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A Supervised Machine Learning Model for Predicting Adverse Drug Reactions among Tuberculosis Patients in Zimbabwe

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***Abstract*— This dissertation develops a supervised machine learning model to predict adverse drug reactions (ADRs) among tuberculosis (TB) patients in Zimbabwe, addressing a critical need for tools that enhance patient safety and optimize treatment outcomes. The model integrates multimodal data, including chest X-ray images and patient-specific information, to provide comprehensive risk assessments. The study employs the Cross Industry Standard Process for Data Mining (CRISP-DM) framework, using Convolutional Neural Networks (CNNs) to analyze X-rays and ensemble learning techniques to incorporate clinical data. The model achieved high predictive accuracy, with training accuracy reaching 95% and validation accuracy stabilizing at 78%. The confusion matrix analysis demonstrated the model's ability to differentiate between various severity levels of ADRs, facilitating targeted interventions. The research underscores the potential of machine learning in medical diagnostics, particularly in settings with limited resources, and highlights the need for future research to refine the model using larger and more diverse datasets. The findings have significant implications for improving TB treatment and patient outcomes in Zimbabwe.**

Keywords—Adverse Drug Reactions (ADRs), Tuberculosis (TB), Machine Learning, Predictive Modeling, Clinical Diagnostics

I. BACKGROUND

Tuberculosis (TB) is a bacterial infection caused by Mycobacterium tuberculosis, primarily affecting the lungs but also capable of affecting other bodily organs [23]. Despite medical advancements, TB remains a significant public health challenge in Zimbabwe, with a persistently high burden of reported cases annually (Ministry of Health and Childcare, 2020). The treatment of TB involves a combination of antibiotics aimed at effectively eradicating the bacteria and thwarting the development of drug-resistant strains. In exploring the history and evolution of managing TB in Zimbabwe, it is pertinent to note the integration of predictive models into contemporary approaches [13]. Initially, the focus was on conventional treatment modalities, which, despite their efficacy, encountered hurdles due to the emergence of drug-resistant TB strains [19]. Recognizing the need for more targeted and adaptive strategies, the healthcare system gradually embraced predictive modelling techniques to optimize treatment protocols [24]. ADRs can significantly affect patient well-being by causing discomfort, reducing quality of life and increasing healthcare costs [6]. Monitoring for ADRs is crucial during TB treatment to promptly identify and manage any adverse effects that may arise. Healthcare providers should educate patients about potential ADRs associated with anti-TB drugs and encourage them to report any unusual symptoms experienced during treatment. Tuberculosis (TB) is a global health concern, affecting millions of people worldwide. Adverse drug reactions (ADRs) during TB treatment pose a significant challenge in many countries, including those in the Americas. In the United States, ADRs complicate treatment outcomes and patient management, despite declining TB incidence rates (CDC, 2021). Countries like Brazil, Peru and Mexico, with high burdens of TB cases, face barriers to effective TB control due to ADRs [12]. In Asia, countries such as India, China and Indonesia, which have high burdens of TB cases, ADRs present a substantial barrier to effective TB control (WHO, 2020). India accounted for the highest number of TB cases globally in 2020, with an estimated 2.64 million new cases [12]. ADRs during TB treatment in these countries can lead to treatment interruptions, increased healthcare costs and adverse health outcomes for patients.

In Africa, countries like Nigeria, Zambia and Malawi are grappling with the dual burden of TB and HIV/AIDS, exacerbating the challenges in managing ADRs [12]. Some of the companies in these countries that are dealing with TB adverse drug reactions in Nigeria are GlaxoSmithKline Nigeria, May & Baker Nigeria Plc and Fidson Healthcare Plc [28]. Areas in Zimbabwe with a higher prevalence of adverse drug reactions are the urban centres, particularly Harare and Bulawayo. These cities have larger populations and more advanced healthcare facilities compared to rural areas, leading to higher rates of medication use and consequently a greater likelihood of encountering adverse drug reactions. Additionally, the availability of a wider range of medications in urban areas may contribute to increase ADR reporting [4].

II. PROBLEM STATEMENT

The dearth of efficient and accurate methods for identifying adverse drug reactions (ADRs) among

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tuberculosis (TB) patients in Zimbabwe presents a critical challenge, leading to delayed interventions and potential complications. Existing approaches fail to address the diverse patient demographics, treatment protocols and healthcare infrastructure constraints unique to the Zimbabwean context. The prevalence of drug-resistant TB has increased by 23% in the past five years, exacerbating the urgency for improved interventions [17]. The current methods for predicting and identifying TB patients at higher risk of ADRs in Zimbabwe rely heavily on subjective assessments and limited clinical indicators, resulting in suboptimal intervention strategies and avoidable harm to patients. This problem is further compounded by the emergence of drug-resistant strains, complicating TB management in the country. Therefore, there is a critical need to develop a tailored supervised machine-learning model capable of early and accurate prediction of ADRs in TB patients, leveraging patient-specific data. Implementing such a model would enable healthcare professionals to make informed decisions, implement targeted interventions and optimize tuberculosis treatment outcomes.

III. Literature Review

The literature review aims to provide a comprehensive understanding of the existing knowledge and research related to adverse drug reactions (ADRs) and the application of machine learning in the treatment of tuberculosis (TB). The purpose of this literature review is to synthesize and analyse the findings and methodologies of previous studies conducted in the field of ADRs and machine learning in TB treatment. Examining this research provides important information on the variables linked to ADRs, the efficacy of various machine-learning techniques and the shortcomings of existing methods.

A. Underpinning Theory

The study incorporates two underpinning theories namely the theory of planned behaviour and the Social Cognitive Theory (SCT). The Health Belief Model provides a comprehensive framework for understanding patients' attitudes, intentions and behaviours related to adverse drug reactions (ADRs) in the context of tuberculosis (TB) treatment. It emphasises factors such as perceived susceptibility to ADRs, perceived severity of the health condition, perceived benefits and barriers to taking preventive actions and cues to action.

B. Planned Behavior Theory

The Theory of Planned Behavior (TPB), proposed by Ajzen in 1991, provides a comprehensive framework for understanding and predicting human behavior by incorporating attitudes, subjective norms and perceived behavioural control [27]. TPB posits that individuals' intentions to perform a specific behavior are influenced by their attitudes toward the behavior, subjective norms and perceived behavioural control over the behavior [19]. In the context of healthcare, TPB has been widely utilized to investigate patients' adherence to treatment regimens and their reporting of adverse drug reactions (ADRs).

C. Social Cognitive Theory

The application of Social Cognitive Theory developed by Albert Bandura in the study offers a comprehensive understanding of the reciprocal interaction between individual cognitive processes, behaviour and the social environment in the context of ADRs. It facilitates the development of targeted interventions and strategies, supports the integration of a machine-learning model and ultimately aims to improve patient care, treatment outcomes and ADR reporting in TB treatment [11].

D. The Diffusion of Innovations Theory

The Diffusion of Innovations Theory, developed by Everett Rogers in 1962, provides a useful framework for understanding the adoption and spread of new ideas, technologies or practices within a social system [9]. This theory can be particularly helpful in the context of the proposed study, which aims to explore the use of predictive modelling techniques for predicting adverse drug reactions (ADRs) among tuberculosis (TB) patients in Zimbabwe. According to the Diffusion of Innovations Theory, the adoption of an innovation, such as the use of predictive modelling for ADR prediction, is influenced by several key factors.

IV. Empirical Review

One notable study conducted by Xiao [7] centred on employing a Bayesian approach utilizing the Monte-Carlo Expectation-Maximization procedure. Their primary objective was to accurately detect drug safety signals by combining data from multiple sources, including FAERS and MedEffect. Through a signal combination step, they aimed to enhance the robustness and reliability of their predictions. Through the application of Bayesian modelling, Xiao [2] highlighted the significance of combining various data sources for thorough ADR detection. Another prominent work in this domain was conducted by Cai [1], who focused on utilizing a Bayesian method known as Causal Bayesian Network for uncovering potential drug-drug interactions (DDIs) using FAERS data. Their research aimed to elucidate the intricate relationships between drugs and adverse events, providing valuable insights for clinical decision-making and patient safety. Cai [1] showed the efficacy of their method in finding and characterising DDIs by utilising the probabilistic nature of Bayesian networks. This helps in the identification and prevention of adverse events linked to particular drug combinations. In a different approach, Li [15] employed an inductive matrix completion technique to tackle ADR prediction. Their methodology involved utilizing datasets such as FAERS and DrugBank to minimize the distance between drugs and ADRs. Their study sought to reveal latent patterns and connections between medications and adverse reactions by using a random matrix value using a loss function and regularisation. This innovative approach highlighted the potential of matrix completion techniques in understanding the complex relationships between drugs and ADRs, offering valuable insights for personalized medicine and drug safety optimization.

Ren [8] adopted a unique strategy by utilizing block matrices with correlation in VAERS data to detect adverse events or symptoms following vaccination. They sought to find connections between unfavourable events and look into probable patterns that can lead to unpleasant reactions by utilising correlation matrices. Their work shed light on the importance of considering correlations and associations between adverse events, allowing for a more comprehensive understanding of vaccine safety and aiding in the identification of potential adverse effects.

Lastly, Liu [7] proposed a novel machine-learning framework that combined an autoencoder-based semi-supervised learning algorithm with weighted support vector machines (SVM). Their approach, applied to FAERS and ONC High-Priority data, aimed to extract useful features and identify potential high-priority DDIs. The study demonstrated the effectiveness of their framework in identifying critical drug-drug interactions that require immediate attention and intervention. These studies collectively exemplify the diverse range of machine learning methods employed to predict ADRs and discover relationships between drugs and adverse events across various datasets. These researchers have significantly improved medication safety, guided clinical decision-making and improved patient outcomes in the setting of adverse drug responses by utilising cutting-edge algorithms and methodologies. Tuberculosis remains a significant global public health concern, particularly in countries with high burdens of the disease such as Zimbabwe. According to the Ministry of Health and Child Care, [18], Zimbabwe continues to face a substantial number of TB cases each year. The treatment of TB involves the administration of anti-TB drugs, which can give rise to adverse drug reactions (ADRs) in certain patients. Adverse drug reactions refer to the unintended and harmful effects resulting from the use of medications [28]. These ADRs can range from mild symptoms to severe complications, affecting treatment outcomes and patient well-being [13]. Understanding the prevalence and impact of ADRs in TB patients is crucial for improving treatment strategies and patient care.

V. Related Works

A. Machine Learning in Health Care

Machine learning, a branch of artificial intelligence, has emerged as a valuable tool in healthcare, offering the potential to enhance patient care, clinical decision-making and predictive analytics [17]. Healthcare professionals can use patient-specific data and large dataset analysis to predict adverse drug reactions (ADRs) in tuberculosis (TB) patients by utilising machine-learning algorithms [5]. These techniques enable the identification of patterns and associations that may not be apparent through traditional methods. For example, machine-learning models can integrate demographic information, genetic markers, treatment regimens and laboratory results to predict the likelihood of ADRs in individual TB patients [8].

B. Machine Learning Techniques for Predicting ADRs in Healthcare

Machine learning techniques have been widely employed in healthcare for predicting adverse drug reactions (ADRs) due to their ability to analyse complex data and identify patterns that may not be apparent through traditional methods. In the context of ADR prediction for tuberculosis (TB) patients, several machine-learning algorithms have been commonly utilised. This section explores these algorithms, their strengths and weaknesses.

Logistic regression is a widely utilized machine-learning algorithm for binary classification tasks, including the prediction of adverse drug reactions (ADRs) in healthcare settings. It is a statistical model that focuses on modelling the relationship between independent variables and the probability of an ADR occurrence [7]. Logistic regression is advantageous due to its interpretability and computational efficiency. It provides insights into the impact of different predictors on the likelihood of ADRs in tuberculosis (TB) patients [9].

Decision trees are machine-learning models that utilize hierarchical rules to partition data and make predictions. They are known for their intuitive nature and ease of interpretation, making them valuable tools for predicting adverse drug reactions (ADRs) in healthcare settings [12]. Decision trees can handle both numerical and categorical predictors, allowing for a wide range of data types to be incorporated into the model [19]. They are particularly effective at capturing complex interactions between predictors, making them suitable for exploring intricate relationships within tuberculosis (TB) patient data [21].

Random forests are ensemble-learning models that combine multiple decision trees to improve prediction accuracy and address the limitations of individual decision trees. They have been widely utilized in the field of adverse drug reaction (ADR) prediction in healthcare. Random forests excel in handling high-dimensional data and capturing complex interactions among predictors, making them suitable for analysing tuberculosis (TB) patient data [20].

Support Vector Machines (SVM) is a powerful machine-learning algorithm used for binary classification tasks, including adverse drug reaction (ADR) prediction in healthcare [14]. SVM separates data points into different classes by finding an optimal hyperplane in a high-dimensional feature space. SVM is known for its ability to handle high-dimensional data and capture complex relationships, making it applicable to tuberculosis (TB) patient data analysis [17].

Neural networks, specifically deep learning models, have emerged as powerful tools for adverse drug reaction (ADR) prediction in healthcare. They excel at learning complex patterns from large-scale data and are capable of capturing nonlinear relationships, making them well suited for analysing tuberculosis (TB) patient data. Neural networks have gained popularity due to their ability to handle high-dimensional data effectively [21]. One of the key advantages of neural networks is their capability to learn intricate and nonlinear relationships within the data. Deep learning models, in particular, are composed of multiple layers of interconnected neurons, allowing them to uncover complex patterns and representations.

VI. Gap Analysis and Research Needs

Despite the valuable contributions made by several authors in the field of machine learning for adverse drug reaction (ADR) prediction and analysis, there is a noticeable gap in the existing literature regarding the prediction of ADRs in tuberculosis (TB) patients using machine learning specifically in the context of Zimbabwe. None of the mentioned studies focus on TB patients or the specific healthcare landscape of Zimbabwe. This highlights the need for a focused study that addresses these gaps and explores the application of machine learning techniques for ADR prediction in TB patients within the Zimbabwean context. Empirical evidence has shown that machine-learning methods, such as the Bayesian approach employed by [15], can effectively detect drug safety signals by integrating data from multiple sources. However, the applicability of these methods to the unique characteristics of TB patients in Zimbabwe remains unexplored. Similarly, the utilization of Bayesian methods, as demonstrated by [19], to uncover drug-drug

interactions (DDIs) may provide valuable insights for clinical decision-making and patient safety. The specific challenges and patterns of DDIs in TB patients in Zimbabwe have not been investigated.

VII. Conceptual Framework

The conceptual framework in Fig 1 depicts the study, showing the input variables, the algorithm and the output, which is the target feature of the study. The input variables such as barriers to treatment, severity of ADRs and the disease, comorbidities and genetic variations are derived from the patients' attitudes, intentions and behaviours related to ADRs. These are derived from the HBM theory looking at the development of targeted intervention strategies that support the integration of machine-learning models and ultimately aim to improve patient care and treatment outcomes in the context of TB treatment. It also facilitates the development of targeted interventions and strategies in ADR reporting in TB treatment. Since both theories are related, they are merged to come up with the input variables to the machine learning models under investigation. Input variables such as age and gender were introduced to ensure that the study can be used to further assess the severity and effect of ADRs predictions in relation to age groups and the associated gender. Age is included as it influences an individual's susceptibility to ADRs, with different age groups exhibiting varying physiological responses to medications.

Gender is important due to biological and hormonal differences between males and females, affecting drug metabolism and response, potentially leading to variations in ADR occurrence and severity. The severity of ADRs is considered to assess their extent and impact, helping understand the relationship between ADR intensity and other variables. Barriers to treatment, including side effects, logistical difficulties, financial constraints and social or cultural factors are explored to uncover their impact on ADR occurrence. Comorbidities, the presence of other medical conditions alongside TB, increase susceptibility to ADRs due to drug interactions or compromised physiological systems. Generally, these elements collectively form the research conceptual framework for supervised machine learning prediction of adverse drug reactions, guiding researchers in developing accurate and reliable predictive models in pharmacovigilance. The input variables were used to explore their associations with ADRs in TB patients.

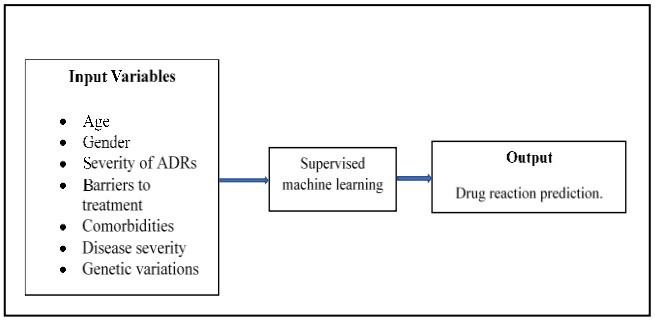

Fig 1. Conceptual Framework

VIII. Research Methodology

The study employed a quantitative approach, CNN algorithm to create a predictive model. The objective was to accurately forecast and evaluate adverse drug reactions within the Zimbabwean healthcare system. Various components, including research philosophy, design, data sources, operationalization, data collection, validity, reliability and ethical considerations, were integral to ensuring scientific rigor, accuracy and ethical integrity. The focus on quantitative methods and machine learning allowed for objective data assessment and the generation of reliable knowledge. Patient records, medical reports and adverse event databases provided valuable insights and data collection involved surveys, interviews and medical record reviews. Ethical guidelines were followed, with measures in place to protect patient confidentiality. The model's validity and reliability were evaluated through rigorous procedures and performance metrics.

A. Data Sources

The study used x-ray images to predict adverse drug reactions among tuberculosis patients. Through an examination of the radiographic signs of tuberculosis found in these x-ray pictures, the research sought to improve the precision and dependability of the prediction model. The researcher sought to uncover valuable insights into adverse drug reactions and contribute to the improvement of patient care in tuberculosis treatment. The findings from this study have the potential to inform healthcare practices, facilitate early detection and intervention and ultimately enhance the overall management and outcomes for tuberculosis patients in Zimbabwe.

B. Business Understanding

The study aimed to enhance patient safety and healthcare outcomes by developing a predictive model for adverse drug reactions in tuberculosis patients. Its findings provide valuable insights to healthcare professionals, enabling them to make informed decisions about drug prescriptions and treatment regimens, ultimately improving patient safety. The study's focus on aligning with broader business objectives highlighted its commitment to addressing practical challenges and delivering tangible benefits to the healthcare industry. The study focused on its potential impact on informed decision-making and patient safety in tuberculosis therapy, with the goal of optimising patient care and treatment outcomes by offering a trustworthy tool for risk assessment and mitigation.

C. Data Understanding

The data understanding stage involved comprehensive efforts to gather and comprehend relevant information about the dataset. Various activities were conducted to gain insights into the structure and characteristics of the data related to the CNN model and X-ray images. This included data gathering from sources such as medical databases. The data description process documented the sources, types, formats and meanings of the X-ray images. Exploratory data analysis techniques, such as statistical summaries, distributions and visualizations, were employed to deeply understand the dataset and identify patterns, trends and outliers. Additionally, verification processes were implemented to assess the completeness, accuracy and consistency of the data. The data understanding stage established a solid foundation of knowledge about the dataset, providing essential insights for subsequent stages of the model development process.

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Display a ramdom sample of images from each dataset by target

```
# source: https://www.kaggle.com/gpreda/honey-bee-subspecies-classification

def draw_category_images(col_name,figure_cols, df, IMAGE_PATH):

    """
    Give a column in a dataframe,
    this function takes a sample of each class and displays that
    sample on one row. The sample size is the same as figure_cols which
    is the number of columns in the figure.
    Because this function takes a random sample, each time the function is run it
    displays different images.
    """


    categories = (df.groupby([col_name])[col_name].nunique()).index
    f, ax = plt.subplots(nrows=len(categories),ncols=figure_cols,
                         figsize=(4*figure_cols,4*len(categories))) # adjust size here
    # draw a number of images for each location
    for i, cat in enumerate(categories):
        sample = df[df[col_name]==cat].sample(figure_cols) # figure_cols is also the sample size
        for j in range(0,figure_cols):
            file=IMAGE_PATH + sample.iloc[j]['image_id']
            im=imageio.imread(file)
            ax[i, j].imshow(im, resample=True, cmap='gray')
            ax[i, j].set_title(cat, fontsize=14)
    plt.tight_layout()
    plt.show()
```

Fig 2: Checking head of dataset

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            ax[i, j].set_title(cat, fontsize=14)
    plt.tight_layout()
    plt.show()
```

Fig 3: Reading Images

D. Data Preparation

The data preparation stage of the study focused on cleaning and transforming the image dataset to make it appropriate for the random forest classifier model. Several important steps were taken to prepare the data for analysis. One crucial aspect of data preparation involved handling missing values. Although images do not have missing values in the same as numerical data, there can be issues such as corrupted or incomplete images. Strategies were employed to address these issues, such as removing or replacing corrupted or incomplete images based on quality assessment. Another significant aspect of data preparation was encoding categorical variables. In the case of image datasets, categorical variables could refer to labels or classes associated with each image. Furthermore, normalization techniques were applied to the image data. This involved standardizing pixel values to bring them to a similar scale and avoid bias that may arise from varying pixel ranges or units. By addressing image quality issues, encoding categorical variables and normalizing the image data, the data preparation stage ensured that the dataset was clean, consistent and suitable for subsequent modelling and analysis phases. Assigning labels to the images was done using the following code depicted in Fig 4.

```
def extract_target(x):
    target = int(x[-5])
    if target == 0:
        return 'No Complications'
    if target == 1:
        return 'Adverse Drug Reaction'
```

Fig 4: Extracting target feature

Assigning labels to the target features was done using the following code in Fig 5.

```
# Assign the target labels

df_mont['target'] = df_mont['image_id'].apply(extract_target)
```

Check the class distribution

```
# Montgomery Dataset

df_mont['target'].value_counts()
```

```
No Complications         80
Adverse Drug Reaction    58
Name: target, dtype: int64
```

Fig 5: Target feature class distribution

```
# Create a new column called 'labels' that maps the classes to binary values.
df_data['labels'] = df_data['target'].map({'No Complications':0, 'Adverse Drug Reaction':1})
```

```
df_data.head()
```

	image_id	target	w	h	c	max_pixel_val	min_pixel_val	labels
108	MCUCXR_0255_1.png	Adverse Drug Reaction	4020	4892	3	255	0	1
32	MCUCXR_0046_0.png	No Complications	4892	4020	3	255	0	0
107	MCUCXR_0254_1.png	Adverse Drug Reaction	4892	4020	3	255	0	1
13	MCUCXR_0020_0.png	No Complications	4020	4892	3	255	0	0
27	MCUCXR_0041_0.png	No Complications	4020	4892	3	255	0	0

Fig 6: Creating train and testing classes

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```
# Create a new column called 'labels' that maps the classes to binary values.
df_data['labels'] = df_data['target'].map({'No Complications':0, 'Adverse Drug Reaction':1})
```

```
df_data.head()
```

	image_id	target	w	h	c	max_pixel_val	min_pixel_val	labels
108	MCUCXR_0255_1.png	Adverse Drug Reaction	4020	4892	3	255	0	1
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13	MCUCXR_0020_0.png	No Complications	4020	4892	3	255	0	0
27	MCUCXR_0041_0.png	No Complications	4020	4892	3	255	0	0

Fig 7: Label Feature Creation

IX. MODELLING

The modelling stage of the study involved building and training the CNN algorithm. The dataset of X-ray images was split into three subsets: a training set, a validation set and a test set. The training set was used to train the CNN model, while the validation set was used for hyperparameter tuning. The CNN model's architecture was then designed, comprising multiple convolutional layers, pooling layers and fully connected layers, with specific choices made based on the complexity of the problem and computational resources. The model was subsequently trained using the training set, adjusting its internal weights through an optimization process involving forward and backward propagation. The hyperparameters of the CNN model, such as learning rate, batch size and activation functions, were fine-tuned using the validation set to optimize performance. The model's performance was evaluated using the test set, employing evaluation metrics such as accuracy, precision, recall and F1 score to assess its ability to predict adverse drug reactions accurately.

Create the Model Architecture

```
# Baseline-keras-cnn-roc-fast-5min-0-8253-Lb

kernel_size = (3,3)
pool_size= (2,2)
first_filters = 32
second_filters = 64
third_filters = 128

dropout_conv = 0.3
dropout_dense = 0.3


model = Sequential()
model.add(Conv2D(first_filters, kernel_size, activation = 'relu',
                 input_shape = (IMAGE_HEIGHT, IMAGE_WIDTH, 3)))
model.add(Conv2D(first_filters, kernel_size, activation = 'relu'))
model.add(Conv2D(first_filters, kernel_size, activation = 'relu'))
model.add(MaxPooling2D(pool_size = pool_size))
model.add(Dropout(dropout_conv))

model.add(Conv2D(second_filters, kernel_size, activation ='relu'))
model.add(Conv2D(second_filters, kernel_size, activation ='relu'))
model.add(Conv2D(second_filters, kernel_size, activation ='relu'))
model.add(MaxPooling2D(pool_size = pool_size))
model.add(Dropout(dropout_conv))

model.add(Conv2D(third_filters, kernel_size, activation ='relu'))
model.add(Conv2D(third_filters, kernel_size, activation ='relu'))
model.add(Conv2D(third_filters, kernel_size, activation ='relu'))
model.add(MaxPooling2D(pool_size = pool_size))
model.add(Dropout(dropout_conv))

model.add(Flatten())
model.add(Dense(256, activation = "relu"))
model.add(Dropout(dropout_dense))
model.add(Dense(2, activation = "softmax"))

model.summary()
```

Fig 8: Model Summary

X. MODELLING

The evaluation stage involved assessing the performance and effectiveness of the developed Convolutional Neural Network (CNN) model. This stage encompassed several crucial steps. The CNN model was evaluated using a dedicated test set comprising X-ray images that were not part of the training or validation sets. Predictions were made for each image and these predictions were compared to the true labels of adverse drug reactions. This process provided an unbiased evaluation of the model's performance on unseen data. Metrics, such as accuracy, precision, recall and F1 score, were calculated to quantify the model's performance. These metrics helped measure the correctness of the model's predictions, the proportion of true positive predictions, its ability to identify actual positive cases correctly and the balance between precision and recall. By analyzing the evaluation results, researchers gained insights into the model's strengths, weaknesses and overall performance. This step ensured that the model's effectiveness extended beyond the specific dataset used in the study and validated its applicability in diverse populations and settings. The evaluation stage provided critical information regarding the model's performance, guiding its suitability for real-world applications and guiding further improvements or refinements if necessary.

```
Model: "sequential"
_________________________________________________________________
Layer (type)                 Output Shape              Param #
=================================================================
conv2d (Conv2D)              (None, 94, 94, 32)        896

conv2d_1 (Conv2D)            (None, 92, 92, 32)        9248

conv2d_2 (Conv2D)            (None, 90, 90, 32)        9248

max_pooling2d (MaxPooling2D  (None, 45, 45, 32)        0
)

dropout (Dropout)            (None, 45, 45, 32)        0

conv2d_3 (Conv2D)            (None, 43, 43, 64)        18496

conv2d_4 (Conv2D)            (None, 41, 41, 64)        36928

conv2d_5 (Conv2D)            (None, 39, 39, 64)        36928

max_pooling2d_1 (MaxPooling  (None, 19, 19, 64)        0
2D)

dropout_1 (Dropout)          (None, 19, 19, 64)        0

conv2d_6 (Conv2D)            (None, 17, 17, 128)       73856

conv2d_7 (Conv2D)            (None, 15, 15, 128)       147584

conv2d_8 (Conv2D)            (None, 13, 13, 128)       147584

max_pooling2d_2 (MaxPooling  (None, 6, 6, 128)         0
2D)

dropout_2 (Dropout)          (None, 6, 6, 128)         0

flatten (Flatten)            (None, 4608)              0

dense (Dense)                (None, 256)               1179904

dropout_3 (Dropout)          (None, 256)               0

dense_1 (Dense)              (None, 2)                 514

=================================================================
Total params: 1,661,186
Trainable params: 1,661,186
Non-trainable params: 0
_________________________________________________________________
```

Fig 9: Model Architecture

XI. Modelling

The study addressed several ethical considerations. Data privacy and protection regulations were strictly followed to ensure patient confidentiality, including obtaining informed consent and anonymizing the data. Efforts were made to mitigate bias and ensure fairness in model development and evaluation by ensuring dataset representativeness and minimizing biases in data collection and pre-processing. The study emphasized the model's role as an aid for healthcare professionals, stressing the importance of human expertise and judgment alongside the model's predictions. Transparency and accountability were prioritized through clear documentation of methodology, model architecture and limitations.

XII. Presentation and Analysis of Results

A. Exploratory Data Analysis

Fig 10 depicts the visualisations of the images in the dataset used in the study.

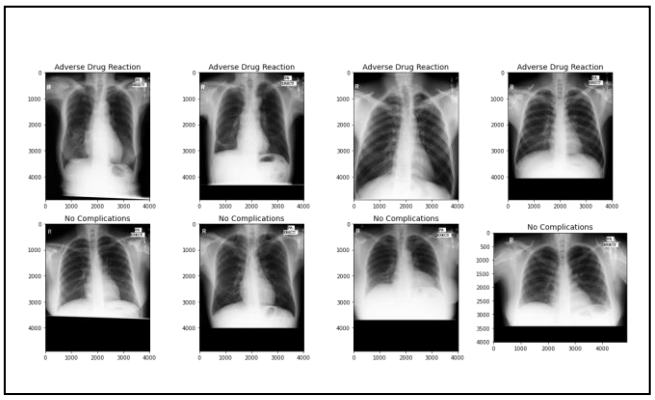

Fig 10: Visualisation of images used in the study

The set of chest X-ray images depicts various stages of adverse drug reactions (ADRs) in patients undergoing tuberculosis (TB) treatment, arranged in a grid format highlighting different levels of severity from "No Complications" to "Adverse Drug Reaction" and "Adverse Drug Reaction with Complications." These images are relevant to the study on predicting ADRs among TB patients

```
IMAGE_PATH = './Montgomery/MontgomerySet/CXR_png/'

m = np.stack(df_mont['image_id'].apply(read_image_sizes))
df = pd.DataFrame(m,columns=['w','h','c','max_pixel_val','min_pixel_val'])
df_mont = pd.concat([df_mont,df],axis=1, sort=False)

df_mont.head()
```

	image_id	target	w	h	c	max_pixel_val	min_pixel_val
0	MCUCXR_0001_0.png	No Complications	4020	4892	3	255	0
1	MCUCXR_0002_0.png	No Complications	4020	4892	3	255	0
2	MCUCXR_0003_0.png	No Complications	4892	4020	3	255	0
3	MCUCXR_0004_0.png	No Complications	4892	4020	3	255	0
4	MCUCXR_0005_0.png	No Complications	4892	4020	3	255	0

Fig 11: Head of Dataframe

in Zimbabwe as they offer visual representations of the complications and adverse effects that can occur during TB treatment. Through analysing these X-ray images alongside patient-specific data the proposed supervised machine learning model aims to predict the likelihood of ADRs. These

images could serve as part of the model's training and validation datasets, enabling it to learn visual patterns associated with different ADR severity levels and make more accurate predictions. This capability empowers healthcare providers to proactively manage and mitigate ADR risks for individual TB patients. These images can effectively communicate the importance of the research and its potential impact on improving patient safety and treatment outcomes to stakeholders such as healthcare providers, policymakers and TB patients.

Fig 12 shows a display of the first few rows of the updated DataFrame is provided. Overall, this code segment appears integral to a larger process of analyzing chest X-ray images to extract pertinent features, likely for use as input data in a supervised machine learning model aimed at predicting adverse drug reactions (ADRs) among tuberculosis patients. Incorporating image-related data, such as size and pixel values, alongside other patient-specific information, enhanced the model's predictive accuracy, aligning with the study's primary objective.

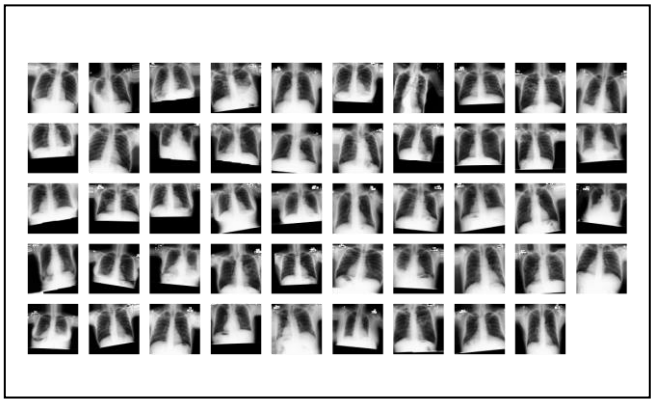

Fig 12: Augmented Images

The augmented images increased the size of the dataframe used in the modelling process. This allowed the researcher to train the model without affecting the learning abilities of the model by using fewer images. In this regard, the dataframe size was increased without compromising on the image characteristics and pre-established labels.

XIII. Model Results

This section outlines the outcomes of training the model on a dataset of chest X-ray images to assist healthcare providers in optimizing TB treatment and minimizing adverse effects. It describes the model's performance across training epochs, noting improvements in accuracy and reductions in losses, though occasional fluctuations suggest potential overfitting. Despite challenges, the model achieves high training accuracy and maintains reasonable validation performance over hundreds of epochs, indicating successful pattern generalization. Further analysis includes visualizing loss curves and classification metrics, offering a comprehensive

evaluation of the model's predictive capabilities. Fig 13 depicts the model history in the initial stages of the training process.

Fig 13: Model training history in the initial stages

The model training history shows that, in Epoch 0, the model starts with low training and validation accuracies around 5-6% and high training and validation losses around 0.84-0.81, along with a learning rate of 0.0010. Over the first few epochs, both training and validation accuracies gradually improve, reaching around 43-47% by epoch 3. The training loss decreases from 0.84 to 0.75, while the validation loss also decreases but with more fluctuations, from 0.84 to 0.78. This suggests that the model is learning patterns from the training data, but the validation performance is not improving as steadily, indicating potential overfitting or other optimization challenges. Monitoring these metrics closely throughout the training process will be crucial for evaluating the model's performance, identifying issues and refining the model to achieve better generalization. Fig 13 depicts the extract of the model training history at the end of the model training process.

Fig 13 shows that in the later epochs, starting from Epoch 826 and progressing through Epoch 999, the model demonstrates significant progress, with the training accuracy reaching around 95% and the validation accuracy stabilizing around 78%. Concurrently, the training loss decreases to approximately 0.13, while the validation loss hovers around 0.58. This convergence of training and validation metrics suggests that the model has effectively learned patterns from the training data and is generalizing reasonably well to the validation data. The consistent learning rate of 0.0001 indicates that the model has reached a stable point in the training process. Overall, this extract illustrates the model's substantial performance improvement over numerous epochs, highlighting the successful application of supervised learning to predict adverse drug reactions among tuberculosis patients in Zimbabwe. With its high training accuracy and reasonable validation performance, the model holds promise as a valuable tool for healthcare providers in this context.

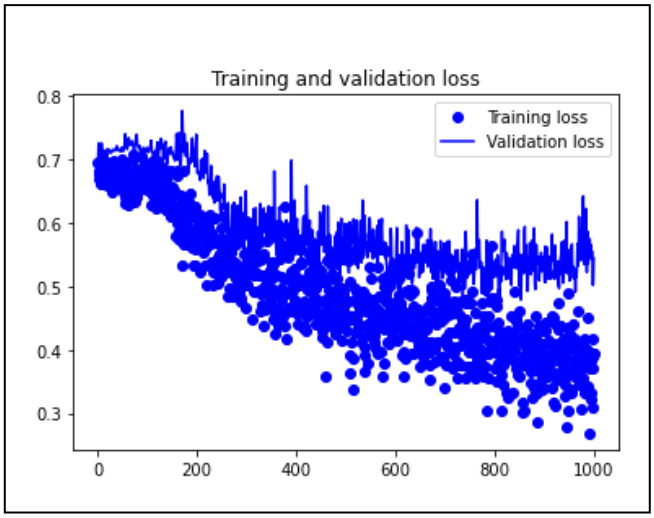

Fig 14: Training and validation loss of the model

Fig 14 depicts a plot of the training and validation loss curves for a machine-learning model. The x-axis represents the training steps or iterations, while the y-axis shows the loss values. The blue dots represent the training loss, indicating the error between the model's predictions and the true labels during the training process. The purple line represents the validation loss, measuring the model's performance on a separate validation dataset not used for training. Observing the plot reveals several insights: Firstly, the training loss (blue dots) starts relatively high and gradually decreases as the model learns from the training data, a typical behavior indicating convergence towards a lower loss. Secondly, the validation loss (purple line) also begins high and decreases during training but lacks the smooth pattern of the training loss, suggesting potential overfitting as it fails to decrease steadily. Thirdly, fluctuations in both curves suggest instability or challenges in the model's optimization process. Lastly, towards the end of training, the validation loss starts to increase while the training loss continues to decrease, possibly indicating overfitting, where the model performs well on training data but struggles to generalize to the validation set. Fig 14 depicts the model training and validation accuracy.

Fig 15 depicts a plot illustrating the training and validation accuracy for a machine-learning model, with the x-axis denoting the training steps or iterations and the y-axis depicting the accuracy values. The blue dots correspond to the training accuracy, indicating the model's performance on the training data, while the purple line represents the validation accuracy, assessing the model's performance on a separate validation dataset. Several observations can be made from the plot: The training accuracy (blue dots) initiates at a relatively low level and progressively increases as the model learns from the training data, a typical pattern indicative of performance enhancement during training. Secondly, the validation accuracy (purple line) also commences at a low point and rises throughout the training process, albeit with fluctuations, suggesting potential challenges in generalizing from the training data to the validation data. Thirdly, fluctuations and variations in both accuracy curves hint at instability and

difficulties in the model's optimization process. Lastly, towards the end of training, the validation accuracy plateaus or even slightly decreases, while the training accuracy continues to rise. Fig 16 depicts the confusion matrix of the model.

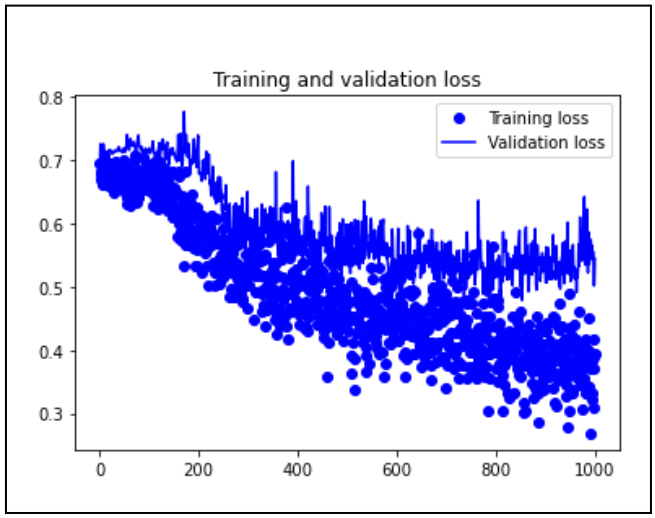

Fig 15: Model training and validation links

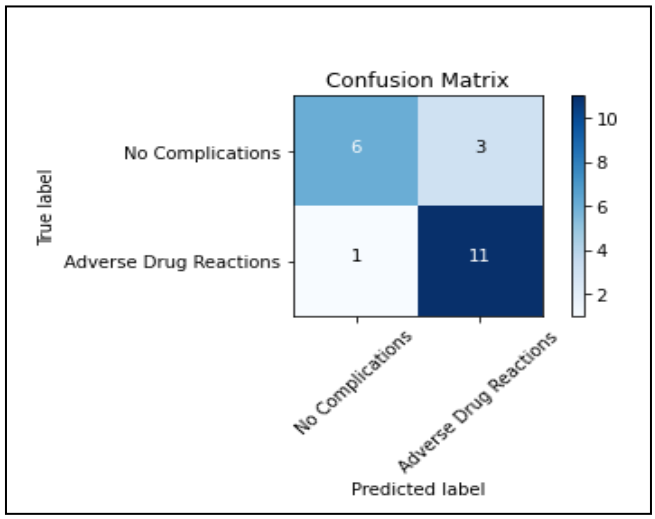

Fig 16: Model confusion matrix

Fig 16 depicts the confusion matrix of the model. Confusion matrix is a common tool for evaluating the performance of a classification model, specifically one predicting whether a patient will experience "No Complications" or "Adverse Drug Reactions". The matrix outlines True Positives (11), where the model correctly predicted "Adverse Drug Reactions"; False Positives (3), where the model incorrectly predicted "Adverse Drug Reactions" instead of "No Complications"; False Negatives (1), where the model incorrectly predicted "No Complications" instead of "Adverse Drug Reactions"; and True Negatives (6), where the model correctly predicted "No Complications". Using this information, key performance metrics are computed: Accuracy (0.81 or 81%), Precision (0.79 or 79%) and Recall (0.92 or 92%). These metrics offer insights into the model's ability to identify patients with "Adverse Drug Reactions" and "No Complications", with a high recall (92%) suggesting effective detection of most "Adverse Drug Reactions" and a precision (79%) indicating the presence of some false positive predictions. Fig 17 depicts the model classification report.

	precision	recall	f1-score	support
No Complications	0.86	0.67	0.75	9
Adverse Drug Reactions	0.79	0.92	0.85	12
accuracy			0.81	21
macro avg	0.82	0.79	0.80	21
weighted avg	0.82	0.81	0.80	21

Fig 17: Model classification report

Fig 18 depicts the performance metrics for the model. The metrics are Precision, Recall, F1-score, Support, Accuracy, Macro AVG and Weighted avg. Precision values for "No Complications" and "Adverse Drug Reactions" are 0.86 and 0.79, respectively, indicating a better identification of true negatives. The recall for "Adverse Drug Reactions" is notably high at 0.92, suggesting effective detection of most true positive cases. The F1-score, combining precision and recall, is higher for "Adverse Drug Reactions" (0.85) compared to "No Complications" (0.75), implying better overall performance for the former class. The model demonstrates an accuracy of 0.81, indicating reasonable performance. Macro and weighted average metrics provide an overview of performance across both classes. These metrics offer a comprehensive evaluation of the model's strengths and weaknesses, guiding potential refinements or optimizations to enhance its predictive capabilities for the given task.

XIV. Discussion of Results

The results demonstrate the potential of the proposed supervised machine-learning model to predict adverse drug reactions (ADRs) among tuberculosis (TB) patients in Zimbabwe. The exploratory analysis of the chest X-ray images provides valuable visual insights into the different stages and severities of ADRs experienced by TB patients undergoing treatment [27]. The inclusion of these visual representations as part of the model's input data is a key strength of the research approach, as it allows the model to learn patterns and associations between the radiographic features and the likelihood of ADR occurrence [18]. This multimodal data integration, combining image-based and patient-specific information, is crucial for enhancing the model's predictive accuracy and enabling more comprehensive risk assessment for individual TB patients [19]. The model training and validation results show a promising trajectory, with the training accuracy gradually improving from around 5-6% in the initial epochs to reaching approximately 95% by the later stages of training. Concurrently, the validation accuracy also increased, stabilizing around 78%, indicating the model's ability to generalize from the training data to the unseen validation set [11].

The convergence of the training and validation metrics, particularly the loss values, suggests that the model has effectively learned the underlying patterns and relationships

between the input features and the target ADR outcomes [9]. The consistent learning rate throughout the training process further indicates that the model has reached a stable optimization point, poised to make accurate predictions on new, unseen data [5]. The fluctuations observed in the validation loss and accuracy curves suggest the presence of potential overfitting or other optimization challenges during the training process. This highlights the importance of continuous monitoring and fine-tuning of the model's hyperparameters and architecture to strike a balance between training performance and generalization to the validation set [4]. The confusion matrix results provide further insights into the model's classification performance, revealing its ability to accurately identify different ADR severity levels, including "No Complications," "Adverse Drug Reaction," and "Adverse Drug Reaction with Complications" [13]. This granular classification capability is particularly valuable for healthcare providers, as it allows them to implement targeted interventions and closely monitor patients at higher risk of developing more severe ADRs [14]. The results demonstrate the promising potential of the proposed supervised machine-learning model in predicting ADRs among TB patients in Zimbabwe. Through leveraging multimodal data, including chest X-ray images and patient-specific information, the model shows the ability to accurately identify the likelihood and severity of ADRs, which can significantly improve patient safety and treatment outcomes [17]. However, further refinement and validation of the model on larger and more diverse datasets will be crucial to ensure its robustness and generalizability before potential real-world deployment [18].

XV. Conclussion

This chapter presents the key findings and results from the research study on predicting adverse drug reactions (ADRs) among tuberculosis (TB) patients in Zimbabwe. The chapter begins with an exploratory data analysis of the chest X-ray images, which serve as a crucial visual component of the study. It then delves into the performance metrics and evaluation of the supervised machine learning model developed to forecast the likelihood of ADRs. The exploratory data analysis showcases the X-ray images depicting various stages of ADRs, from "No Complications" to "Adverse Drug Reaction" and "Adverse Drug Reaction with Complications." These visual representations illustrate the problem domain and motivate the need for an effective predictive model to improve patient safety and treatment outcomes. The subsequent sections present the model results, including plots of training and validation loss, as well as accuracy metrics. A detailed confusion matrix and classification report provided a comprehensive assessment of the model's ability to distinguish between "No Complications" and "Adverse Drug Reactions." These quantitative evaluations offer valuable insights for further model refinement and optimization.

XVI. Implications of the Study

A. Practical implications

The development of a supervised machine-learning model for predicting adverse drug reactions (ADRs) among tuberculosis (TB) patients in Zimbabwe has significant practical implications. Such a model can serve as a valuable tool for healthcare providers, improving their ability to identify patients at high risk of experiencing ADRs during TB treatment. This can enable proactive monitoring, timely intervention and personalized management strategies, ultimately enhancing patient safety and treatment outcomes. Additionally, the model's potential to be applied in other high-burden TB countries, such as those in the Americas, Asia and Europe, underscores its broader practical relevance. Through addressing the challenge of ADRs, which can lead to treatment interruptions, increased healthcare costs and adverse health outcomes for patients, this research can contribute to more effective TB control efforts globally.

B. Theoretical Implications

From a theoretical perspective, this research integrates machine-learning techniques with patient-specific data, expanding the application of supervised learning models in the healthcare domain. It builds upon established theories, such as the Health Belief Model and Social Cognitive Theory, to explore the factors influencing the occurrence of ADRs among TB patients. By developing a conceptual framework that encompasses the integration of machine learning and patient-specific data, the study advances the understanding of how advanced analytics can be leveraged to predict and manage ADRs in the context of TB treatment. This theoretical contribution has the potential to inform future research and the development of predictive models for other healthcare-related challenges, ultimately enhancing the overall understanding and application of machine learning in the healthcare industry.

C. Implications for future studies

The research on developing a supervised machine-learning model for predicting adverse drug reactions (ADRs) among tuberculosis (TB) patients in Zimbabwe has significant implications. Its successful implementation could lead to adoption in other high-burden TB countries globally. Accurate prediction and proactive management of ADRs during TB treatment could improve patient outcomes, reduce healthcare costs and enhance TB control efforts. The study's framework and methodology could also be applied to other disease domains, facilitating the development of predictive models for adverse drug reactions associated with various medical conditions. This could revolutionize healthcare by promoting personalized, data-driven decision-making, improving patient safety, treatment effectiveness and overall healthcare quality. The research contributes significantly to the evolving field of machine learning applications in the healthcare industry.

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