

Accordingly, this raises the second research question of this study: how to enable personalized models with structures independent of the global model to sufficiently learn the global collective data knowledge.

III. Generating personalized models with diverse structures for all FL participants is challenging, unlike the straightforward approach of directly adapting the global model. The parameter space corresponding to personalized models that encompass diverse structures is exceedingly vast. Manually constructing, training, and searching for the ideal personalized models of all FL participants is extremely difficult and impracticable (Tan et al., 2022).

For example, a novel Model-Heterogenous Aggregation Training FL scheme (MHAT) (Hu et al., 2021) further explores the model structure personalization based on KD technique. It provides a mechanism for FL to generate heterogeneous models for all participating clients, thereby improving the prediction accuracy. However, these heterogeneous models, customized for each client, can only be manually designed, and selected. Although it enhances prediction accuracy, tremendous labor and time are required to search for the optimal personalized model for each FL client.

Consequently, the third research question is how to efficiently and practically find ideal personalized models with structural differences for all ICU centers without manual intervention.

1.3 Research Objective

The main objective of this study is to propose a PFL method that can effectively improve the model accuracy of mortality prediction for each center under the actual multi-center ICU scenarios. To accomplish this general objective, the following sub-objectives are required to be achieved:

I. To propose a modified approach on the baseline FL to alleviate the instability in performance of the FL global model across differently skewed non-IID data, thereby better facilitating subsequent local adaptation.

II. To propose an approach to tackle the drawback that personalized models with structures independent of the global model cannot acquire sufficient collective data knowledge, thereby enhancing model prediction accuracy.

III. To propose an approach to address the challenge of manually obtaining ideal personalized models with diverse structures for all ICU centers, thereby enhancing the overall efficiency and practicality of the method.

1.4 Research Scope

This study implements FL to predict the mortality of inpatients within a certain period after admission in a multi-center ICU scenario. Its main concern is whether the survival status of patients can be predicted accurately while introducing FL. Essentially, it is a binary classification prediction task involving

ML.

The primary issue in this study is to address the non-IID problem present in separate datasets stored across various independent clients in FL, with a focus on enhancing the accuracy of mortality prediction. To authentically simulate this data environment, the study utilizes the actual dataset, eICU Collaborative Research Database (eICU-CRD) (Pollard et al., 2019), which preserves the natural non-IID data distribution.

The database was generated by an actual program and encompasses over 200,000 admissions related to 335 ICU units at 208 independent hospitals, providing a suitable data environment for this research due to its independently distributed sources and abundance of data.

This study is to propose a novel PFL method to address the research problem in the specific data environment. The proposed method is evaluated using ROC AUC and PR AUC metrics and compared against three benchmark methods, namely FederatedAveraging (FedAvg) (Brendan et al., 2017), FedDistill (Jiang, Shan, & Zhang, 2020), and pFedMe (Dinh et al., 2020), to validate its effectiveness.

1.5 Contribution of the Thesis

This study mainly proposes an effective PFL method in an actual multi-center ICU scenario to improve the mortality prediction performance of each independent center. It accomplishes this by sequentially addressing the challenges of PFL in various non-IID data environments, thus achieving the following specific contributions:

- An approach to modifying the standard FL to obtain a more stable global model across different skewed non-IID data environments has been proposed. The global model obtained by the modified FL has been proven to be more stable in terms of prediction accuracy, which is conducive to subsequent local adaptation.
- An approach allowing the highly personalized model of each ICU center to effectively acquire collective data knowledge in the global model has been proposed. This approach enables individual centers to possess highly personalized local models while extracting sufficient collective data knowledge from the global model to enhance model accuracy.
- An approach to automatically constructing and searching for the best-fitting personalized parameters for all ICU center models has been proposed. This approach automates the laborious task of manually determining the personalized model designs in FL, ensuring the stability of the whole PFL algorithm while enhancing its practicality.

1.6 Thesis Outline

Chapter 1 is an introductory chapter that includes the research background, research problem, research objectives, research scope, and contributions of this study.

Chapter 2 gives a comprehensive review and summary of the related research and techniques. Firstly, the concepts, classifications, challenges, and EHR applications of FL are introduced. Secondly, the non-IID data problem in FL is elaborated on. Thirdly, prevailing optimization strategies in FL that aim to address the challenge of non-IID data are reviewed and summarized. Finally, the content in this chapter is summarized.

Chapter 3 integrally illustrates the methodology used in this study. It contains all stages of the whole research, which refers to optimization problem definition, experimental environment setup, data analysis and processing, basic model implementation, and evaluation metrics.

Chapter 4 elaborates the proposed PFL method, POLA. It first provides an overview of the implementation framework for POLA and then proceeds to explain the specific implementation process of POLA in three optimization steps.

Chapter 5 presents the experimental results and offers a comprehensive analysis and discussion. It starts by showcasing the foundational experimental settings. Then, it demonstrates the predictive performance of the baseline FL under the specific non-IID data environment of this research. Following that, it presents the results of the POLA algorithm step by step. Subsequently, a comparison between POLA and benchmark PFL methods is presented. Finally, these experimental results are discussed.

Chapter 6 concludes the whole research and recommends several future research directions.

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