# **A systematic review of SARS-CoV-2 epidemiological interpretable machine learning models**

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## **Abstract**

Artificial intelligence has shown substantial achievements to control the spread of SARS-CoV-2 by application of numerous machine & deep learning techniques to variety of pandemic relevant fields. Epidemiological machine learning studies of SARS-CoV-2 are among the frequently performed researches within the scope of the recent pandemic. While these models can be perceived as precise and policy relevant to guide governments towards selecting optimal containment policies, their black box nature might hamper to build trust and rely confidently on the prescriptions proposed. This paper focuses on the question of interpretability of AI based epidemiological models (XAI) in the context of the recent SARS-CoV-2 pandemic. We systematically review the studies, which has focused on jointly incorporation of AI, SARS-CoV-2 epidemiology and XAI. Thereby, we first propose a generic framework of the SARS-CoV-2 interpretable machine learning pipelines. Upon analyzing the relevant studies, we reflect around upcoming research ideas based on the existing gaps in the scope of the reviewed studies.

## **Introduction**

The application of Artificial Intelligence (AI) especially machine learning and deep learning models in variety of contexts such as computer vision, robotics, epidemiology, medical imaging, etc. have been evidenced as one of the most powerful approaches to contain the spread of the SARS-CoV-2 pandemic. While the excellence of AI models, in terms of their accuracy and performances are broadly admitted, the results and decision prescriptions made based on these models are not always as transparent as required to represent them as completely understandable and or trustworthy solutions. In other words, AI model, despite being highly accurate, are not enough *interpretable*. Interpretability is defined as the degree to which a human can understand the cause of a decision (Miller, 2019). The basic domain of *Explainable Artificial Intelligence* (XAI) has been devoted a high attention in the recent time to propose approaches to resolve the question of interpretability. Its goal is to understanding the corresponded processes behind the algorithms, which lead to the AI models’ generated predictions (Allgaier et al., 2023; Lu et al., 2023; Confalonieri et al., 2020; Angelov et al., 2021; Vilone & Longo, 2021; Tjoa & Guan, 2020).

In the context of AI studies of the SARS-CoV-2 pandemic, the XAI remains one of the main concerns, especially with regard to medical AI systems (Abiodun et al., 2022), as AI based medical diagnosis are directly linked to human lives. For example, the human legible explanations in practice and their legal implications are being legally stabilized in the practice under the European union’s scope of the General Data Protection Regulation (GDPR) for the medical diagnosis of patients.

While the significance of XAI in health care systems is self-evident, the substantial role XAI might play in AI based *government policy* related problems is either a noticeable subject. The AI based epidemiological models are conspicuous examples of applying machine learning techniques to the problems, where XAI can efficiently influence the AI’s understandability at policy level as well as at system development’s level. Indeed, XAI enables the AI to precisely and transparently shed light on the magnitude of the influential factors of a pandemic. These factors are ranging from pharmaceutical PIs and non-pharmaceutical interventions NPIs to seasonality effects to health infrastructure attributes etc. Figure 1 summarizes, how the effects of applying AI analysis (at policy level as well as at system development’s level), with and without implementation of XAI can seem unlike. When not utilizing the XAI, not only the system development level cannot identify the source of odd results or extraordinary errors in its system, the policy level might also barely trust in the outcomes produced at the development’s level. Though, utilizing XAI can handle the potential pitfalls emerged at system development level by looking at behind the algorithms procedures, it enables moreover the policy making system to see the evidences for model predictions letting him to build more trust and rely more confidently on the conclusions proposed by AI.

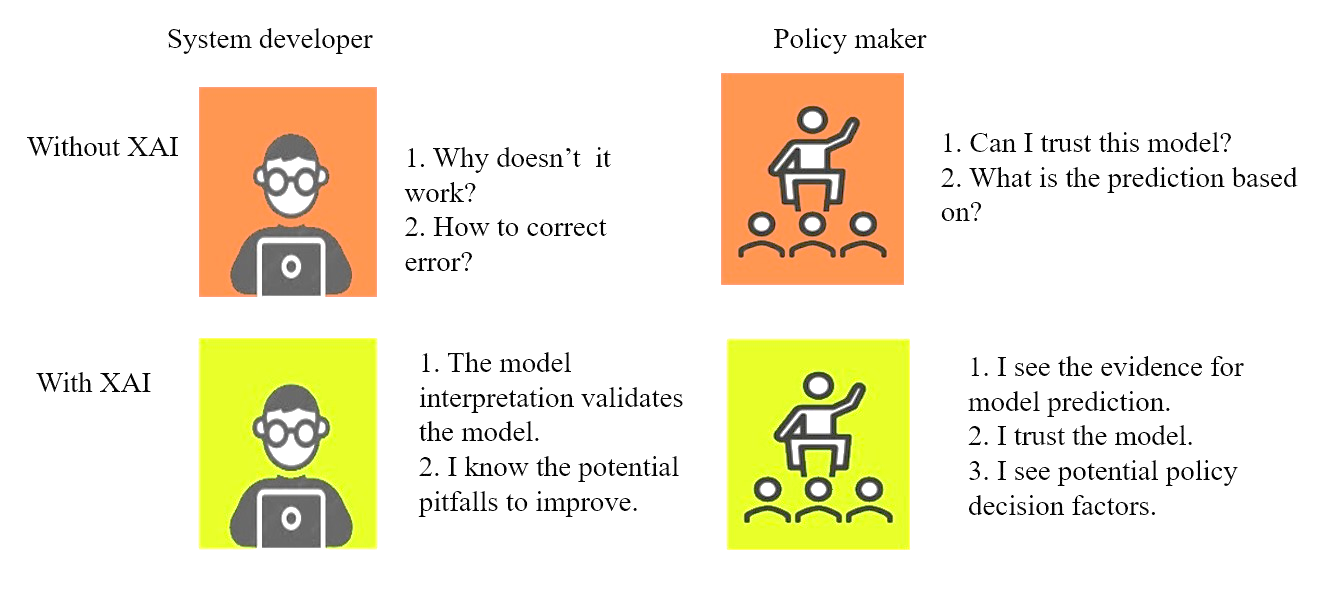


Figure 1: Motivation for model developers and policy makers to implement XAI in AI-enabled decision support systems (adopted from the motivation for model developers and clinicians to implement XAI in AI-enabled clinical decision support systems proposed by Sun et al., 2023).

In this study we aim at providing a complete survey of interpretable epidemiological machine learning models used to forecast and analyze the SARS-CoV-2 pandemic. Even when the current pandemic recedes, summarizing and analyzing this area of research can contribute to solve the complexities, which might arise within the potential forthcoming epidemic waves. It can also enhance the use of XAI within the general context of AI based government policies.

To fulfil the purpose of a consistent literature review, a systematic study is designed adapted from the preferred reporting items for systematic reviews and meta-analyses PRISMA (Moher et al., 2009). Figure 2 presents the flowchart of selecting papers in our study consisting of 4 consequent phases i.e. identification, screening, eligibility and inclusion.

The identification phase is carried out by filtering titles and content in the Google Scholar database. Thereby we opted for a broad coverage identification strategy by using the search engine to identify all papers, which incorporate first, the search word “covid” in their title, as well as, they incorporate one of the semantically exchangeable search words “interpretable machine learning”, “interpretable deep learning”, “explainable machine learning” and “explainable deep learning” in their text content resulting in 4 subsequent search categories. Summing up of the search results obtained from the aforementioned categories, altogether 1503 studies were identified and collected by us. As among the collected papers, there were studies, which coexist in the 4 aforementioned categories, the duplicated papers are filtered in the summing step to come out with about 1320 papers. Based on the identified papers, the screening phase is performed to mark each paper with regard to specific area it belongs to. Thereby, more than 7 groups of papers are characterized. Most of the papers are ascribed to the group of computer vision especially X-ray and CT imaging classification methods, as well as SARS-CoV-2 diagnosis approaches based on clinical markers (i.e. blood tests, patient symptoms etc.). Besides, 88 epidemiological studies as the targeted zone of this study are identified as the 4th most frequently observed group. The eligibility phase is then implemented based on the XAI criteria with regard to the screened epidemiological papers. The inclusion criterion consists of three rules comprising (a) being pier reviewed journal paper (b) using at least one ML model rather than statistical regression models in the paper and (c) that paper applies XAI within its pipeline. By stepwise filtering based on the three above mentioned inclusion criteria, we come out finally with 26 papers, which are included, categorized again and explored more in detail in section 3 of this paper. It is worth noting that by the screening phase of our research and under the “other categories” (figure 2), we came across 188 literature review articles. Most of these articles have analyzed AI technologies that can be used to fight SARS-CoV-2 from different perspectives (The complete list of these review articles together with a short description corresponded to each of them is provided by us in the supplementary material of this paper). However, none of these studies has focused on jointly incorporation of AI, SARS-CoV-2 epidemiology and XAI.

The remainder of the paper is as follows. In section 2, a generic framework of the interpretable machine learning pipelines in the context of SARS-CoV-2 is proposed. In section 3, the included papers’ pipelines are analyzed. Section 4 reflects around upcoming research ideas based on the existing gaps in the scope of literature we reviewed in this study. Section 5 concludes.

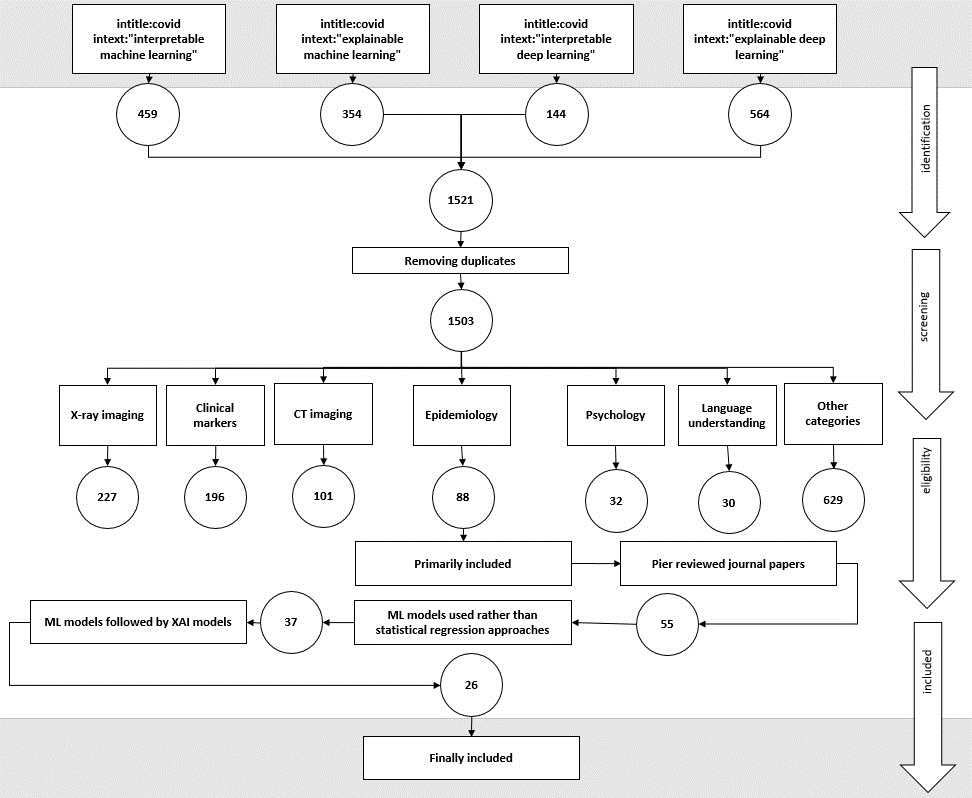
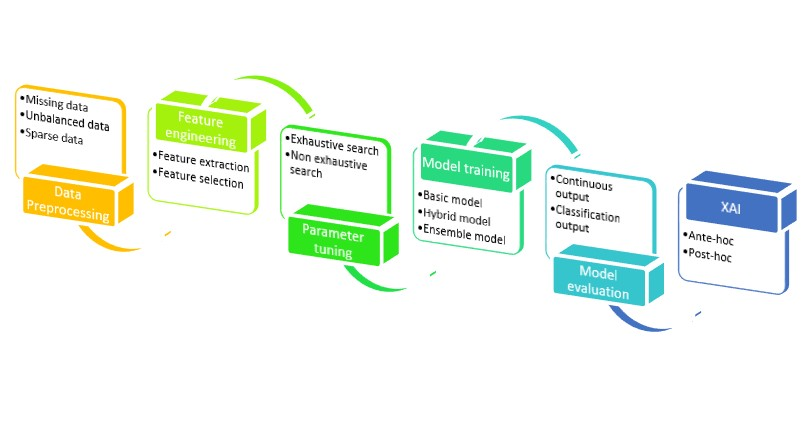


Figure 2: Flowchart of the study search and selection process.

## **Background**

In this section we deliver a comprehensive framework of the pipeline of ML papers applied in the context of SARS-CoV-2 literature. A simplified version of the pipeline from the data sources as the most primary existing inputs until achieving human understandable outcomes is depicted in figure 3. Note that even if the model XAI stage in figure 3 is realized at the end of the pipeline, each step of the research pipeline might have interactive influential on XAI. Hence the review of preceding steps prior to the model interpretation is of importance.

Figure 3: A generic depiction of the ML pipelines in the context of SARS-CoV-2.

### **Data preprocessing**

Data preprocessing step is thought to handle missing, unbalanced and sparse data. Missing data values are inherently handled by some techniques e.g. by the gradient-boosting predictors (Zoabi et al., 2021), nonetheless they remain a basic problem on top of the pipeline in numerous studies.

#### Missing data

Missing data can cause concerns not only to the model precision but furthermore to the interpretation of the achieved output. The lack of enough data is shown to burden the prediction accuracy of SARS-COV-2 cases while having larger data can lead to improved results in Jayanthi & MuraliKrishna (2023). Basically as the amount of data increases, the epistemic uncertainty related to the model decreases (Aldhahi & Sull, 2023). In contrast, the problem of lacking data becomes amplified when facing with problems with a large number of inputs. Docquier et al. (2022) show how the inclusion of extra parameters (to incorporate day specific effects – i.e., 366 day specific time dummies) to their models deteriorates the predictive power of the ML model and conclude that given a dataset, the gains from adding information, is indeed outbalanced by the costs linked to the inflated dimensionality of the AI computation problem. Hinns et al. (2021) study the XAI generated by various predictors on a dataset and show how *inconsistent* model interpretations emerge among a set of random data sub-sets when using little data and that by increasing the size of data, interpretations of the random data sub-sets converge towards each other. Andonov et al. (2023) show how sudden shift in the input data impacts AI model performances as well as the XAI of the models.

In the context of SARS-COV-2 studies, k-nearest neighbors’ algorithm KNN is frequently used (Cabitza et al., 2020) to imputing the missing values in the dataset. By trying to compare an unlabeled data point to the training dataset, the KNN finds the K most related data points. Thereby, a metric that measures distance such as Euclidean or Manhattan distance is utilized to determine proximity. This technique then assigns the given data point to the most familiar class (Chadaga et al., 2022). Another possible imputation approach is the usage of Generative Adversarial Neural Networks GANN, which learn to generate ‘‘missing’’ data with the same distribution as the training set. This is done by training a ‘‘generative’’ network, which generates possible imputed values and proposes them to a ‘‘discriminative’’ network, which is trained to accept only those generated values that properly fill the missing ones according to the underlying data distribution (Casiraghi et al., 2020).

#### Unbalanced data

The unbalanced data can lead the model performance to be biased in favor of the classes or ranges of outputs, which are overrepresented. The unbalanced data is often handled by the synthetic minority oversampling technique SMOTE (Alle et al., 2022) algorithm. SMOTE works based on identifying the k nearest neighbors principle and deploys the principles of interpolation (Khanna et al., 2023). It creates synthetic data that is close to the minority class to oversample the minority class in the feature space (Adeoye et al., 2022; Rezapour & Elmshaeuser, 2022). To handle the problem of data unbalanced, there are moreover other alternatives. Data partitioning i.e. utilizing dichotomous variables is one of such techniques. Discretizing the variable spaces might not worsen the model performance in all circumstances in a large extent. For example, Wendland et al. (2023) show that models using only dichotomous features perform only slightly worse than models based on a complex combination of numerical input values. Another way of managing unbalanced data is during the training step. In Croci et al. (2022), during the fitting procedure, the class slight unbalancing is tackled by penalizing the misclassification of the minority class with a multiplicative factor inversely proportional to the class frequencies. In Hu et al. (2021), a novel self-adaptive auxiliary loss is proposed to help the training with imbalanced data. The self-adaptive factor reflects the feature distribution and emphasizes minority class. There are other data imputation methods used in the SARS-COV-2 literature based on decision tree based tools e.g. isolation-forest (Aljame et al., 2020), miss-forest (Cortes et al., 2022) and random-forest (Esposito et al., 2021). Meanwhile the range of possible data imputation techniques is not restricted to the those frequently used. For example, predictive mean matching to impute numeric features, logistic regression to impute binary variables and Bayesian polytomous regression to impute factor features are used in Liang et al. (2020). In addition, time series augmentation technique to create new series with the same temporal dependencies that exist in the original series to create new data are presented in the SARS-COV-2 literature e.g. in (Abbasimehr et al., 2021).

#### Sparse data

For resolving the generic problem of sparse training data, the use of generative networks GAN to generate ample training synthetic data is applied in various studies (Amin et al., 2022; Singh et al., 2021; Rangarajan et al., 2021).

In addition, in the presence of the limited data in the SARS-CoV-2 studies context, synthetic data is generated using the auto encoder AE methods (Laatifi et al., 2023; Khozeimeh et al., 2021, Khobahi et al., 2020). AEs belong to the realm of unsupervised learning, as they do not need labelled data for their training and process consists of providing labeled sample data to the *encoder*, which captures the distribution of the deep feature, and the *decoder*, which generates data from the deep feature by decompressing the latent space.

### **Feature engineering**

Feature engineering is generally covering feature selection and feature extraction (Ntakolia et al., 2022). Feature selection is about selecting the subset of the original feature set, whereas feature extraction creates new features (Sulaiman et al., 2022).

#### Pre-trained feature extracting

As the most ML models require inputs in the form of numerical vectors, feature extraction techniques can aim at e.g. translating features like the vocabulary (Beranová et al., 2022), images (De Falco et al., 2022) or parts of speech into numerical representations. This task is done in the most image recognition (Gomes et al., 2021) as well as natural language processing studies (Beranová et al., 2022) by means of pre-trained deep learning models. The pre-trained model acts as an early feature extractor, followed by a fine tuning (Nguyen et al., 2022) and or downstream classification step (Chamberlin et al., 2022).

It is worth noting that, the upstream part of an ML pipelines can comprise the translation of e.g. text and image in both directions to extract desired features. For example, Shang et al. (2022) utilize a text-guided visual feature generator to generate visual features from the news text, as well as an image-guided textual feature decoder to generate the corresponding textual features from the news image.

#### Reduced dimensional feature extraction

Feature extraction techniques can aim at learning the reduced structure of the data by finding a low dimensional embedding representation that preserves the essential structure of the data. A variety of algorithms depicted in table 1 are applied in the context of SARS-CoV-2 literature including K-Means, principal component analysis PCA, auto encoders AE, t-stochastic neighborhood embedding t-SNE, uniform manifold approximation and projection UMAP, self-organizing maps SOM, random fourier features RFF, Latent Dirichlet Allocation LDA etc.

|  |  |  |
| --- | --- | --- |
| Method | Explanation | Reference |
| K-Means | clustering algorithms that can detect complex patterns based on a partition system to group data into several clusters | Thenata & Suryadi , 2022; Janko et al., 2021 |
| PCA | a statistical procedure, which relies on linear transformation for reducing the dimensionality of datasets while preserving crucial information | Chieregato et al., 2022; Adeoye et al., 2022; Hueniken et al., 2021; Janko et al., 2021 |
| AE | perform dimensionality reduction Similar to PCA, however, unlike PCA, which relies on linear transformation, AEs carry out nonlinear transformation using deep neural networks | Khozeimeh et al., 2021 |
| SOM | is an unsupervised machine learning technique to cluster the high-dimensional data into low-dimensional outputs consisting of a similar structure like ANNs, with the difference that the organizing maps in SOM use competitive learning whereas the ANNs use error correction learning such as back-propagation with gradient descent | Yu et al., 2022; de Souza et al., 2023; |
| LDA | is a Bayesian unsupervised clustering method that is often employed to clustering topics of a set of documents in each cluster | Lannou et al., 2021 |
| t-SNE | is an unsupervised non-linear embedding dimensionality reduction. It embeds the points from a higher dimension to a lower dimension trying to preserve the local structure of data | Higaki et al., 2022 |
| UMAP | is a flexible non-linear dimension reduction algorithm based in Riemannian geometry and algebraic topology to learn the manifold structure of the data and find a low dimensional embedding that preserves the essential topological structure of that manifold | Cooper et al., 2022; Lande et al., 2023 |
| RFF | an approximate kernel method, which maps the given data to a low dimensional randomized feature space based on Euclidean inner product space | Ali et al., 2022 |

Table 1: Dimensionality reduction algorithms

Docquier et al. (2022) use a PCA analysis to reduce the dimensionality of the origin- and destination specific containment measures and extract the first two components of the PCA and propose the first PCA component can be interpreted as an average index of stringency of containment measures and the second component captures testing and tracing policies. Trajanoska et al. (2022) cluster countries with similarly balanced diets using SOM. In addition to presenting the SOM clusters, an explainable decision map corresponded to the SOM clusters is presented with squares representing the most dominant feature leading to the decision for clustering the countries.

Beside the above mentioned methods, the knowledge graph embedding techniques to encode the entities and relations in a Knowledge graph as dense and low-dimensional vector representations are utilized in the literature of SARS-CoV-2 (Wong et al., 2023; Ma et al., 2022). In addition, functional data analysis following the principle of “breaking up the whole into pieces” of big data analysis, to transfer discrete and high-frequency sequences of data to continuous smooth functions treating the whole functions as a single entity with an internal unified structure are used in the literature(Zhu et al., 2022)

It is worth noting that, while the above mentioned techniques to reduce the number of variables can eliminate redundant and irrelevant features, however, it is not always clear whether these methods may result in improvements in the predictive power of ML models (de Paiva et al., 2023). Furthermore, even though some of above mentioned studies has provided explanations together with the corresponding algorithms, as these methods project the features to a new dimension, and the features on the new dimension become mixed features, these new features might not necessarily provide a strong explanatory basis (Cao et al., 2022). Despite that, features with the strongest impact on the clustering can be always examined by examining their importance to emerging each cluster through utilizing supervised machine learning models (Lingelbach et al., 2021). For example, Cooper et al. (2021) constructs discriminative decision-rules that identify and differentiate the clusters, forming the subgroup descriptions.

#### Feature selection

Feature selection aims at eliminating the irrelevant and redundant features. Irrelevant and redundant features not only increase the computational complexity of a model but also increase the probability of overfitting (Rostami & Oussalah, 2022; Estiri et al., 2021).

Statistical correlation analysis is the first milestone to observe if e.g. there is a high degree of correlation between multiple independent variables. Existing a high correlation between two variables e.g. the share of population with cancer and the share of elderly is easy to understand. After the correlation analysis, such variables can be reduced to a lower representing number (Cui et al., 2021). The factor analysis technique is an alternative statistical method, which extracts maximum common variance from all variables and puts them into a common score. This contributes to identify latent composite variables for example between GDPs per capita and other development metrics e.g., access to electricity (Hegde et al., 2023).

Various statistical methods can contribute to evaluate the association between independent variables and the dependent variables (leading to sorting the priority of influential variables and eliminating the irrelevant ones) including H-statistics (Youha et al., 2020), Pearson’s correlation analysis (Kianfar et al., 2022), chi-square (Harmouche-Karaki et al., 2023), T-test (Baqui et al., 2021), U-test (Janko et al., 2021), univariate logistic regression (Sun et al., 2021) etc. Note that while statistical methods can indicate overall interaction strength of each feature with the other features, they do not convey how the interactions looks like. That is what XAI are for.

Next to the statistical approaches, the selection of the feature selection model is often based on training an ML model. This ML model could be identical to the training model at the upcoming stage of the pipeline or not. Various approaches undertake a kind of stepwise wrapping feature selection by removing (or adding) features one by one from (to) a set of features and evaluating the model error (or statistical significance of the added factor) through training the model at the upcoming stage of the pipeline (Cao et al., 2020; Cui et al., 2021).

Alternatively, the selection of the feature selection model can be done based on training an ML model and computing the significance of each feature through the subsequent XAI corresponded to the chosen ML model (Rinderknecht & Klopfenstein, 2021; Doblhammer et al., 2021; Digamarthi, 2022; Baldassarri et al., 2020). For example, various studies utilize the XAI-based SHAP concept (see the model interpretation subsection) to undertake the task of feature selection in their pipeline (de Moura et al., 2021; Abbaspour et al., 2022; Chieregato et al., 2022; Nguyen & Byeon, 2023; Jiang et al., 2022).

Beside the above mentioned categories i.e. statistical analysis, Error based and XAI based feature selection methods, different evolutionary techniques like genetic algorithm and particle swarm optimization are utilized in the context of SARS-CoV-2 literature for feature selection (Chadagaa et al., 2023; Khozeimeh et al., 2021; Hu et al., 20222).

An alternative kind of explainable feature selection is proposed by Kalustian (2021) by initializing a weighted graph to comprise features with Pearson similarity criteria for the feature similarities calculation as well as integration of Fisher Score (FS) and the Node Centrality to determine the score of each feature. That way, the feature selection approach considers not only feature importance but also feature similarity.

### **Model parameter tuning**

To achieve high precise results through ML algorithms, fine tuning the models’ hyper parameters is done using various approaches. The hyper parameters to tune by DL models comprise e.g. the number of layers, number of neurons, activation function, learning rate, etc (Kianfar et al., 2022). For example, Vernikou et al., 2022 show that the Bert Tokenizer LSTM model responds better with a very low learning rate. The hyper parameter to tune in decision tree based models would comprise the maximum depths of trees and maximum number of features used in each split. Hyper parameter tuning is conducted in the most pipelines with Grid search algorithm. The grid search algorithm tests all combinations of hyper parameters and narrows the model parameters to the optimal ones. (Khanna et al., 2023; Taye et al., 2023; Croci et al., 2021; Maitre et al., 2022)

Due to the computational costs for information processing in grid search strategies, evolutionary and swarm intelligent based optimization algorithms are applied as well (Kareem et al., 2023, Najaran, 2023). In addition, the search for hyper parameters is carried out frequently using a Bayesian search (Mora-Garcia et al., 2022; Shade et al., 2022; Qiu et al., 2022).

### **Model training**

Model training approaches are based on different categories consisting of statistical regression models, pre-trained DL models, ML basic models, DL basic models, Graph models, ensemble models and hybrid models. A complete list of detailed training (as well as interpretation) methods used in the identification phase of the literature in our paper can be found in the attached supplementary material to this paper. Among statistical regression models, logistic regression model is used frequently to take classification and or regression tasks in various studies (Hasan et al., 2022; Shiri et al., 2022, Thimoteo et al., 2022). Model training in the context of natural language processing and medical imaging is often elaborated through pre-trained models e.g. Bert in Beranová et al. (2022), ResNet in Xu et al. (2021) etc. Among ML basic models extreme gradient boosting algorithm XGB is elaborated frequently in variety of classification and or regression tasks in the context of SARS-CoV-2 literature. XGB is on itself an ensemble model encompassing multiple weak tree based models which work together (Yagin et al., 2023) based on the boosting approach. Boosting is a sequential ensemble method that iteratively adjusts the weight of observation as per the last model output. LSTM and CNN are prominent examples of basic DL models applied frequently in the context of SARS-CoV-2 studies. While LSTM excels at capturing time data dependencies, making it ideal for sequence prediction tasks (Du et al., 2023), CNN is specifically used for image classification and tasks that consider the processing of spatial dimensions of data (Cardoso et al., 2022). It is worth noting that while CNNs are primarily used for computer vision applications, they are shown to work on different time series problems too (Sengupta et al., 2022). Ensemble models incorporate a number of basic ML or DL models to achieve higher degrees of accuracy. Four main alternatives to create ensembles comprising Bagging, Boosting, Stacking and Mixture of Experts are addressed in Hasan et al. (2022). Hybrid models concatenate different combinations of ML and DL models at different model architecture levels (Li et al., 2021; Zhang et al., 2023, Xu et al., 2021). Graph models reflect the underlying logical connection of the model components in a graphical style (Segovia-Dominguez et al., 2021; Alqaissi et al., 2023). Graph neural networks GNNs are among novel utilized graph models, comprising inputs as each graphs component e.g. nodes and edges, which get updated by a machine learning model e.g. based on the features networks of its neighbors and the edges connecting them (Fritz et al., 2021).

### **Model evaluation**

The evaluation of the performance of a ML or DL model depends on the model outputs. For the pipelines with classification output types, the evaluation criteria are often AUC (area under receiver operating characteristic curve), Precision, Recall, F1-score and accuracy (Karthikeyan et al., 2021). To aforementioned criteria can be elucidated further in details based on the notions of the receiver operating characteristic (ROC) curve (Fawcett, 2006) as well as the precision and recall (PR) curve (Powers, 2011). To evaluate the performance of pipelines with continuous outputs, mean absolute error MAE, mean square error MSE, root mean squared error RMSE and goodness-of-fit (R2 score) are used (Mora-Garcia et al., 2022). Furthermore, often instead of evaluating the performance of the models on a single validation dataset, as performance may change depending on the choice of split, multiple random splits (k-fold validation) are utilized (Bottrighi et al., 2022). For the time series ML models, since all records of the test data of each split come from a time window which has not been seen during training of the respective split, a sliding window can be applied on the dataset to alter the test data set in a non-random manner from a time point to the next time point onward. Thus, if e.g. for the first split, the test set covers 20% of the earliest data records from a certain time point on, the test set of the last split corresponded to the last 20% i.e. the most recent data records (Rinderknecht & Klopfenstein, 2021).

### **Model interpretation**

Basically ML and DL models can be grouped into two categories i.e. intrinsically interpretable and non-intrinsically interpretable. A complete list of detailed interpretations (as well as training) methods used in the identification phase of the literature in our paper can be found in the attached supplementary material.

#### intrinsically interpretable models

Statistical regression models e.g. logistic regression LR model can be seen as examples of intrinsically interpretable models. In these models, a coefficient or odds ratio summarizes the positive or negative strength of association between exposure and an event. The coefficients from LR model can be moreover utilized to build a nomogram predicting the model outcome (Hong et al., 2022). Regressions remain one of the simplest and most explainable models with clear formulation. Despite this, they might not precisely accommodate the non-linear and non-monotonic patterns in the data. The literature of SARS-CoV-2 studies has proposed a range of intrinsically interpretable methods rather than statistical models. The performance degree of these methods at global level cannot be effortlessly compared to non-intrinsically interpretable models and depends on the problem contexts. Table 2 summarizes a list of intrinsically interpretable methods.

|  |  |  |
| --- | --- | --- |
| Method | Explaining | Source |
| J48 | is a machine learning decision tree classification algorithm based on Iterative Dichotomies. | Nopour et al., 2021 |
| RIPPER | is a rule-based ML algorithm, in which rules are learned from the data directly. | Onari et al., 2022, Schiesser et al., 2023 |
| pyFUME | can create rules based on fuzzy logic. | Onari et al., 2022 |
| GAMs | are used as nonlinear regression tools that allow for nonparametric fittings of complex dependences of response. | Seguel et al., 2022 |
| GNAMs | a hybrid ML-DL and belongs to the GAMs family and learn a linear combination of multi-layer perceptron models. | Moslehi et al., 2022 |
| EBM | is constructed with multiple hierarchically organized simple classifiers consisting of sequences of binary decisions and tree-based decision system. | Zhou et al., 2020, Hegde et al., 2023 |
| JRip | is a rule-based classifier which creates propositional rules that can be used to classify elements | Bottrighi et al., 2022 |
| Quantum Lattice | inspired by the Richard Feynman’s path creates multiple possible graphical models composed of different mathematical operations. On selection of the best model, a Qgraph is created to provide the rationale behind a prediction. Further, a simplified equation for the model is obtained that provides insights into the mapping of inputs to outputs. | Khanna et al., 2023 |
| Bayesian networks | a probabilistic graphical model for representing knowledge about an uncertain domain. | Derevitskii et al., 2022 |

Table 2: Intrinsically interpretable ML methods

#### non-intrinsically interpretable models

The non-intrinsically interpretable models are analyzed in two alternative ways in the literature i.e. post-hoc approaches and ante-hoc approaches. Post-hoc approaches presume ML models as a black-box and try to convey specific XAI either by means of employing intrinsically interpretable meta explaining models or by means of employing perturbation mechanisms. Ante-hoc approaches, conversely, try to embed XAI into the model to observe the feature influences during the training procedure. Among Post-hoc approaches the Shapley value based explanations SHAP is elaborated frequently in variety of model interpretation tasks in the context of SARS-CoV-2 literature. The SHAP is a perturbation based concept stemming from the game theoretical literature, which computes the average marginal contribution of a feature on the output predicted by the ML model considering all possible combinations of features (Fan et al., 2023). The SHAP computation time increases exponentially with the number of features.

LIME is another most frequently applied interpretation post-hoc methods, which is based on perturbation and meta modeling. LIME tunes the values of the features of a selected predicted instance and generates new samples based on the proximity to the instance being picked. It then optimizes a line based on all generated samples and gives a local interpretable explanation of the instance being picked (Rabby & Berka, 2022). SHAP and LIME can be effectively used e.g. to get insights into a black box model when some features might get confused (in the cases the models makes significant prediction mistakes) by the corresponding model and contribute to debug the model.

Variety of studies in the context of SARS-CoV-2 literature, has utilized intrinsically interpretable meta -models to explain the logic behind the decisions made by the original model. Examples of such approaches include using Formal concept analysis FCA to create a set of association rules with different confidence intervals in Saleh et al. (2022) , a Bayesian network to visualize the effect of the potential influencers for decision making in Alle et al. (2022), a single associated decision tree DT to present the ransom forest RF model in Rostami & Oussalah (2022) and Espositi et al. (2021), Anchors method to assist explain predictions by decision rules in Casiraghi et al. (2020), PGM-Explainer as a simpler interpretable Bayesian network in order to interpretation of GNNs in Alharbi et al. (2023) and symbolic meta modelling approach, which integrates various simple parameterized functions to get a closed-form and interpretable expression for the meta model (Jana et al., 2021).

Despite wide range of practical applications of post-hoc models, these approaches might not be ideal XAI approaches representing the original training model, they are devoted to. Post-hoc models are indeed surrogates, which first presume an ML model as a black box, then derive their interpretations (after the model training is finished) from a different modelling perspective with priors that are not necessarily in line with internal procedures of the original model. Ante-hoc approaches try to fill this gap by trying to provide information regarding actual reasoning process within the model by embedding explain ability into the model through the training e.g. by incorporating gradients or weights from a DL model’s specific layers. Different such techniques based on the product of final weights, connections from input neurons to the output neurons etc. are introduced in Mahmoudi et al. (2021) and Kianfar et al. (2022). Another examples are the CAM and Grad-CAM explanation methods, which are applied frequently in the literature to interpret the CNN network models. Class activation map (CAM) uses the notion of global average pooling (GAP) and learns weights from the output of the GAP layer onto the output classes. Grad-CAM generates a localization map that shows the critical features by using gradients from the target class settling into the final convolutional layer in the CNN network (Suri et al., 2022).

Another alternative is the integrated gradient IG method, which is applied to examine the inputs of a deep learning model on their importance for the output by integrating the gradients of the output with respect to the input along an arbitrary path from the baseline to the input data point (Du et al., 2023).

In addition, the advantage of embedding attention mechanism into the architecture of DL models has gained a high attention in the SARS-CoV-2 literature (Islam et al., 2022). The attention approaches are inspired from human attention visual mechanism, which uses limited attention to quickly screen high value information from a large amount of information. This not only contributes to increase the prediction performance but also is efficient in gaining insight to information that are more critical to the model outputs instead of learning non useful information (Chatzitifos et al., 2021; Jing et al., 2021, Singh et al., 2021, Nazir et al., 2022).

## **Epidemiological machine learning research analysis**

In this section, 26 papers, which are included in our study, are explored more in details. A detailed representation of the 26 paper comprising research question, data, pipeline & significant results is presented in appendix 1 of this paper.

These models are designed to analyze different epidemiologic aspects of the SARS-CoV-2 in different geographical scopes. A subset of papers (8 papers) incorporate data of multiple number of countries including Nader et al. (2021) analyzing NPIs in 176 countries, Docquier et al. (2022) analyzing the evolution of cross-border movements of people during the Covid-19 in Europe, Balogh et al. (2022) studying the influential of NPIs, PIs, virus variants etc. on Covid spread in Europe, Zhou et al. (2023) investigating the role of booster vaccine in 32 countries, Trajanoska et al. (2022) focusing on the role of dietary imbalances in 154 countries, Qiu et al. (2022) assessing the role of NPIs against COVID-19 at containing seasonal influenza transmission in 33 countries, Zhang et al. (2023) forecasting Confirmed cases prediction in 8 countries, Janko et al., 2021 assessing the effect of Non-Countermeasure Factors (e.g. cultural factors) to classify countries into those more and less prone to the fast spread of COVID-19 and Kianfar et al. (2022) explaining a variety of socio-temporal variables on COVID-19 prevalence and mortality at a global scale. The rest of papers are mostly utilizing the data of one country or region especially from US (e.g. Du et al., 2023, Jing et al., 2022 & Zheng et al., 2022).

The analyzed studies are applied based on different research objectives resulting in significance of different influential pandemic factors i.e. compliance with interventions (Bakkeli, 2023), population density (Paul et al., 2021), population movement and gathering (Cao et al., 2020; Doblhammer et al., 2021; Qiu et al., 2022), lock down effects (Saleh et al., 2022; Docquier et al., 2022), labor and unemployment effects (Jian et al., 2022; Kianfar et al., 2022), closure and regulation of schools (Nader et al., 2021; Arık et al., 2021), vaccination (Balogh et al., 2022; Zhou et al., 2023; Zheng et al., 2022), spatial effects (Dlamini et al., 2022; Baquie et al., 2021), weather condition (Ren et al., 2023; Jing et al., 2022; Zeng et al., 2021), countries dietary and cultural effects (Trajanoska et al., 2022; Janko et al., 2021), virus variants (Du et al., 2023) and health infrastructural impacts (Flores et al., 2021).

The data preprocessing stage in the most studies encompasses a data imputation step. In rare cases, the data unbalanced is handled e.g. by SMOT in Zeng et al. (2021) and by excluding those NPIs, which were used in less than 20 countries in Nader et al. (2021). Data discretization in Dlamini et al., 2022 is done by means of a relevant algorithm due to the necessity of discretization of feature values in Bayesian network analysis (but not for the sake of handling data unbalance).

Feature extraction techniques are applied in 3 studies i.e. PCA analysis in Docquier et al. (2022), SOM in Trajanoska et al. (2022) and K-means in Janko et al. (2021). Feature selection step is performed in the most of the studies consisting e.g. statistical analysis in Kianfar et al. (2022) and Bakkeli (2023) and stepwise wrapping methods based on k-fold validation in various studies (Cao et al., 2020; Dlamini et al., 2022; Ren et al., 2023; Trajanoska et al., 2022; Qiu et al., 2022; Flores et al., 2021).

SHAP-based feature selection methods (Trajanoska et al., 2022; Doblhammer et al., 2021; Qiu et al., 2022) and feature selection based on alternative ML methods (Qiu et al., 2022; Janko et al. 2021) are applied as well. It is worth noting that -relying on the inherent advantage of tree based models (XGB) to deal with data imputation and in coping with correlations between the covariates-, data preprocessing and data engineering steps in Baquie et al. (2021) are not explicit parts of the pipeline.

Parameter tuning as well as model evaluation stages in the most models are done based on grid search algorithm and the metrics for continuous and discrete output evaluation methods introduced in section 2, respectively.

Figure 4 depicts the main ML and XAI approaches types & frequencies used in the epidemiological context. A list of method abbreviations existing in figure 4 is presented in appendix 2.

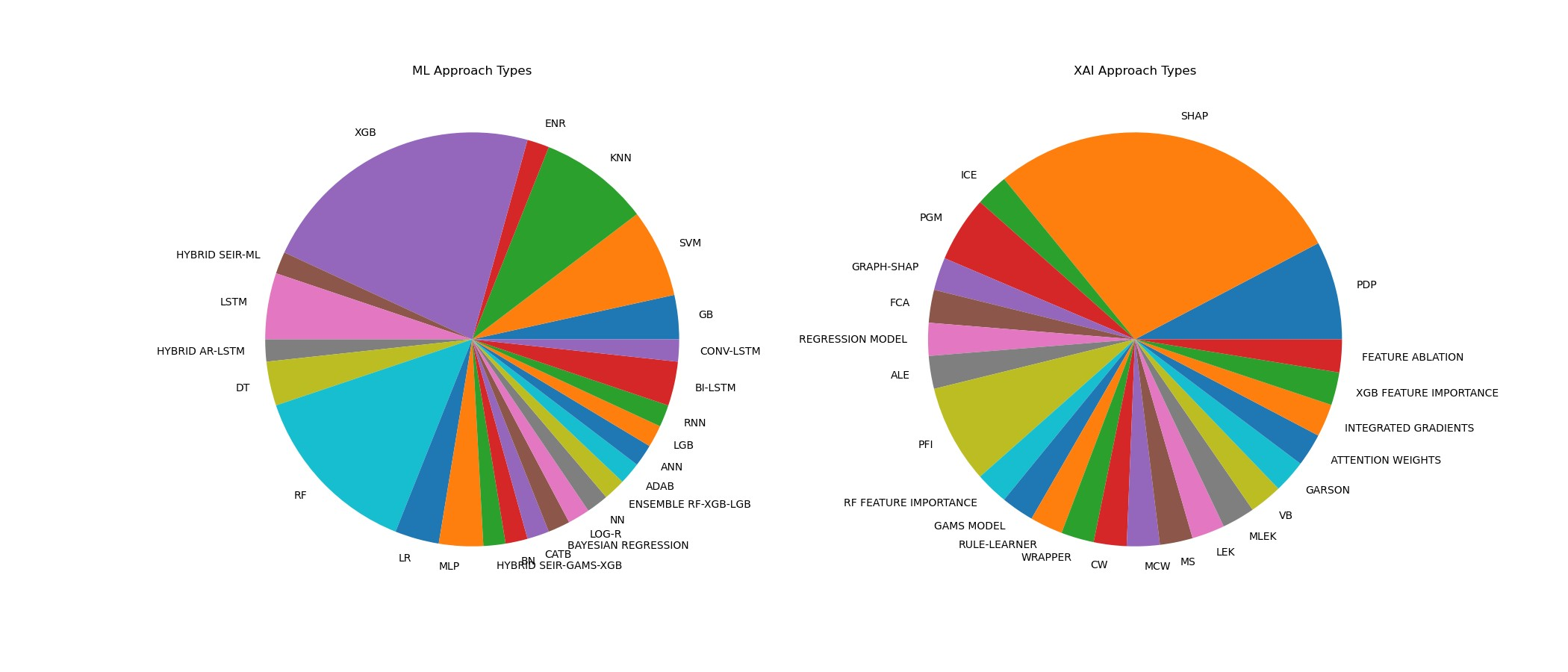


Figure 4: ML (left hand panel) & XAI (right hand panel) approaches types & frequencies used in the epidemiological context

The prevalence of XGB and SHAP method as well as their joint application as frequently used techniques to train and interpret ML models in the literature are evident from the figure 4. While we are not going to in depth assessment of this observation, it might be referred to the solid game theoretical basis of SHAP (Molnar, 2022) as well as XGB’s speed and performance based on parallelization, tree pruning, and hardware optimization (Zopluoglu, 2019).

Figure 5 illustrates the ML & XAI studies crucial aspects from different perspectives.

Figure 5: the ML & XAI studies crucial aspects from different perspectives

The main idea behind SEIR based ML models is combining compartmental models with machine learning models to replace the fixed parameters of the former with time-varying parameters that are fitted using machine learning methods. While Vega et al. (2022) uses a simplified probabilistic graph model PGM (e.g. probabilistic version of linear regression) to update the SEIR model parameters based on past information and estimated parameters in a previous iteration, in Arık et al. (2021) a generalized additive model is adopted for each variable into the SEIR model to represent the transmission rates.

Note that, not all studies are designed to be used as a real time forecasting tools. Indeed, most of the studies approaches are fitted models to enhance the overall understanding regarding the effect of various influential features on the pandemic progression, mortality rates etc. and hence they did not explicitly model the factor time. In contrast, the studies, which are listed in the second column of figure 5 have explicitly modeled the factor time. These studies must be analyzed either in two distinct categories: The studies, which utilize dynamic time series models (i.e. RNN, LSTM or CNN) to systematically incorporate the dependencies between consequent time points (studies which are listed in the third column in figure 5) and the studies, which treat each variable at each time point as a distinct input to the model (studies which are listed in the second column but not listed in the third column in figure 5). For example, Nader et al. (2021) represent a combination of each NPI variable with how long the corresponded NPI has been in place as a distinct variable. In Qiu et al. (2022), for each NPI the lagged day with the largest Spearman correlation coefficient was selected. Nonetheless, in Jing et al. (2022) a multi-stage (4 stages) LSTM is used, which, at each stage forecasts a chosen target variable for one-week ahead. It builds off the initial first stage prediction to forecast an additional week out and continues to implement this iterative approach one stage at a time, to predict further into the future.

Graphical causal structure of the data is used in a minority subset of study not only for the sake of intrinsically interpretable model training (Dlamini et al., 2022) but also for incorporating prior knowledge to the resulting SHAP values (Banerjee et al., 2022).

In addition, creating associative rules as interpretable post-hoc models are practiced in Janko et al. (2021) and Saleh et al. (2022).

Explanation provided by models in the 6the column of table 5 are ante-hoc explanation types reflecting ML model’s internal mechanism, hence these XAIs might be more reproducing the corresponded models’ decision making than explanations produced by post-hoc methods. These XAI methods are the internal connected neurons’ weights in Kianfar et al. (2022), attention weights (to determine which input features should be given more attention than the others as well as the weight of importance for each historical temporal step) in Jing et al. (2022), integrated gradient in Du et al. (2023) and the XGB feature importance in Zeng et al., (2021) representing the percentage of trees that use a variable in the ensemble tree model.

## **Discussion**

Analyzing the pipelines of epidemiological papers shed light on a wide range of methods used in the literature from data preprocessing phase up to the interpretation phase. However, there is still play room to reflect around upcoming research ideas based on the existing gaps in the scope of literature we reviewed in this study. In the current state of the literature the unbalanced data is not addressed or handled in a great extent. It is expected that necessity of data availability will more drive the successor literature researches towards using e.g. GANs to resolving the generic problem of sparse training data. Similarly, the current feature engineering methods rarely have incorporated the existing rich set of embedding techniques especially t-SNE, UMAP, SOM, RFF etc. Whether the inclusion of these methods enhance the performance and interpretability of the models cannot be extensively discussed in this paper. While the field of parameter tuning in the current literature of epidemiological ML is performed often by means of the grid search, however the potential of using non-exhaustive methods e.g. various evolutionary and swarm intelligent based optimization algorithms can be seen as a research gap. Model evaluation methods based on k-fold validation and with standard error optimization measures are used in accordance with the main body of AI literature.

Elaborating more on the SARS-CoV-2 machine learning techniques can further develop this literature to come up with added practical credibility in terms of performance and XAI. The SEIR compartmental models as a solid foundation of epidemiologic models can be maintained to design enhanced and modular pipelines. The SEIR can be enriched by using further DL models. Hereby, GNN graph based approaches can be utilized as interpretable and robust alternatives to update the time varying character of SEIR models’ parameters.

Furthermore, while the usage of CNN based architecture approaches in the context of *clinical* studies is practiced (e.g. in Solayman et. al., 2023), using the rich potential of performance and interpretability of CNN models is rarely utilized in the context of epidemiological studies. Numerous ante-hoc and post-hoc efficient CNN’s XAI approaches are proposed in the computer vision literature i.e. in the papers belonging to the group of X-ray and CT imaging methods in the screening phase of this research in section 1. For example, the imaging based Grad-CAM interpretation method is one of the most frequently applied approaches in the SARS-CoV-2 computer vision. This technique uses the gradients of the target class flowing into the final convolutional layer and hence, can be used to produce visual explanations for *any* CNN-based model. Note that, CNNs perform convolution operations in the upstream layers of the network where the filters extract the most critical features to generate a feature map. These features can not only be of spatial or temporal nature but also could be used e.g. to recognize a range of interactive policies e.g. a set of NPIs in a certain region. This property of CNNs can be combined with time dependency based architecture of LSTM models to present multi-dimensional spatial-temporal representation of the pandemic. Each dimension of epidemiological images can be determined based on the geographical context or time or based on the set of influential pandemic factors e.g. NPIs. Attention mechanism can be then utilized within the LSTM part of the network to enhance the system’s temporal XAI.

Additionally, the literature can benefit from the incorporation of uncertainty in XAI outcomes. The effect of data scarcity both on model training and on model interpretation is argued in section 2.1.1 (Hinns et al., 2021). Scarce data necessitates the incorporation of uncertainty in the generated model and the XAI outcomes (Aldhahi and Sull, 2023). While incorporating the uncertainty in model training level is incorporated rarely based on Bayesian approaches e.g. in Ren et al. (2023), the interpretations’ uncertainty is not accomplished in the scope of literature we reviewed.

It is worth noting that, beside the prediction and interpretation tasks, upon the feedbacks generated from DL based SEIR models, the GANs generative models can be employed to the context of AI based SEIR models to generate the optimal combination of NPIs strategies, which will lead to e.g. maximized reduction of pandemic reproducibility. The task of generating the best strategies or vice versa is not applied in the scope of literature we reviewed.

## **Conclusion**

Various AI-based SARS-CoV-2 epidemiological research have analyzed the effect of significant dynamics on the pandemic containment and have come out with diverse policy relevant prescriptions. To be credible at the system developing level as well as at policy setting level, these studies are required to shed light on the procedures behind the algorithms they developed. Understanding XAI necessitates studying each step a research pipeline is gone through until providing human understandable results. In this paper we conveyed a generic framework of the SARS-CoV-2 interpretable machine learning pipelines. We systematically selected the studies, which has focused on jointly incorporation of AI, SARS-CoV-2 epidemiology and XAI. Then, the reviewed papers’ research question, data, pipeline & significant results are analyzed. Upon analyzing the relevant studies, we reflected around upcoming research ideas based on the existing gaps in the scope of the reviewed studies.

## **Appendix**

### Appendix 1: Description of selected studies’ research question, data, pipeline & significant results

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Paper** | **Research Question** | **Data** | **Data preprocessing** | **Feature engineering** | **Parameter tuning** | **Model training** | **Model evaluation** | **XAI** | **Significant results** |
| Bakkeli, 2023 | Factors impacting self-perceived exposure risk to covid in Norway | Norwegian survey data collected with regard to important predictors of Self-perceived exposure risk to covid e.g. persons NPI-compliance, mobility pattern and work life conflicts etc. | data imputation depending on the type of missing data with reference to a paper & data partitioning | correlation statistics analysis based on bivariate ordinary least squares for the predictor variables and the target variable but no feature selection or feature extraction in the pipeline before model training | grid search | GB, SVM, KNN, ENR | rmse, mae,rsq | PDP, SHAP, ICE | The most significance predictors of perceived exposure risk are compliance with interventions, work-life conflict, age and gender. |
| Paul et al., 2021 | Factors impacting county level spread of COVID-19 & death rates in USA | local socio-economic conditions of counties i.g. income per capita, population density etc. data collected from the 5 years American Census Survey | data imputation is done for a few values with reference to the code | discard evidently unimportant variables via correlation analysis | 0 | XGB | rsq | SHAP | The spread of COVID-19 can be an urban phenomenon when the population density is very high. |
| Vega et al., 2022 | the number of new infections one to four weeks in advance in USA & Canada | tracked regional changes in the policies implemented at the government level in data from United States and the six biggest provinces of Canada | handling missing values based on basic logics | 0 | ML model learns to set the seir models time varying parameter based on change in government policy | HYBRID SEIR-ML | mape,mae | PGM | A model that explicitly models government policies can potentially produce one- to four-week forecasts of the number of COVID-19 infections. |
| Cao et al., 2020 | main contributors to the number of new cases and COVID-19 growth rates in China | Multiple data e.g. travel-related factors, population density, medical endowments, socioeconomic, environmental policy, and etc. in China | 0 | stepwise wrapping feature selection | 0 | XGB | mse | SHAP | Travel-related population movement was the main contributing factor for new cases and COVID-19 growth rates in China. |
| Banerjee et al., 2022 | spread of COVID-19 in the USA | socioeconomic disparities that have a causal link to the spread of COVID-19 in the USA | data imputation is done for a few values with reference to the code | 0 | 0 | XGB | rsq | GRAPH-SHAP | Causal Shapley values can be used to understand the causal connections between the socioeconomic metrics and the spread of COVID-19. |
| Saleh et al., 2022 | New hospital admissions per day in UK | Six attributes comprising total cases, new cases, seasons, national lockdown, number of people who have received the first dose vaccine, and second vaccine. | 0 | 63 possible combinations of the 6 variables is examined | exogenously assigned | LSTM | rmse | FCA | National Lockdown, New Cases and First Vaccine have a strong correlation with the total admission number due to COVID-19 in hospitals in the UK. |
| Zhang et al., 2023 | Confirmed cases prediction in 8 counties in the state of California, USA, and 7 other different countries | information on populations, positive and total tests, number of deaths, and positive cases and vaccine utilization obtained from California and WHO data sources | 0 | 0 | 0 | HYBRID AR-LSTM | mape | REGRESSION MODEL | Hybrid deep learning regression model can be useful in simultaneously providing accurate prediction as well as shedding light into policy guided understanding of the virus transiotion. |
| Jian et al., 2022 | Identifying the High-Risk Hongkong territory units for COVID-19 Transmission | Population specific socioeconomic features e.g. population density, educational, income, household and housing variables etc. | 0 | 0 | grid search | DT, KNN, RF, LR, XGB | mae, rsq | SHAP | The top three most important indicators of high risk territories are people in accommodation and food services, low income, and high population density. |
| Nader et al., 2021 | Analyzing COVID-19 growth rates and the effects of NPIs combined with how long they have been in place in 176 countries | NPIs of 176 countries using Corona net data during the initial phase of the outbreak presenting if and how long which NPI has been in place in a specific country at a specific day | NPIs that were used in less than 20 countries are excluded to balance data | 0 | random search | RF | 0 | ALE | Closure and regulation of schools was the most important NPI, associated with a pronounced effect about 10 days after implementation. |
| Docquier et al., 2022 | changes in daily evolution of cross-border movements of people during the Covid-19 in Europe | Data on international travel bans, the stringency of countries containment policies & Facebook users’ mobility data | 0 | synthetic policy indices are obtained by conducting PCA and extract the first two components of the PCA and propose the first PCA component can be interpreted as an average index of stringency of containment measures and the second component captures testing and tracing policies | exogenously assigned | LR, KNN, GB, MLP | mae,rmse | PFI | Countries containment policies are more important in explaining changes in cross-border traffic as compared with international travel bans and fears of being infected. |
| Balogh et al., 2022 | Main time series Predictors of COVID-19 cases in EU | Country-specific response measures, the spread of different variants, the average daily temperature, country population characteristics , health expenditures, cultural participation etc. | missing values are checked with reference to code | Sensitivity tests on feature dimensionality reduction, i.e., new versions of restrictions produced by merging restrictions with partially relaxed measures | the final rf parameters are reported | RF | rmse | PDP, RF FEATURE IMPORTANCE | The most important predictors of new COVID-19 cases in the EU include proportion of vaccinated people, the spread of different variants, the average daily temperature, self-reported COVID-like symptoms, and the use of protective masks. |
| Arık et al., 2021 | Daily predictions of the expected number of confirmed COVID-19 deaths, cases, and hospitalizations in USA & Japan | confirmed cases, deaths, publicly available Google Mobility Reports, government restrictions, demographic etc. | median imputation for static variables & forward & backward filling for time-varying variables | 0 | hyper parameter tuning to optimize the validation loss with reference to the literature | HYBRID SEIR-GAMS-XGB | mape, aape | GAMS MODEL | School closures are associated with the highest reduction in predicted exposed counts among all NPIs. |
| Dlamini et al., 2022 | to examine the factors that determine the spatial distribution of COVID-19 transmission risk in Eswatini | geographic factors e.g. proximity to major health facilities, churches, shopping centers and supermarkets as well as average annual traffic density in Eswatini | discretizing data based on the minimal description length algortihm to minimize the class variable entropy for each variable | The Incremental Wrapper Feature Subset Selection with Naive Bayes is used for feature selection | different BN structures are examined | BN | Logarithmic loss | PGM | The proximity to health facilities, churches, shopping centres and supermarkets as well as average annual traffic density were the strongest predictors of transmission risk during strict lockdown. After relaxation of the lockdown, the proportion of the youth in an area became the strongest predictor of COVID-19 transmission. |
| Zhou et al., 2023 | key factors including booster vaccination affecting the COVID-19 age-adjusted case fatality rate in 32 countries | Country specific level of health services index HAQ, GDP, behavioral risk factors etc. data from 32 countries | XGBs advantage to handle missing data by assigning it to a default direction and finding the best imputation value | recursive feature elimination | grid search | XGB | rmse | SHAP | The key risk factors for countries with higher age-adjusted case fatality rates (CFR) than crude CFR are low GDP *per capita* and low booster vaccination rates |
| Doblhammer et al., 2021 | The effect of local socioeconomic characteristics on COVID-19 incidence rates in Germany | data on demographic, social, economic, health care, unemployment, education, emission etc. | 0 | the 10 most frequent features from each top 10 ranking of SHAP values over all subsamples are selected | exogenously assigned | RF, CAT | rmse,rsq | SHAP | High mobility of high socioeconomc status (SES) groups may drive the pandemic at the beginning of waves, while mitigation measures and beliefs about the seriousness of the pandemic as well as the compliance with mitigation measures may put lower SES groups at higher risks later on. |
| Ren et al., 2023 | Assessing socioexposomic associations with COVID-19 mortality rates across New Jersey | spatially , demographic and socioeconomic factors including air pollution, proximity to industrial facilities, neighborhood and housing characteristics, age, poverty, etc. | The paper investigates how sparse data do not drastically affect the association estimates but increase uncertainties in Bayesian spatial models | Forward stepwise algorithm starting with a predefined set based on variables with variance inflation factor below 5 & Poisson and Negative binomial Bayesian regression | repeated coarse-fine grid search | BAYESIAN REGRESSION, RF, XGB | rsq | SHAP | Robust positive associations of COVID-19 mortality is found with historic exposures to NO2, population density, percentage of minority and below high school education. |
| Trajanoska et al., 2022 | Dietary, comorbidity, and geo-economic data for explaining country wise COVID-19 mortality rates | 154 countries’ dietary habits fused with data on past comorbidity prevalence and environmental policy factors such as seasonally averaged temperature geolocation, economic and development indices etc. | Only countries for which there were no missing mortality rates are included | Wrapper methods i.e. recursive feature elimination with feature importance, recursive feature importance with shap, Boruta shap | hyper parameter space search | XGB | mse, mae, rsq | SHAP | Countries with imbalanced dietary habits generally tend to have higher COVID-19 mortality predictions. |
| Baquie et al., 2021 | the importance of non-laboratorial and socio-geographic factors on COVID-19 hospital survival in Brazil | non-laboratorial data e.g. sex, age, ethnicity, comorbidities, socioeconomic etc. of COVID-19 patients in Brazil | XGB algorithm imputes missing data | The study highlights the beneficial use of the XGB model in coping with correlations between the covariates | 0 | XGB, SVM, KNN, LOG-R, RF, XGB, NN | AUC-ROC metric i.e. area under the receiver-operating curve | PFI | The most important non-laboratorial and socio-geographic factors on COVID-19 patients hospital survival in Brazil, are the state of residence and its development index, the distance to the hospital, the level of education, hospital funding model and strain. |
| Qiu et al., 2022 | The effects of governmental NPIs against COVID-19 at seasonal influenza transmission | Data for 14 NPIs implemented in 33 countries and the corresponding influenza virological surveillance | countries excluded based on with no infuenza surveillance data not exhibition of a typical seasonal epidemic curve | For each NPI, the lagged day with the largest Spearman correlation coefficient was selected. Wrapper methods based on svm & rf, a shap-based rf & a lasso regression are utilized to feature selection | Bayesian optimization | XGB | 0 | SHAP | The three most effective Covid-19 related NPIs to suppressing influenza transmission were gathering limitations, international travel restrictions, and school closures. |
| Zheng et al., 2022 | important factors related to occurrence of COVID-19 in the USA | Data on vaccination, wearing masks, mobility, government interventions etc. | There were no missing data in this study | Although some features had a statistically weak association with daily cases, they were still included to ensure the integrity of the features | hyper parametric optimization (Hyperopt) | ENSEMBLE RF-XGB-LGB | mae, rmse, mape | SHAP | Vaccination, wearing masks, less mobility, and government interventions identified as the most significant factors on the control and prevention of COVID-19. |
| Janko et al., 2021 | The effect of Non-Countermeasure Factors to classify countries into those more and less prone to the fast spread of COVID-19 | Data on non-countermeasure factors including weather, culture, travel, health, economic effects, development etc. of several countries | Iterative imputer a multivariate imputation approach | Features manually categorized (A synthetic categorization based on k-means & PCA is tried beside the manual categorization) & some features were excluded due to high internal correlation in the same category. Wrapper method, rf feature importance & Boruta are used for feature selection. | grid search | KNN, DT, RF, XGB, SVM, ADABOOST | AUC, accuracy | RULE-LEARNER | Culture and Development, followed by Travel and Health (excluding countermeasures) contribute the most to the virus’s fast spread. |
| Kianfar et al., 2022 | explanatory variables on COVID-19 prevalence and mortality at a global scale | Data on unemployment, population density, air and rail transportation, urban population, GNI per capita etc. of all countries. | 0 | variance inflation factor and Pearson’s correlation analysis are used for feature selection | optimum number of neurons in the hidden layer is determined using WIC index | ANN | root mean square error interquartile index | PFI, WRAPPER, CW, MCW, MS, LEK, MLEK, VB, PDP, GARSON | Unemployment and population density were the most influential variables regarding the COVID-19 prevalence. Health-related variables such as diabetes prevalence and number of hospital beds were the most significant variables regarding COVID-19 mortality. |
| Jing et al., 2022 | Impacting factors on total number of confirmed COVID-19 cases across the US | Demographic, public health, and other relevant COVID-19 predictors e.g. population density, transportation, pollution, sex ration etc. | 0 | XGB algorithm imputes missing data | Parameter setting is given | XGB, RF, LGB, RNN | mae,rmse,rsq | SHAP, ATTENTION WEIGHTS | The most important three factors affecting the spread rate of COVID-19 are temperature, age 65+ and pollution. |
| Du et al., 2023 | forecast the number of COVID-19 cases and deaths for each US state at a weekly level for a forecast horizon of 1–4 weeks | Data on epidemiological, mobility, survey, climate, demographic, and SARS-CoV-2 variant frequencies | 0 | Four models are constructed which include different combinations of available features | different LSTM model settings are explored | LSTM | ae,pae,wis | INTEGRATED GRADIENTS | The variant specific data are the most important predictors in short-term Covid-19 cases forecasting |
| Zeng et al., 2021 | The effects of additional factors i.e. local weather conditions as well as country-specific research sentiment to reflect patients progression of the disease | Data on weather situation in the location of the infected person as well as medRxiv, and bioRxiv COVID-19 literature databases | SMOTE | 0 | GridSearchCV | XGB, MLP, BI-LSTM | AUC, accuracy, Precision, Recall, F1-score | XGB FEATURE IMPORTANCE | The weather textual description in particular air pollution, followed by local temperature, humidity, and age, appear as the most important features to forecast Covid-19 patients progression of the disease |
| Flores et al., 2021 | Analyzing the relative importance of factors in predicting the COVID-19 incidence in the Chilean urban commune of Concepción | Data on mobility, death, patients in icu, hospitalization by region from the official COVID-19 repository of Ministry of Science Chile | 0 | Wrap around method to select features based on XAI step | Parameter setting is given | CONV-LSTM, LSTM, SVM, BI-LSTM | accuracy, Precision, Recall, F1-score | FEATURE ABLATION | Number of patients in ICU, bed types, deaths and features related to the type of mechanical ventilators rank first to predict the incidence of disease. |

### Appendix 2: List of Abbreviations

|  |  |
| --- | --- |
| **ML abbreviations** | |
| ADAB | adaptive boosting model |
| ANN | artificial neural network |
| AR | autoregressive model |
| BI-LSTM | bidirectional long short term memory network |
| BN | Bayesian network model |
| CATB | categorical boosting model |
| CONV-LSTM | convolutional long short term memory network |
| DT | decision tree |
| ENR | elastic net regularization regression |
| GAMS | generalized additive model |
| GB | gradient boosting model |
| KNN | k nearest neighbors model |
| LGB | light gradient boosting model |
| LOG-R | logistic regression |
| LR | linear regression |
| LSTM | long short term memory network |
| MLP | multi-layer perception network |
| NN | neural network |
| RF | random forest |
| RNN | recurrent neural network |
| SEIR | susceptible exposed infected recovered model |
| SVM | support vector machine |
| XGB | extreme gradient boosting model |
| **XAI abbreviations** | |
| ALE | accumulated local effects |
| CW | connection weights |
| FCA | formal concept analysis |
| ICE | individual conditional expectation |
| IG | integrated gradients |
| MCW | modified connection weights |
| MS | most squares |
| PDP | partial dependence plot |
| PFI | permutation feature importance |
| PGM | probabilistic graphical model |
| VB | variance based model |

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## **Supplementary material**

Further material such as data, results and figures related to this paper can be found in the GitLab account, provided by University of Koblenz.

## **Conflicts of interest**

All authors have no conflicts of interest.

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