

Forecasting Post-Patent Time Series Pharmaceutical Sales: A Comparative Study of Statistical and Machine Learning Models

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Abstract - Volatility in the pharmaceutical industry can be caused by expiration of drug patents, leading to a gap between actual and target sales values, which necessitates accurate sales forecasting for pharmaceutical marketers. This study utilizes the sales data from PT. Q, an Indonesian pharmaceutical firm. The comparative performance within the specific context of the post-patent period for pharmaceutical sales remains relatively unexplored. This research aims to compare forecasting models for post-patent pharmaceutical sales. The research method utilized is based on the CRISP-DM data mining framework. The forecasting process is done on a 4.5-year timeframe using forecasting models such as ARIMA, SARIMA, LSTM, and Prophet. The results show that multivariate LSTM works better for forecasting in smaller aggregations in the dataset such as by product type and branch, with a R^2 score value of up to 0.64 in the aggregation level of Bandung_Sales, and with the smallest error metric values, such as MAE in many aggregation levels, example being regional sales, such as Lampung_Sales with 1.31 and Makassar_Sales with 0.26, which outperforms the other compared models in the majority of cases. This research concludes that multivariate LSTM is a better way to replace outdated methods to set sales targets.

Keywords: Sales prediction; machine learning; AI; pharmaceutical sales; time series analysis.

I. INTRODUCTION

In Indonesia, one major pharmaceutical marketing company, PT. Q has iron chelation medicine as its leading product, and the medicine's sales volume is consistently high. However, some factors, such as the high cost of pharmaceutical production and the end of patent protection, pose issues for further expansion. Orally administered medicine has a relatively higher cost due to a complex production cycle and patent protection in pharmaceutical corporations. These factors cause market expansion to slow down as patients in lower-

income countries struggle to afford them, despite global healthcare programs [1-3]. The end of a patent period, even amidst the ongoing growth of the thalassemia market. This caused a gap between the targeted sales value and the actual sales numbers of the medicine.

This research compares and explores the usage of forecasting models to determine the best forecasting model for sales target setting, using the sales data of the company's product. Out of the eight years of data, this research utilizes a 4.5-year subset, specifically pharmaceutical sales data from January 2021 to June 2025. In order to better understand the data, the CRISP-DM method is used. This approach enables a better understanding of the business problem. The implementation of the CRISP-DM method to heighten understanding regarding a business problem and formulating a solution includes research by Wen et al., where CRISP-DM is considered and used as the best approach to develop a web application to predict Big Mart sales [4]. Another example of the usage of CRISP-DM was in the research by Jox et al., where CRISP-DM was used as the approach to implement a proper workflow that starts with the selection of suitable data, to the implementation of a machine-learning oriented solution to enhance dairy processing [5]. A study by Tummers et al., compares various data mining frameworks, including CRISP-DM [6]. Another study by Sebastian & Juliane utilized CRISP-DM as a data mining method to better understand the issues regarding stroke prediction from databases, and assists in the decision-making process [7].

This study aims to compare sales prediction approaches for post-patent pharmaceutical sales using time-series data. The data is then processed using the CRISP-DM model for data processing, and then the forecasting models ARIMA, SARIMA, LSTM, and Prophet are used to predict the sales quantity value of the thalassemia iron chelation medicine. These models are

chosen for their high compatibility with time-series data, the number of prior studies exploring these models, and that they enable accurate prediction over data with fixed time intervals. Some examples include the usage of ARIMA and SARIMA models to predict sales numbers for product stock management data by [8] and predicting the movement of NASDAQ stock exchange by [9] the usage of LSTM for predicting medicine demand by Mbonyinshuti et al., [10] and forecasting the spread of contagious diseases by [11] and the usage of Prophet to create a prediction framework on solar energy usage by [12] predicting energy demand within Colombia's market [13] and compared with other forecasting methods to forecast drinking water extraction by [14]. A study by evaluated ARIMA and GRU models in the case of chili price prediction, which is highly susceptible to fluctuations in price, which leads to sales-related changes [15]. The results of the three models are analyzed and compared for the best performance to be applied to the gap issue between the actual sales value and the targeted sales value.

The previously stated bodies of literature explore various forecasting methods that use statistical methods and machine learning across different domains. A research gap can be found in the lack of previous comparative performance within the specific context of the post-patent period for pharmaceutical sales, which still remains relatively unexplored. An evaluation to compare the performance and resilience to disruptive characteristics of post-patent protection sales data for each model is not only academic, but also necessary.

Research on the pharmaceutical context is focused on stable-market conditions or planning related to medicine demands. This is evidently shown in the study by Mbonyinshuti et al., which compares the usage of ARIMA and LSTM for general medicine demand, and by Fourkiotis & Tsadiras, whose study applies machine learning methods to predict stable pharmaceutical sales. The volatility of medicine sales is introduced due to the entry of generic products into the market, which grants a unique forecasting challenge as there are sudden market shifts, which can change preexisting trend and seasonality patterns that can be found, which remained understudied. This differs from constant or stable demand datasets. This research aims to address this gap by comparing the performance of pharmaceutical models on post-patent medicine sales, as there is a lack of evidence on the most robust method to predict time-series values in the unique conditions after the expiration of the patent protection period. The performance of forecasting models such as ARIMA, Prophet, and LSTM

has not been rigorously evaluated and compared. This gap leaves pharmaceutical marketing companies lacking evidence-based guidance for forecasting model selection in a particularly volatile business phase, which leads to outdated target-setting methods, as the case described in this study.

The remainder of this paper is constructed as follows: Section 2 details the method utilized in this research, which is based on the CRISP-DM framework. Section 3 presents the forecasting results alongside a discussion of the findings. The last section, section 4, concludes the contents of the rest of the paper, which contains the summary of key findings, contributions both scientific and practical, and the limitations and direction of possible future research.

II. METHOD

The research methodology utilized in this research is structured in sections that constitute the CRISP-DM data mining method, which can be divided into six segments, as illustrated in Fig. 1. These include the processes of business understanding, data understanding, data preparation, modelling, evaluation, and deployment.

A. Business Understanding

PT. Q, the subject of this study, showed that the leading factor in the reduction of sales numbers is the end of the patent protection period, which lasts for twenty years in 2021. Lower costs on generic products are preferred for governmental health policies, which leads loss of sales. Before the end of the iron chelation medicine patent protection period, the target determination for the sales numbers is set by checking the sales data within the last five years, and the peak value among the sales data number is chosen, and is increased by any percentage value depending on the sales manager's orders as the method of determining the target value of a set month. The usage of forecasting models can be used to assist in target setting from data that is based on actual sales value.

From the yearly sales report, a dataset was created to serve the data in a forecastable manner. The data captures the sale of iron chelation medicine that fluctuates within the timeframe of the dataset. In order to process the dataset, it is uploaded to Google Colab directly to gain the values and variables contained in the dataset. The information contained within the dataset can be seen in Table 1.

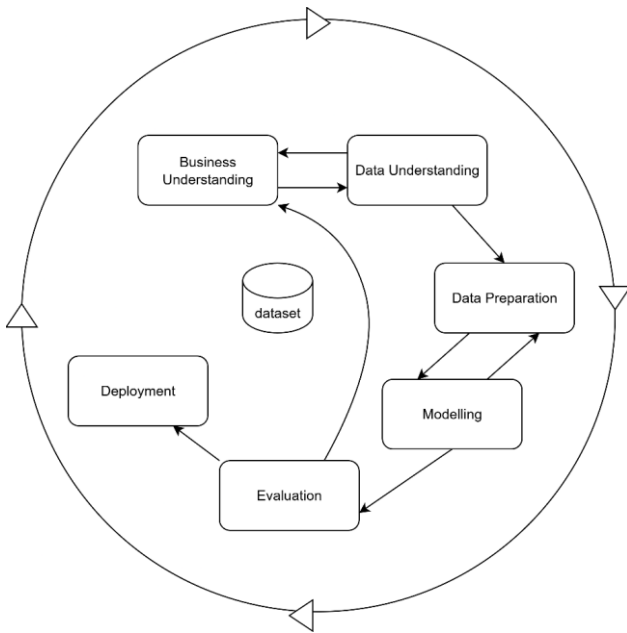


Fig. 1 The Crisp-DM method structure

B. Data Preparation

The data preparation steps involve boxplot checking to determine the number of outliers in the dataset, ACF and PACF checking, and dataset differencing. Also, due to the large number of outliers in the dataset, the data is capped for forecasts with ARIMA, SARIMA, single-variable LSTM, and Prophet. Using Tukey’s method

with $k=1.5$, reveals that 208 data points in the dataset, or 16.05% of the dataset, exceeded the calculated upper and lower bounds, which are -51.0 as the lower bound, and 85.0 as the upper bound. This substantial amount of outliers shows the volatility of the post-patent period sales, where the entry of generic products causes volatile changes to sales amounts. The capping process at the 95th and the 5th percentiles ensures that the market signals are still captured rather than being discarded outright. This will preserve the temporal continuity of the dataset and reduce the influence of extreme values on statistical models and simpler forecasting approaches. Additional features, such as the standard deviation of the dataset and the moving average for 6 months, are also added to the dataset.

The Multivariate LSTM was excluded in the data capping process due to its inherent architectural robustness to data outliers in extreme values during the training process. However, the output layer is indicated by linear activation in the activation function hyperparameter. This potentially generates negative values in forecasts. For real-life case implementation, post-processing is required using constraints that limit the value to zero or above. This research retains the limitation to preserve the consistency of methods across different models.

**TABLE I
RELEVANT DATASET VARIABLES**

Variable	Explanation
Periode	The period when medicine sales occur, the period is formatted in YMD form. The historical sales data of PT. Q is recorded monthly.
Branch	The PT. Q Branch that handles iron chelation medication sales.
Product_Type	The type of iron chelation products that are sold: KBT for tablets and KBS for syrup.
Quarter	The quarter of a year in which a transaction happened.
Product_Price	Varies by product type and stays consistent within a year.
Product_Sales	The actual number of sales within a period and product type.
Total_Customers	The total number of customer instances in a single year within a branch. This accounts for active and inactive customers.
Active _Customers	The number of active customer instances in a single year within a branch.
Lag_1	The number of sales in the previous month
Is_Holiday_Month	Indicates if a month is considered a holiday season or not.

C. Modelling

Three forecasting model classes are implemented and compared, which are statistical models (ARIMA and SARIMA), machine learning models (LSTM), and Prophet. These models were chosen due to their capabilities of creating a prediction based on time-series data. The statistical models work by utilizing statistical data to determine the set contained within the data. Historical value of the dataset, alongside prediction errors and lag values, is considered part of a set [10]. These represent the statistical benchmark and are effective for time-series forecasting with clear seasonality. The LSTM model utilizes hidden Recurrent Neural Network (RNN) cells and other internal cell conditions to store long-term data, and is suitable for complex and non-linear data, which are the characteristics of post-patent volatility [16]. The multivariate variant incorporates more features of the dataset, which captures the multi-factor nature of medicine sales dynamics. The Prophet model takes seasonality and holiday effects in forecasts, and is highly responsive to those factors.

All of the models are implemented in Python using the standard libraries, such as statsmodels for ARIMA, Keras for LSTM, and the Prophet library. Grid searches are done to determine the best hyperparameter values on some models. Table II shows what hyperparameter values are used for each model to give the best performance while avoiding overfitting.

D. Evaluation

In the evaluation phase, some metrics are used as a way to gauge the quality of each forecasting model to predict post-patent iron chelation medicine sales. To evaluate the performance of each model, from statistical to machine learning methods, alongside Prophet, some statistical metrics were utilized to determine each model's accuracy to the dataset, and the quality of each model by showing the average error values that are usually better if the value is smaller. The metrics that are used in this study are Mean Absolute Error (MAE) and R^2 score. The error metric utilizes the number of observed rows of the dataset, the index of each processed data point, starting from the earliest data point to the value of n , the actual data value, the predicted data value, and the error values or residuals gained from the absolute, or squared difference between the actual and predicted values, depending on the metric used. On the other hand, the R^2 score utilizes the dependent variable variation, which was influenced by the independent variable, and works in two parts: the unexplained variation and the total variation. The value of the R^2 score determines the

performance of the model in explaining data variability, and ranges from -1 to 1. The closer the value gets to 1, the better the model is [17].

E. Deployment

Depending on the model, be it ARIMA, LSTM, or Prophet, forecasting results are monitored to detect any issues, as changes to trend and seasonality happened in the dataset. The result of deploying the models can be seen as plots that showcase the actual and predicted values of the dataset alongside the projected values in the next three periods.

III. RESULT AND DISCUSSION

In this section, we present the results of the forecasts to project the values for the next three months, and the MAE and R^2 score performance metrics give the results that can be seen in Table III-V. Table III shows the projected sales as forecasting results for the next three months in various levels of aggregation, Table IV shows the evaluation results utilizing MAE as the performance indicator metric, and Table V shows the evaluation results utilizing R^2 score as the performance indicator metric. The usage of different performance metrics allows more insights from the dataset, as better insights can be gained from using the error metric in some datasets, and others with the accuracy metric or R^2 score.

The forecasting result for the next three data values of the dataset of several models, such as ARIMA, SARIMA, Multivariate LSTM, and Prophet, shows negative values, as seen in Table 3. This is nonsensical in a practical context, as the sales amount cannot be negative. The occurrence of the forecasting artifact is caused by multiple factors, with the main cause being the presence of negative values from the training data itself, which was caused by frozen transactions due to market shock linked to the entry of generic products with lower prices. The national health insurance regulation uses the cheapest available product. The other causes include the limitations of extrapolation in statistical models such as ARIMA and SARIMA, which extend trends beyond feasible ranges, and the lack of constraints in output layers of all models. This includes multivariate LSTM, which could be considered the most robust among the compared models, and can produce forecasts with negative values if trained in volatile, near-zero datasets with negative values. In operational deployment, strategies such as flooring the forecast value to zero at the lowest or using log transformation to prevent negative values are essential.

The occurrence of negative R^2 scores, such as -7.096 for the ARIMA model on KBT_Total and the worst

being -69.666 for the Prophet model on Semarang_Sales, needs careful interpretation. The negative values of R^2 indicate that the performance of the models is worse compared to simply using the mean as the constant forecast value in forecasting contexts, or considered

deficient, according to [19]. This can be caused by the extreme volatility of the dataset that disrupts stable, observable patterns that are relied upon by statistical models. Another cause of a negative R^2 score is structural

TABLE II
HYPERPARAMETER VALUES FOR EACH MODEL

Forecasting Models	Hyperparameters	Values
ARIMA	p Range	(0-4)
	d Range	(0-1)
	q Range	(0-4)
SARIMA	Split Ratio	67:33
	p Range	(0-1)
	d Range	(0-1)
	q Range	(0-1)
	P Range	(0-1)
	D Range	(0-1)
	Q Range	(0-1)
	S Value	(12)
Monovariate LSTM	Split Ratio	67:33
	Model Type	Sequential
	Time Steps	12
	Number of Features	1
	LSTM Layers	1
	LSTM Units	50
	Dense Layer	1
	Dense Units	1
	Loss Function	'mse'
	Epochs	100
Multivariate LSTM	Batch Size	32
	Model Type	Sequential
	Time Steps	12
	Number of Features	6
	Split Ratio	80:20
	Forecast Steps	3
	LSTM Layers	2
	LSTM Units	Varied (Layer 1: 100 > Layer 2: 50)
	Activation Function	'ReLU' Rectified Linear Unit Activation
	Dropout Rate	0.3
	Dense Layers	2
	Dense Units	Varied (Layer 3: 25 > Layer4: 1)
	Optimizer	Adam
	Loss Function	'mse'
Epochs	100	
Prophet	Batch Size	16
	Yearly Seasonality	linear
	Changepoint Prior Scale	0.05
	Seasonality Prior Scale	10.0
	Holiday Prior Scale	10.0
	Interval Width	0.80

breaks, such as a sudden decline in sales caused by the expiration of the patent protection period, which render prior data relationships invalid. This finding shows that simpler forecasting models perform worse under high-

volatility and low-signal situations. The limitation showed an additional consideration of choosing a performance metric. R^2 score might not be a suitable primary metric for post-patent protection medicine sales

data, which are volatile and prone to market shocks. Within the context of large and meaningful outliers, error-based metrics such as MAE can provide better reliability with an interpretable indicator of model performance.

The overall result shows that multivariate LSTM generally performs the best, as evidenced in the MAE, RMSE, and R² score value for product sales aggregated by product type and branch. However, this is not the case with overall aggregation, as the R² score shown, and the error metrics show that it performs worse than SARIMA and Prophet. This may be caused by the mismatch between the time series data within the dataset and the model.

Prophet shows the best forecasting result for overall product sales at a broader aggregation level, which shows that the model performs well as a way to capture broad statistics in iron chelation medicine sales. However, this model does not work as well in granular, smaller-scale forecasting. Machine learning models, such as the variations of LSTM works as a way to capture the complicated relationships between variables within pharmaceutical or medicine sales data, such as in the case of iron chelation medication sales. Due to the patent protection period of the product having already run out, the sales amount had become volatile, as generic products entered the pharmaceutical market.

TABLE III
PROJECTED SALES OF THE NEXT THREE MONTHS USING EACH FORECASTING MODEL

Product_Sales	ARIMA	SARIMA	Mono-LSTM	Prophet	Multi-LSTM
All_Products	[1109 1109 1109]	[1088 746 787]	[1000 1001 1000]	[373 578 482]	[510 497 482]
KBS_Total	[405 405 405]	[398 329 358]	[366 372 373]	[310 442 373]	[70 72 59]
KBT_Total	[175 175 175]	[99 161 114]	[150 154 157]	[63 137 109]	[5 5 5]
Aceh_Sales	[44 -2 7]	[10 -11 45]	[55 40 24]	[13 -20 66]	[-2 68 85]
Bandung_Sales	[71 77 59]	[61 65 70]	[79 74 81]	[49 74 84]	[-8 91 92]
Bogor_Sales	[84 87 103]	[70 84 95]	[81 73 73]	[73 61 97]	[23 20 16]
Jakarta_Sales	[160 153 159]	[143 138 145]	[147 144 149]	[150 145 132]	[151 145 144]
Jambi_Sales	[7 10 11]	[4 5 4]	[15 15 15]	[-3 7 3]	[1 1 1]
Lampung_Sales	[10 9 8]	[13 10 10]	[6 6 5]	[-1 1 6]	[2 1 2]
Makassar_Sales	[0 0 0]	[0 0 0]	[0 1 1]	[-2 -1 0]	[0 0 1]
Palembang_Sales	[39 33 35]	[50 69 52]	[32 32 32]	[92 35 15]	[5 3 3]
Pekanbaru_Sales	[21 14 5]	[-19 -6 1]	[16 16 18]	[-24 2 3]	[7 6 6]
Semarang_Sales	[5 5 4]	[-10 -4 -4]	[13 14 16]	[-9 -42 -4]	[6 7 6]
Surabaya_Sales	[26 43 26]	[-14 3 40]	[30 26 28]	[-35 27 36]	[6 7 7]
Yogyakarta_Sales	[62 33 29]	[29 69 13]	[69 58 64]	[181 80 94]	[60 172 84]

TABLE IV
EVALUATION RESULTS USING MAE

Product_Sales	ARIMA	SARIMA	Mono-LSTM	Prophet	Multi-LSTM
All_Products	407.123	291.172	431.550	140.881	397.191
KBS_Total	102.295	116.645	108.714	87.917	86.826
KBT_Total	86.916	79.182	82.281	89.509	17.49
Aceh_Sales	22.439	28.007	30.655	48.672	29.384
Bandung_Sales	16.543	19.054	24.412	25.093	54.700
Bogor_Sales	22.921	25.45	23.755	28.583	27.070
Jakarta_Sales	22.919	35.737	21.781	32.631	123.819
Jambi_Sales	5.619	4.743	8.113	10.318	4.107
Lampung_Sales	4.204	7.618	3.651	12.89	1.309
Makassar_Sales	0.958	0.791	0.885	2.614	0.258
Palembang_Sales	14.714	14.199	18.556	31.58	8.266
Pekanbaru_Sales	5.042	21.408	28.997	39.86	11.950
Semarang_Sales	6.774	14.506	21.232	31.746	6.937
Surabaya_Sales	15.85	21.491	31.907	32.378	15.206
Yogyakarta_Sales	102.752	151.528	42.813	103.496	54.696

TABLE V
EVALUATION RESULTS USING R² SCORE

Product_Sales	ARIMA	SARIMA	Mono-LSTM	Prophet	Multi-LSTM
All_Products	-1.584	-0.647	-3.279	-0.800	-0.359
KBS_Total	-0.227	-0.262	-0.098	0.145	0.026
KBT_Total	-7.096	-7.330	-23.841	-9.894	0.110
Aceh_Sales	-0.015	-0.082	-0.029	-2.894	0.517
Bandung_Sales	-0.201	0.149	-0.763	-0.113	0.647
Bogor_Sales	-0.172	-0.344	-0.016	-0.372	0.449
Jakarta_Sales	-0.701	-2.304	-0.486	-2.407	0.205
Jambi_Sales	-0.571	-0.253	-1.684	-3.412	0.188
Lampung_Sales	-1.106	-5.089	-0.556	-17.903	0.234
Makassar_Sales	-0.03	-0.355	0.005	-5.012	0.114
Palembang_Sales	-0.121	-0.377	-0.574	-5.195	0.459
Pekanbaru_Sales	-0.019	-3.242	-3.747	-12.815	0.525
Semarang_Sales	-1.744	-14.914	-21.765	-69.666	0.525
Surabaya_Sales	-0.081	-0.797	-1.836	-2.744	0.435
Yogyakarta_Sales	-7.815	-18.287	-1.382	-10.99	0.130

The findings within this study contribute to the discourse of model selection of time series analysis by validating the existing knowledge within the context of post-patent protection sales of pharmaceutical products. The findings of this study align closely with the conclusions found by [10] and [18], which confirms that machine learning methods have a higher capability of capturing more complex and non-linear patterns found in volatile healthcare-related data. As seen in the overall higher R² score in some granularity levels, such as sales by product type and branch level.

Considering the data granularity, a more complex picture can emerge. While this study shows that multivariate LSTM is well-suited for complex datasets, the conclusion shown by the study from [9] showed that the performance of each forecasting model is domain-specific. This study extends the finding by showing that performance can differ with different tasks that are still in the same domain. The performance of the Prophet model shows better results, despite being a simpler model, on highly aggregated, overall sales data. Only on a more granular and volatile product and branch level does the multivariate LSTM's ability to capture complex data give better results.

Determining model performance utilizing metrics also needs to be done contextually, as using MAE for data with large outliers might give greater insights into a model's performance than using the R² score. Also, the choice of variables in multivariate LSTM is important to prevent data leakage and increase the model's accuracy in sales forecasts. The findings of this study show

actionable insights for the management of the pharmaceutical marketing process. The first is the transition to actual data-based methods of target setting, for sales target setting needs to be done in order to reduce unrealistic expectations for salesmen and the conflicts associated with it. For the second finding, the level of dataset granularity in the forecasting process is important, as a single aggregate forecast could be insufficient. The estimation of branch-level and product-level target setting is better done using multivariate LSTM, as it captures post-patent protection volatility better. The third is the product inventory management based on forecast-driven data, particularly for product types or regions with high demand, for example, KBS or syrup iron chelation medicine. Cases of overstocking incidents and wasted products can be reduced using actual data-based approaches. Lastly, investment in machine learning methods, such as multivariate LSTM, can be justified in the post-patent protection period, as outdated target setting methods and statistical forecasting models could fail in capturing volatile and non-linear sales patterns.

IV. CONCLUSION

This study addressed the challenge of forecasting medicine sales in a volatile period of post-patent protection. During periods of high volatility, traditional and heuristic methods of setting sales targets are rendered obsolete and could create operational gaps. A comparative analysis of ARIMA, SARIMA, Prophet, and LSTM variants in multiple aggregation levels

revealed that the performance of each model depends on granularity. Prophet performs the best in capturing broader aggregate trends, with multivariate LSTM generally showing superior performance at granular (by product type and branch) levels, achieving an R^2 score up to 0.64. However, the model still shows a negative sales forecast value due to the unconstrained output layer. This limitation can be addressed by modification with post-processing techniques. The academic contribution of this study is to provide an empirical framework for model selection in a volatile post-patent setting, with non-linearity and complex patterns as the data characteristics, and demonstrating that data granularity affects the efficacy of the models. While the practical contribution is by offering a data-driven alternative to replace outdated sales target setting methods, and in turn enabling pharmaceutical marketing corporations to set realistic and actual sales data-based targets to reduce salesmen pressure, minimize financial losses, optimize inventory management, and prevent conflict with stakeholders from failure in achieving targets. The limitation in the study is in the restricted sets of forecasting architectures, and the lack of exploration of hybrid models and transformers that potentially could show better forecast results. Future research can be done to hybrid approach in forecasting models that combines the use of statistical models and machine learning models, and exploration of external factors to pharmaceutical sales and specific architectural approaches for data related to pharmaceutical sales, such as medicine sales, logistics, and consumption.

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