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Medication correlation analysis for outbreak prediction

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ABSTRACT

Outbreak prediction is a way to predict the epidemic potentials of diseases using the pattern of medication sales values. Successful prediction might result in being cautious of the outbreak of diseases and taking necessary measures to prevent the predicted outcome. As medication sales values are too random, the analysis of medication correlation is one of the most interesting and challenging parts for the researchers. The major objective of this proposed research method is to analyze medication drug sales values for a certain period of a pharmaceutical company using statistical methods. It is also the intent of this research to make a comparative analysis of the output generated by the deep learning model with the real sales values of a month. Our method successfully predicts the outbreak potential of diseases with competent accuracy, so that we will have enough time to take precautions and prevent future pandemics through precautionary measures.

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1. INTRODUCTION

Every year people get affected by several diseases namely dengue fever, diarrhea, dysentery, and cold. Often, people don’t get themselves prescribed by a doctor or go to hospitals for mild symptoms. Rather they prefer to buy conventional medicines from pharmaceutical stores. As a result, pharmaceutical stores' medication sales data indicates what kind of medications people are taking explicitly. There’s been research for predicting disease outbreaks using surveillance data and weather change data. But there are very few studies about disease outbreak prediction using pharmaceutical stores’ sales data. Different genres of medicines are sold in retail pharmaceutical stores and produced by different pharmaceutical companies. But medicines of the same genres are used for some common diseases. These common genres correlate with them. Analysis of these correlations might result in predicting potential disease outbreaks in the nearest future, which plays the primary motivation for research in this area. Using statistical analysis, machine learning, and deep learning with a neural network approach we will try to predict which genres of medicines are likely to increase in their sales soon and make an estimation about potential disease outbreaks.

Correlation is a statistical association between two random variables that can indicate a predictive relationship and can be exploited in practice. Outbreak prediction is a way to predict the epidemic potentials of diseases using the pattern of medication sales values. Long short-term memory (LSTM), a type of artificial recurrent neural network, is best suited to classify and forecast time series data. Retail pharmacy sales data is day-to-day sales information. So, we have applied this method to make a predictive analysis of generic pharmaceutical drug sales for 30 days. Then assume of disease outbreak based on those analyses. We have also made a comparative analysis of our prediction with the actual sales in a month.

Bangladesh and other South Asian countries are comparatively backdated in medical facilities. A large number of people live under the poverty line and don’t even try to reach a doctor unless they are severely sick or wounded. Because of this reason, medical institutions do not have proper information on the sales of medicines or diseases detected by doctors. Most people go to nearby pharmaceutical stores and buy generic drugs that are used regularly for common diseases. Diseases like dysentery, cold symptoms, diarrhea, fever, and gastrointestinal problems are taken very lightly in these regions and are often cured by taking common medicines from pharmacy stores. This raises a huge possibility of predicting disease outbreak potentials more accurately from the prediction of medicine sales in these retail stores. Successful prediction might become highly effective in taking precautionary measures against future outbreaks. For instance, if we notice a significant increase in sales of a particular genre of medicines in a month that might indicate a good probability of a disease outbreak for which those particular medications doctors will prescribe. In this way, we can get a broad view of diseases that people are getting affected with every day, even if they are not getting prescribed by a doctor. But sometimes people make wrong assumptions about their diseases and take unnecessary or wrong medicines to get cured. As a result, these medicine sales values are random, and very hard to predict just by statistical analysis. That’s why we have come up with the idea of applying deep learning in this kind of dataset to make a predictive analysis of potential disease outbreaks. Our system can be used in medical drug research, financially beneficial to pharmaceutical institutions, and greatly useful for public health concerns.

The main contribution of our works is: to propose a model using LSTM and recurrent neural networks (RNN) architecture for predicting medicine sales and compare them with the real sales values. And by using this analysis, predict the potential disease outbreaks at a certain time for that particular region. We organize the paper as related works are described in section 2, the proposed model and dataset description and comparative analysis are addressed in section 3, and results and discussion are placed in section 4. Finally, the conclusion and limitations are provided in section 5.

2. LITERATUR REVIEW

A few studies have been conducted in the domain of illness or epidemic prediction. Deepthi *et al.* [1] used the patients' symptoms to forecast the disease. Over real-life healthcare data, [2] experimented with the revised estimate models. It used a latent factor model to reconstruct the missing data to solve the challenge of incomplete data. Also experimented with a brain infarction-related regional chronic disease. Several algorithms were utilized to analyze structured and unstructured data from the hospital. Mohan *et al.* [3] used machine learning approaches to predict cardiac disease. They suggested a novel strategy for identifying key features which improve the accuracy of cardiovascular disease prediction. They attained an enhanced performance level using a prediction model for heart disease that included a hybrid random forest with a linear model (HRFLM) where an accuracy level of 88.7%.

Several methods have been proposed to predict specific disease outbreaks or increases in any medication dispensed. One of the proposed methods applies a classical model of susceptible-infectious-removed (SIR), which is a classical model that uses differential equations representing disease dynamics and predicts the number of people to be affected by the influenza virus using pharmacy sales data [4]. The study also visualizes a comparison between the results from surveillance data and pharmacy data as well. Another method uses an artificial neural network (ANN) and support vector machine (SVM) to predict malaria cases in a state using parameters such as humidity, temperature, average monthly rainfall, the total number of plasmodium falciparum (pF) cases, and the total number of positive cases [5]. Using similar parameters dengue outbreak prediction studies have also been conducted [6]. Dengue fever predictions have also been studied using Pharmacy sales data as well by applying the Bayesian data analysis technique [7]. To predict disease outbreaks like gastrointestinal illness and respiratory illness pharmaceutical sales data has been used and a method has been proposed that applies ANN that detects changes in the sales trends for over-the-counter (OTC) pharmaceuticals [8]. Drug sales data has been proven to be effective in one of the studies concerning these kinds of illnesses [9]. Another work has been conducted for price movement prediction using a convolutional neural network (CNN) and LSTM [10]. RNNs, use their internal state to process variable length sequences of inputs (memory). As a result, they're ideal for research projects involving connected handwriting or speech recognition and unsegmented [11]–[14]. In contrast to traditional feed-forward neural networks, LSTM has feedback connections [15]. It can handle both single data points (such as photos) and complete data sequences (such as speech or video or time series). Kołecka *et al.* [16] reveal the sold drugs volumes for their presence in the wastewater treatment plants. Smith *et al.* [17] evaluate differentiated the relationship between the traditional patient acuity metric and medication regimen complexity. Wallis *et al.* [18] describe the scenarios of the vast usage of self-prescribed medication for adults and the arisen difficulties. Reyana and Kautish [19] suggest the necessity of ML tools to help hospital administrations and frontlines of hospitals to provide efficient decisions for patient treatment and services. Comito and Pizzuti [20] highlight the limitations of existing practices of learning and interpretability of the labeled data. To effectively combat the pandemic, this study measures the effects of various nonpharmaceutical approaches [21]. Ye *et al.* [22] provide a method for forecasting the energy usage of multiple jobs based on LSTM and multi-task learning techniques. Haag *et al.* [23] identified the influential factors of pre- and post-COVID-19 to reduce the risk and resilience. Yoo *et al.* [24] study the parameters of counting the lymphocyte and albumin for making a correlation between disease severity and laboratory parameters.

3. METHOD

3.1. Proposed model

First of all, we create the dataset. After that, the dataset required some preprocessing before the proposed method could be applied. Then, we applied LSTM RNN for dataset training and testing purposes. Finally, we used this trained model to make a comparative analysis of the predicted output and the real output. Predict disease outbreaks from one month of future sales forecasting. The workflow diagram is depicted in Figure 1.

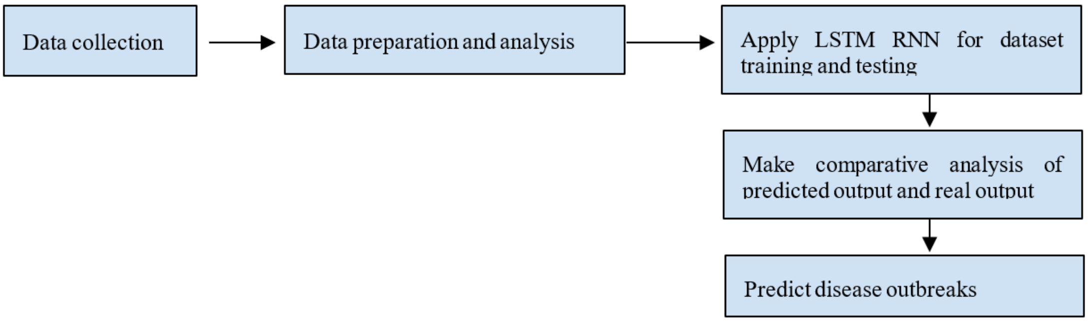

Figure 1. Workflow diagram

3.2. Dataset description

We choose the dataset of daily sales of generic medicines in retail pharmacy stores. We collect the dataset from Kaggle [25]. The dataset is based on an initial collection of 600,000 transactional data exported from individual pharmacies' point-of-sale systems over six years (2014-2019), showing the date and time of sale, pharmaceutical drug brand name, and sold amount. A subset of 57 drugs from the dataset are classified using the anatomical therapeutic chemical (ATC) classification system. There are no null values or dump data in this dataset.

3.3. Dataset preparation and analysis

The dataset contained data on different drugs produced by different companies. But several drugs contained the same molecules and were prescribed for curing similar diseases. All of these similar drugs were labeled under the same genre. A specific genre of medicine is generally prescribed for one or more than one specific disease. Here, the dataset has been classified into 8 groups of generic medicines according to the therapeutic chemical classification system. To receive optimal performance, we have used Scikit-learn's MinMaxScaler to scale our data. Then, data now be in a specified format, a 3D array for LSTMs. We began by generating data in 60 timesteps and then converting it to an array with NumPy. Following that, we created a 3D dimension array of X train samples, 60 timestamps, and one feature at each step. Now, we analyze how the 8 categories of medicine sales are fluctuating in day-to-day sales, what are these categories, and what kinds of diseases these categories are used for.

- M01AB-M01AB in Figure 2(a) refers to medicines that comprise anti-inflammatory and antirheumatic drugs, non-steroids, acetic acid derivatives, and related compounds. This type includes medications like zomepirac (used to alleviate pain ranging from mild to severe), alclofenac (rheumatoid arthritis, ankylosing spondylitis, and as an analgesic in severe arthritic diseases are all treated with this drug), and bufexamac (used to treat atopic eczema and inflammatory dermatoses on the skin) (see in Appendix).
- M01AE- In Figure 2(b) shows anti-inflammatory and anti-rheumatic medicines, non-steroids, and propionic acid derivatives. This class of medicine includes tarenflurbil (a pharmaceutical extensively given for the treatment of cough and related respiratory tract disorders) and levopropoxyphene (a pharmaceutical frequently prescribed for the treatment of cough and related respiratory tract diseases). Dextropropoxyphene (an analgesic enantiomer), and oxaprozin (for osteoarthritis, rheumatoid arthritis, and juvenile rheumatoid arthritis) (see in Appendix).

- N02BA-This category in Figure 2(c) indicates other analgesics and antipyretics, as well as salicylic acid and derivatives. Salicylamide (for the alleviation of pain and discomfort caused by ordinary mouth ulcers, cold sores, denture sore spots, infant teething, mouth ulcers, and sore spots on dentures), acetylsalicylic acid (pain, fever, inflammation, migraines, and lowering the risk of serious adverse cardiovascular events are only a few of the uses for this drug), and acetylsalicylic acid (pain, fever, inflammation, migraines, and lowering the risk of serious adverse cardiovascular events are only a few of the uses for this drug) (see in Appendix).
- N02BE/B- Figure 2(d) refers to the genre-indicated medicines that contain other analgesics and antipyretics, pyrazolones, and Anilides. Common medicines in this genre are propacetamol (in multimodal analgesia therapy, it is utilized to control perioperative fever and discomfort) (see in Appendix).
- N05B- Figure 2(e) refers to the genre of medicines that contain psycholeptics drugs, and anxiolytic drugs. These kinds of medicines are generally used for insomnia, anxiety, sleep disorder, and related diseases (see in Appendix).
- N05C- Figure 2(f) refers to the genre of indicated medicines that contain psycholeptics drugs, hypnotics, and sedative drugs and are generally used as sedatives and prescribed to cure insomnia (see in Appendix).
- R03- Figure 2(g) indicates the medicines that contain drugs for obstructive airway diseases. Flunisolide (used as a prophylactic therapy in the maintenance treatment of asthma), and dyphylline (used to treat asthma, bronchospasm, and COPD) (see in Appendix).
- R06- This category in Figure 2(h) includes antihistamine-containing medicines for systemic use. Terfenadine (an antihistamine used to treat allergy symptoms), dexbrompheniramine (an antihistamine used to treat allergy symptoms, including upper respiratory tract symptoms), and phenindamine (an antihistamine used to treat allergy symptoms) are all antihistamines that are used to treat allergy symptoms (sneezing, runny nose, itching, watery eyes, hives, rashes, itching, other allergies, and cold symptoms are treated with this medicine (see in Appendix).

All together we can see in Figure 3 that the sales information of those 8 medicine genres is too random. Then, it is a challenging task to make a disease outbreak forecasting from these datasets. We have used a deep learning model for predicting sales in the next step.

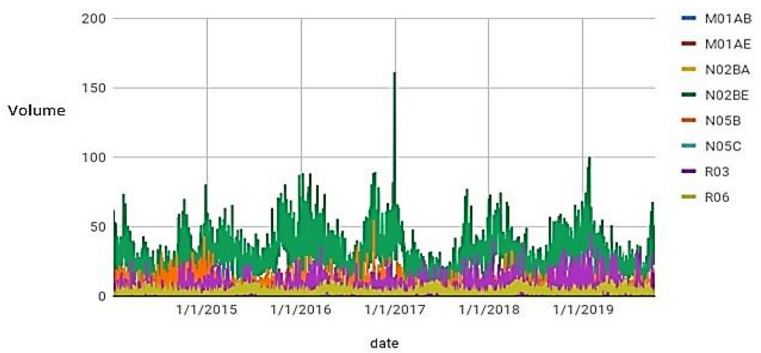

Figure 3. Sales variations of 8 ATC categories

3.4. Model development

We used a sequential model to start our neural network to apply LSTM. The LSTM layer was then added, as well as a highly connected neural network layer. To avoid overfitting, dropout layers have recently been added. We set the value for dropout layers to 0.2, which means that 20% of the layers will be lost during processing. The dense layer was then added, which decides the output of one unit. Our model used the adam optimizer, and the loss was determined using mean squared error. Finally, we optimized the model for a batch size of 32 epochs and 100 epochs. To anticipate sales volume for the following 30 days, we employed RNN LSTM. In September 2019, we compare the actual and predicted sales volume.

3.5. Comparative analysis of the predicted and real output

Different genres of medicines are sold every day in pharmacy stores. The visualization shows a correlation among the generic medicine features changing with time. The changes are regular and symmetric. These genres are significantly correlated and their random change in sales volume affects sales values collectively. A massive probability of an increase in any specific medicine genre might result in the possible outbreak of diseases that are diagnosed with them. The mentioned simulation tools have been applied to the dataset and trained after preprocessing. Trained models are then tested for prediction analysis. We trained our model using medication sales from 2014 to August 2019. And predicted the sales values through September 2019 shown in Figure 4. Then, we compared our predicted outcome with the real values and visualized the comparison shown in Figures 4(a)-(h). In Figures 4(a)-(c) and Figure 4(f), predicted volume is the average sales quantity. Figures 4(d), 4(e), 4(g), and 4(h) shows that model tries to fit the curves but the actual data have high fluctuation, so it's not possible to accurately predict the real scenario. In Figure 5, predicted outcomes of the medication sales from 11th October 2019 to 9th November 2019 are provided. Next, we will predict possible disease outbreaks from the previously observed results.

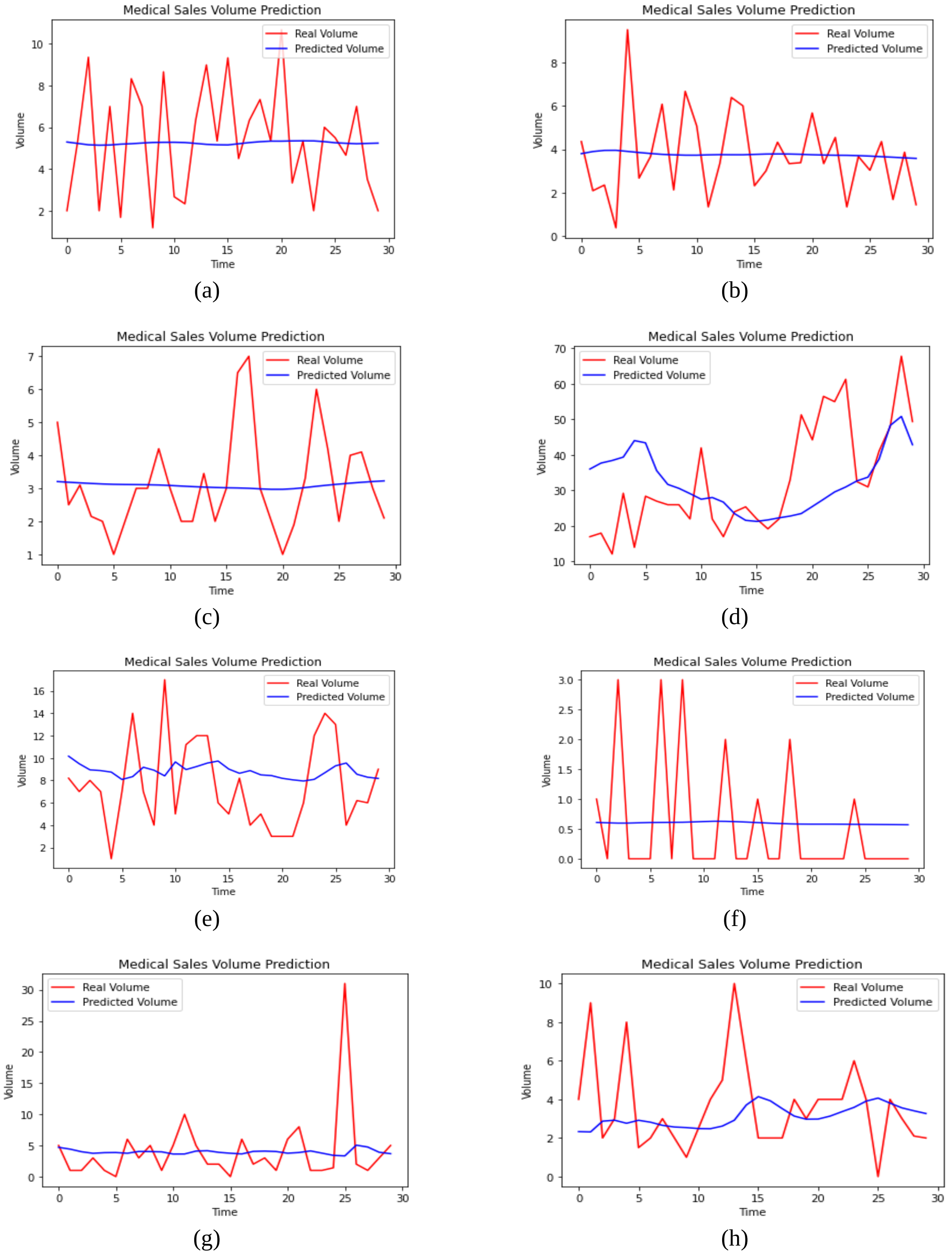

Figure 4. Comparative analysis of predicted outcome vs real outcome for the (a) M01AB, (b) M01AE, (c) N02BA, (d) N02BE, (e) N05B, (f) N05C, (g) R03, and (h) R06 genres

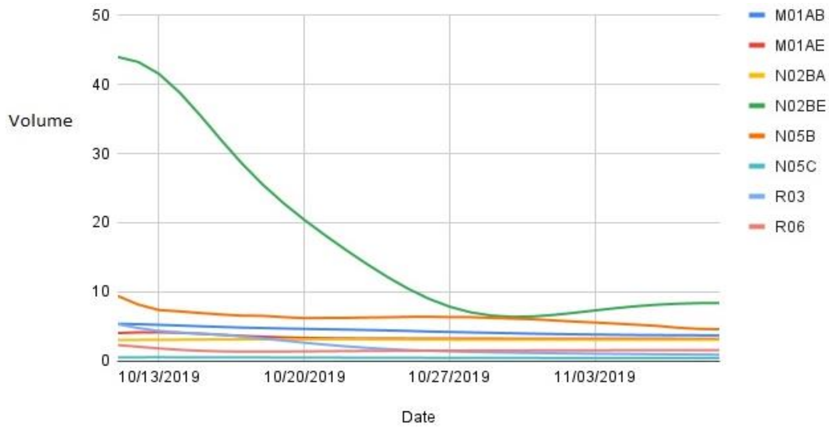

Figure 5. Sales prediction from 11th October, 2019 to 9th November, 2019

4. RESULTS AND DISCUSSION

The analysis of the prediction for one month from 11th October 2019 to 9th November 2019 shows a significant volume of increase in the ATC genre N02BE shown in Figure 4(d). This means there's a high probability of an increase in diseases that are often prescribed to use medicines from N02BE. This genre indicated medicines that contain analgesics and antipyretics, pyrazolones, and anilides. Common medicines in this genre are propacetamol (used in multimodal analgesia therapy to reduce fever and pain during the intraoperative phase). Other medicines are also used to cure several types of fevers and related diseases. This observation leads to the decision that our predicted month has a high possibility of increasing several types of fevers, for instance-dengue, malaria, and chikungunya. Though different medications are prescribed for different types of fevers, people buy generic drugs from pharmacy stores as assumed medication. So, our analysis indicates a possible outbreak of diseases that causes high fever following October 2019. Besides this, another significant increase in the sales of another ATC genre N05B shown in Figure 4(e). This genre indicated medicines that contain psycholeptics drugs, and anxiolytic drugs. These kinds of medicines are generally used for insomnia, anxiety, sleep disorder, and related diseases. These are not severe diseases that could cause outbreaks. But, the increase in these illnesses is not negligible.

5. CONCLUSION

We expect our work to impact several fields of research and development in the future. Our proposed method of using LSTM for disease outbreak prediction might inspire other researchers and encourage researchers to contribute more in this particular field of research. We also expect our work to be efficient and applicable to various fields. The limitation of our research work is that the dataset is inadequate. To predict disease outbreaks over a year or a specific amount of time a dataset of only 6 years is not enough. Dataset collection was a complicated task as financial sales information is confidential and local retail pharmaceutical stores did not want to share them. We plan to extend our research work in the future to predict disease outbreaks of a larger duration of time. We also plan to work with more descriptive genres that will indicate specific disease outbreaks rather than a genre of medicines. Specific genres of medicines can be trained using our proposed model and can predict possible disease outbreaks.

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APPENDIX

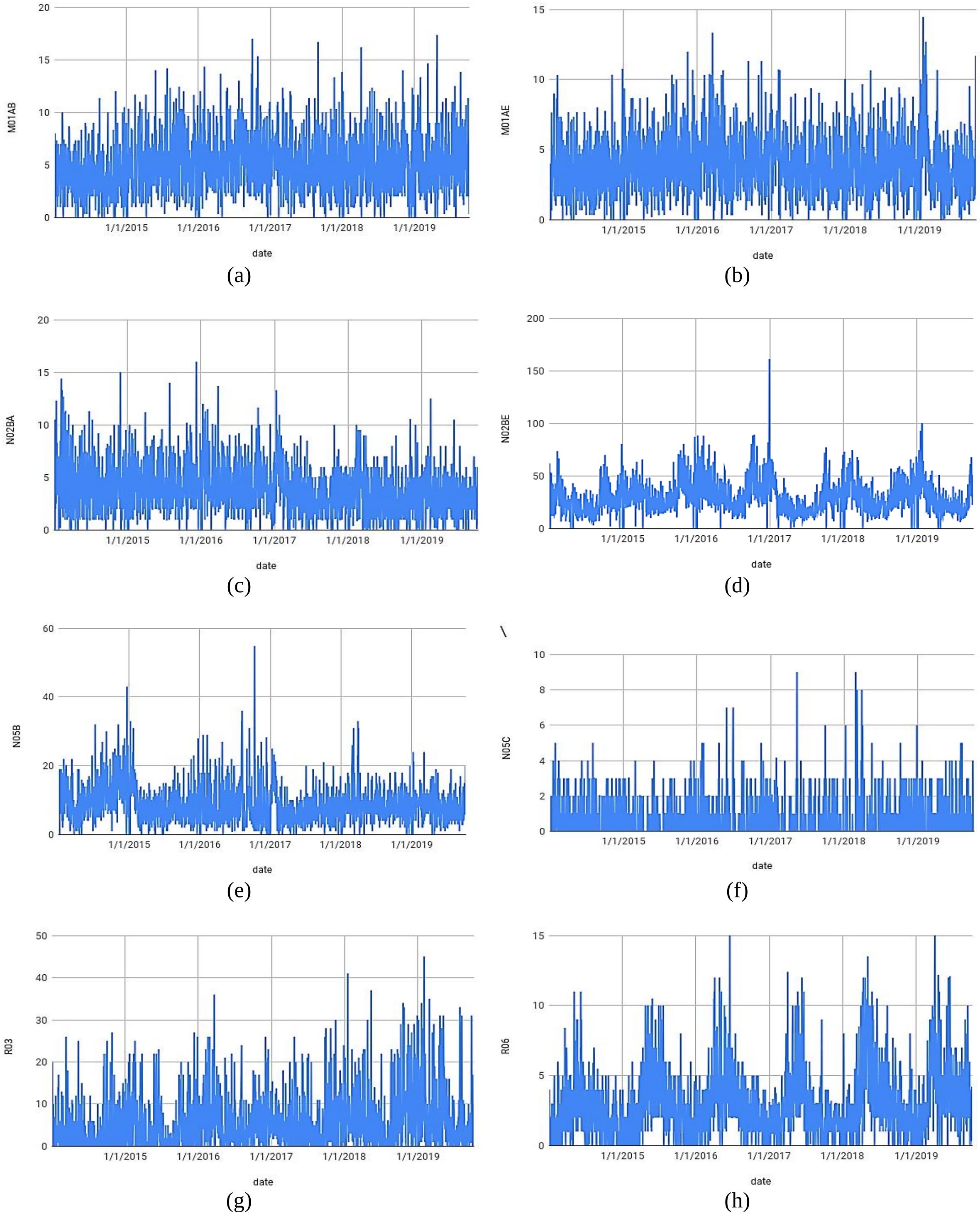

Figure 2. Sales variations of (a) M01AB, (b) M01AE, (c) N02BA, (d) N02BE, (e) N05B, (f) N05C, (g) R03, and (h) R06

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