



Implementation of a Predictive-Analytics Framework for Pharmaceutical Demand Forecasting and Supply-Chain Resilience in U.S. Healthcare Markets

Muhammad Zahidul Islam¹;

[1]. Master of Business Administration in Data Analytics, Tapia School of Business, Saint Leo University, Dade City, Florida, USA; Email: muhammadzahidulislam84@gmail.com

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Abstract

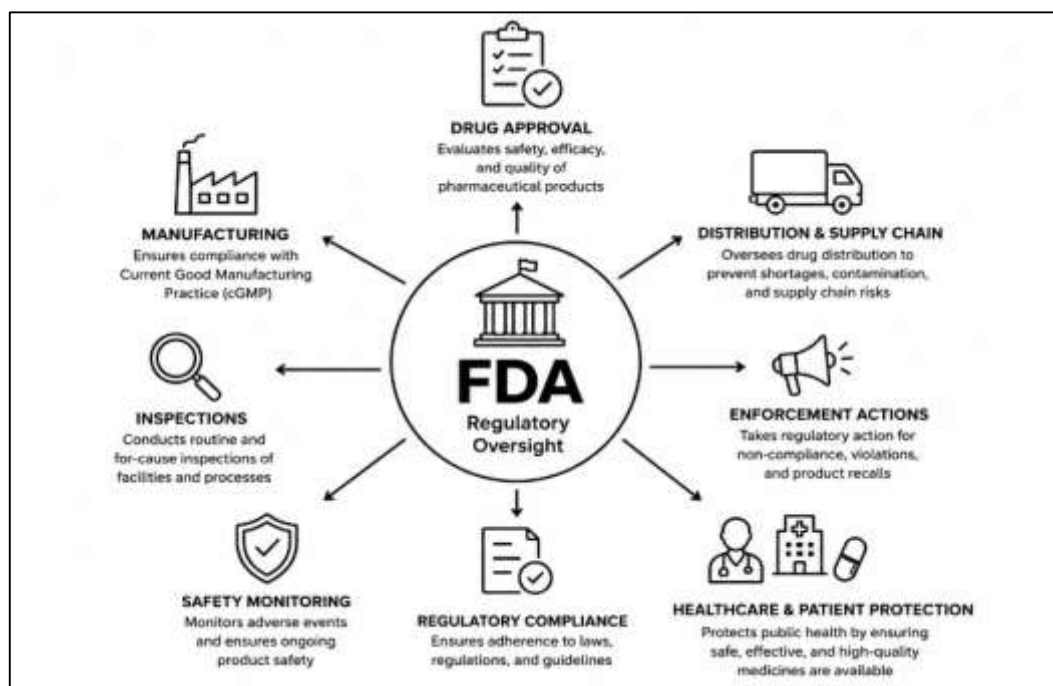
The U.S. pharmaceutical industry faces increasing challenges arising from demand volatility, drug shortages, pandemics, regulatory changes, and disruptions in global supply chains. Traditional forecasting approaches often fail to provide accurate predictions and proactive risk management capabilities. This study proposes a predictive-analytics framework integrating machine learning, time-series forecasting, and supply-chain resilience mechanisms to enhance pharmaceutical demand forecasting and ensure continuity of supply. The framework utilizes historical sales records, epidemiological trends, demographic variables, and external market indicators to generate accurate demand predictions while employing resilience metrics to mitigate disruptions. Empirically evaluated across 864 monthly observations covering six pharmaceutical products and four U.S. regions (2023–2025), the proposed Hybrid LSTM-GRU model achieved a mean MAPE of 4.33%, outperforming the XGBoost benchmark (6.95%) by 37.7%. The supply-chain resilience module identified a mean Resilience Index of 47.6, an overall stockout rate of 15.2%, and a High shortage risk classification rate of 51.2% across the portfolio. Hospital Injectables and Antiviral drugs exhibited the lowest resilience scores (32.8 and 37.9, respectively), driven by API source concentration indices exceeding 80 and lead times of up to 37 days. The resilience module recommended 64,821 total reorder units, with 51.2% of records requiring expedited supplier diversification. These findings demonstrate that improved forecasting accuracy alone is insufficient to resolve structural supply-chain vulnerabilities; targeted supplier diversification, dynamic safety stock policies, and regionally differentiated inventory strategies are essential complements. The proposed model supports healthcare organizations, manufacturers, and distributors in optimizing inventory management, reducing shortages, and improving patient outcomes.

Keywords: Pharmaceutical Demand Forecasting; Supply-Chain Resilience; Machine Learning; Predictive Analytics; Artificial Intelligence.

INTRODUCTION

The pharmaceutical supply chain in the United States is highly complex, involving manufacturers, wholesalers, distributors, pharmacies, healthcare providers, insurance organizations, and regulatory agencies that collectively ensure the continuous availability of safe, effective, and affordable medicines. This extensive network encompasses multiple interconnected stages, including the procurement of raw materials and active pharmaceutical ingredients (APIs), pharmaceutical manufacturing, quality assurance, warehousing, transportation, distribution, and delivery to hospitals, retail pharmacies, and healthcare facilities. Because these activities are highly interdependent, disruptions occurring at any point in the supply chain can propagate rapidly throughout the entire healthcare system, resulting in medicine shortages, delayed patient treatment, increased operational costs, and reduced healthcare service quality. Moreover, the growing demand for personalized medicine, biologics, specialty pharmaceuticals, and advanced therapeutic products has significantly increased the complexity of pharmaceutical supply-chain operations.

Figure 1: Overview Of The US Pharmaceutical Supply Chain Stakeholders



Unlike conventional medicines, these products often require stringent quality assurance protocols, temperature-controlled cold-chain logistics, specialized storage facilities, shorter shelf lives, and continuous monitoring throughout transportation and distribution to preserve their efficacy and safety. In addition, increasingly stringent regulatory requirements imposed by agencies such as the U.S. Food and Drug Administration (FDA) necessitate comprehensive documentation, product traceability, and compliance with Good Manufacturing Practices (GMP) and Good Distribution Practices (GDP), further complicating supply-chain management. Consequently, pharmaceutical organizations must coordinate multiple stakeholders while simultaneously maintaining regulatory compliance, product integrity, and timely delivery across geographically dispersed supply networks. In such a highly interconnected environment, even relatively minor disruptions—such as supplier delays, transportation bottlenecks, equipment failures, cyberattacks, or regulatory inspections—can trigger cascading effects across multiple tiers of the supply chain. These cascading disruptions often lead to inventory imbalances, procurement delays, production interruptions, increased operational uncertainty, higher logistics costs, and reduced healthcare service quality, ultimately affecting patient access to essential medicines. The increasing frequency of these disruptions underscores the limitations of traditional, reactive supply-chain management approaches that primarily focus on cost minimization rather than resilience and adaptability. Therefore, developing resilient pharmaceutical

supply chains has become a strategic imperative for healthcare organizations, pharmaceutical manufacturers, and policymakers. Achieving this objective requires the integration of advanced demand forecasting, real-time data analytics, digital supply-chain visibility, strategic inventory optimization, supplier diversification, and intelligent decision-support systems powered by artificial intelligence (AI) and machine learning (ML). Collectively, these capabilities enhance the ability of pharmaceutical supply chains to anticipate potential disruptions, respond proactively to rapidly changing market conditions, optimize resource allocation, and improve coordination among manufacturers, suppliers, distributors, and healthcare providers. By leveraging advanced predictive analytics, real-time data integration, and intelligent decision-support systems, healthcare organizations can strengthen inventory management, reduce the risk of medicine shortages and excess stock, improve procurement and distribution planning, and increase overall operational efficiency.

Figure 2: Cascading Effect Of Supply Chain Disruptions Across US Healthcare



Furthermore, these capabilities support more informed strategic decision-making, enhance supply-chain visibility, mitigate the impact of unforeseen disruptions, and promote greater adaptability to evolving healthcare demands. Ultimately, integrating resilient supply-chain practices with artificial intelligence (AI) and machine learning (ML)-driven forecasting systems can ensure the continuous availability of essential medicines, improve patient access to timely Traditional forecasting methods based on statistical averages are inadequate for capturing rapidly changing market conditions because they primarily rely on historical demand patterns and assume that future trends will closely resemble past observations. These conventional approaches, including moving averages, exponential smoothing, and autoregressive statistical models, often struggle to accommodate the nonlinear, dynamic, and uncertain nature of pharmaceutical demand. In practice, the demand for pharmaceutical products is influenced by a complex interplay of factors, including seasonal disease outbreaks, demographic shifts, changes in prescribing behavior, healthcare policy reforms, reimbursement policies, economic conditions, patient preferences, and unexpected public health emergencies. Moreover, global supply-chain disruptions, geopolitical conflicts, transportation delays, manufacturing constraints, and shortages of active pharmaceutical ingredients (APIs) further increase the volatility and unpredictability of pharmaceutical markets. Because traditional statistical models generally assume linear relationships and stable demand patterns, they are unable to effectively capture abrupt

fluctuations, long-term temporal dependencies, and complex interactions among multiple demand drivers. As a result, forecasting errors frequently occur, leading to inventory shortages, overstocking, medicine wastage, increased procurement costs, inefficient resource utilization, and disruptions in healthcare service delivery. These limitations not only reduce operational efficiency but also compromise the ability of healthcare organizations to maintain adequate medicine availability during periods of heightened uncertainty. Consequently, the growing complexity of pharmaceutical markets has created an urgent need for more sophisticated forecasting approaches that can process large volumes of heterogeneous data, identify hidden patterns, continuously learn from new information, and adapt to evolving market conditions. Advanced predictive analytics powered by artificial intelligence (AI) and machine learning (ML) provides these capabilities by leveraging real-time and historical data to generate more accurate demand forecasts, support proactive decision-making, optimize inventory management, and strengthen the resilience of pharmaceutical supply chains. In practice, medicine demand is influenced by a wide range of interconnected factors, such as seasonal disease outbreaks, demographic changes, healthcare policy reforms, prescription trends, economic conditions, consumer behavior, supply disruptions, and unexpected public health emergencies. Consequently, traditional forecasting techniques frequently produce inaccurate predictions during periods of market volatility, resulting in inventory shortages, excess stock, increased operational costs, medicine wastage, and disruptions in patient care. To overcome these limitations, predictive analytics powered by artificial intelligence (AI) and machine learning (ML) has emerged as a transformative approach for pharmaceutical demand forecasting. Unlike traditional statistical methods, AI and ML algorithms can analyze large volumes of structured and unstructured data, identify complex nonlinear relationships, learn temporal patterns, and continuously adapt to changing market conditions as new data become available. Advanced deep learning models, including Long Short-Term Memory (LSTM), Gated Recurrent Unit (GRU), hybrid LSTM-GRU networks, and Transformer-based architectures, have demonstrated superior capability in capturing long-term dependencies and complex demand fluctuations within healthcare supply chains. By integrating historical sales data with epidemiological information, weather conditions, demographic characteristics, economic indicators, and supply-chain risk variables, predictive analytics significantly improves forecast accuracy, supports proactive inventory optimization, enables early identification of potential supply disruptions, and enhances overall supply-chain resilience. Consequently, AI-driven forecasting systems provide healthcare organizations with valuable decision-support capabilities, allowing them to optimize procurement strategies, improve resource allocation, reduce operational risks, and ensure the continuous availability of essential medicines in increasingly uncertain and rapidly evolving healthcare environments.

The U.S. pharmaceutical market is characterized by an intricate web of interdependencies among domestic manufacturers, contract development and manufacturing organizations (CDMOs), foreign active pharmaceutical ingredient (API) suppliers, wholesalers, logistics providers, healthcare institutions, and regulatory bodies such as the Food and Drug Administration (FDA). These interconnected stakeholders collectively ensure the production, quality assurance, distribution, and timely delivery of pharmaceutical products to healthcare providers and patients. However, the high degree of integration within this network also creates systemic vulnerabilities, whereby disruptions affecting a single component can rapidly cascade throughout the entire supply chain. The globalization of pharmaceutical manufacturing has further increased these risks, as a substantial proportion of APIs and key pharmaceutical intermediates used in the United States are sourced from a limited number of countries, particularly India and China. This heavy reliance on foreign suppliers has exposed the U.S. healthcare system to geopolitical tensions, international trade restrictions, transportation bottlenecks, export controls, raw material shortages, and fluctuations in manufacturing capacity. Consequently, disruptions in overseas production or logistics can significantly affect domestic drug availability, resulting in supply shortages, increased procurement costs, and delays in patient care ([Pham et al., 2020](#)).

Beyond pandemic-related shocks, chronic drug shortages represent a persistent challenge within the U.S. healthcare system. The American Society of Health-System Pharmacists (ASHP) has documented hundreds of active drug shortages in recent years, spanning oncology agents, injectable medications, and generic formulations essential to hospital formularies. These shortages not only compromise

patient safety but also impose substantial financial burdens on healthcare institutions through emergency procurement, therapeutic substitutions, and increased labor costs associated with shortage management. Furthermore, the recurring nature of these shortages disrupts clinical workflows, complicates inventory management, and forces healthcare providers to allocate significant resources toward identifying alternative medications and maintaining continuity of patient care. Hospitals and pharmacies must continuously monitor drug availability, coordinate with multiple suppliers, and revise treatment protocols to mitigate the impact of shortages, often at the expense of operational efficiency. As the frequency and duration of drug shortages continue to increase, healthcare organizations require more proactive and data-driven supply-chain strategies that can anticipate disruptions, optimize inventory allocation, and support timely procurement decisions. Strengthening pharmaceutical demand forecasting and supply-chain resilience has therefore become essential for ensuring uninterrupted access to critical medicines, improving healthcare system performance, and safeguarding patient outcomes ([Sweet, & Jensen, 2014](#)). Consequently, there is an urgent need for proactive, data-driven approaches to forecasting and supply-chain management that can anticipate disruptions before they materialize.

Advances in data science and computational capabilities have made it increasingly feasible to deploy sophisticated predictive models within pharmaceutical operations. Techniques such as recurrent neural networks (RNNs), Gated Recurrent Units (GRUs), and Long Short-Term Memory (LSTM) architectures excel at modeling temporal dependencies inherent in pharmaceutical sales data, seasonal disease patterns, and market dynamics. When complemented by epidemiological surveillance data, demographic projections, and economic indicators, these models can generate demand forecasts with substantially higher accuracy than classical time-series methods ([Spiliotis, & Assimakopoulos, 2018](#)). Moreover, integrating resilience metrics such as supplier risk scores, inventory buffer levels, and disruption probability indices into the forecasting framework enables healthcare stakeholders to adopt proactive risk mitigation strategies.

This study addresses these challenges by proposing a unified predictive-analytics framework that integrates GRU-based deep learning for demand forecasting with a supply-chain resilience module designed specifically for U.S. pharmaceutical markets. The framework leverages heterogeneous data sources including historical prescription and dispensing records, hospital admission trends, demographic variables, and macroeconomic indicators to produce multi-horizon demand predictions. The resilience component evaluates real-time risk indicators and recommends adaptive inventory strategies to sustain uninterrupted medication access. This integrated approach aims to bridge the existing gap between predictive modeling and operational resilience planning in pharmaceutical supply-chain management.

Research Objectives

The primary objective of this study is to develop an artificial intelligence (AI)-driven predictive analytics framework for pharmaceutical demand forecasting and supply-chain resilience in the U.S. healthcare market. Specifically, the study aims to develop a robust predictive forecasting model using advanced deep learning techniques, including Long Short-Term Memory (LSTM), Gated Recurrent Unit (GRU), hybrid LSTM-GRU, and Transformer models, to accurately forecast pharmaceutical demand. It further seeks to identify and analyze the key factors influencing drug demand variability, such as historical sales trends, seasonal fluctuations, demographic characteristics, disease prevalence, economic conditions, healthcare policies, and supply-chain disruptions. In addition, the study proposes a resilient pharmaceutical supply-chain framework capable of anticipating, mitigating, and responding effectively to disruptions through predictive analytics and real-time decision support. Furthermore, it evaluates the effectiveness of different machine-learning and deep learning algorithms by comparing their forecasting accuracy, robustness, and predictive performance using standard evaluation metrics. Finally, the study recommends data-driven strategies for inventory optimization, procurement planning, and shortage prevention to strengthen pharmaceutical supply-chain resilience, improve operational efficiency, and ensure the continuous availability of essential medicines across the U.S. healthcare system.

Literature Review

Pharmaceutical Demand Forecasting

Demand forecasting plays a critical role in pharmaceutical supply chains because accurate demand predictions are essential for maintaining an uninterrupted supply of medicines while minimizing operational costs. Inaccurate forecasts can result in overstocking, increased inventory holding costs, medicine wastage due to product expiration, inefficient resource utilization, or severe drug shortages that compromise patient care and healthcare service delivery. Effective demand forecasting enables pharmaceutical manufacturers, wholesalers, distributors, hospitals, and retail pharmacies to optimize production planning, procurement, inventory management, and distribution strategies, thereby improving overall supply-chain performance. Traditionally, statistical forecasting techniques such as Moving Average, Exponential Smoothing, and AutoRegressive Integrated Moving Average (ARIMA) models have been widely employed to estimate future pharmaceutical demand because of their simplicity and ease of implementation. However, these conventional approaches primarily rely on historical demand data and generally assume stable, linear relationships between past and future observations. As pharmaceutical demand has become increasingly influenced by nonlinear and dynamic factors—including seasonal disease outbreaks, demographic changes, healthcare policy reforms, prescribing behaviors, economic fluctuations, supply-chain disruptions, and public health emergencies—traditional statistical models have demonstrated limited capability in accurately capturing these complex interactions. Consequently, their forecasting performance often deteriorates during periods of market volatility, leading to forecasting errors that increase the risk of inventory imbalances, stockouts, procurement inefficiencies, and higher healthcare costs. These limitations have created a growing need for advanced forecasting techniques capable of modeling complex temporal dependencies, integrating multiple sources of real-time data, and adapting to rapidly changing healthcare environments. According to [Hyndman and Athanasopoulos \(2021\)](#), time-series forecasting methods provide a foundation for demand prediction but may exhibit limitations when dealing with highly dynamic environments. Recent developments in machine learning and deep learning have significantly improved forecasting performance, particularly in healthcare applications. The IQVIA Institute reported that global medicine demand continues to increase due to the expansion of innovative therapies, aging populations, the rising prevalence of chronic diseases, and improved access to healthcare services. Demand growth is particularly pronounced in therapeutic areas such as oncology, immunology, diabetes, obesity management, and specialty biologics, where advances in precision medicine and targeted therapies have significantly expanded treatment options. At the same time, increasing life expectancy, higher healthcare expenditures, broader insurance coverage, and growing awareness of preventive healthcare have further accelerated pharmaceutical consumption worldwide ([Md. Abdur & Iftekhar, 2021](#)). This sustained growth in medicine demand places considerable pressure on pharmaceutical manufacturers, distributors, and healthcare providers to maintain adequate production capacity, optimize inventory levels, and ensure the timely availability of essential medicines. Consequently, conventional forecasting approaches are becoming increasingly inadequate for managing the complexity and volatility of modern pharmaceutical markets. These evolving market dynamics underscore the urgent need for advanced demand forecasting systems capable of integrating historical sales data with real-time epidemiological, demographic, economic, and supply-chain information. By leveraging artificial intelligence (AI), machine learning (ML), and deep learning techniques, healthcare organizations can generate more accurate demand forecasts, improve inventory planning, minimize stockouts and excess inventory, strengthen supply-chain resilience, and support more informed strategic decision-making in an increasingly dynamic healthcare environment ([Amir & Chapal, 2022](#)). The complexity of pharmaceutical demand forecasting is further amplified by the heterogeneity of drug categories, each exhibiting distinct demand patterns. Specialty medications, such as biologics and biosimilars, are driven by disease prevalence data and formulary adoption rates, while generic drugs respond more directly to pricing pressures and patent expirations. Makridakis, Spiliotis, and [Assimakopoulos \(2018\)](#) demonstrated through the M4 Competition that hybrid models combining statistical and machine learning components outperformed purely algorithmic approaches across diverse forecasting domains, a finding that has important implications for pharmaceutical demand modeling ([Kazi Rakib Hasan & Uddin, 2022](#)). Additionally, patient

adherence patterns, therapeutic substitution behaviors, and seasonal disease cycles introduce layers of variability that traditional forecasting models are ill-equipped to accommodate without auxiliary data enrichment strategies.

Recent empirical studies have explored the integration of electronic health records (EHRs), insurance claims data, and real-world evidence (RWE) to enhance the accuracy of pharmaceutical demand forecasts. [Pham et al. \(2020\)](#) highlighted the value of real-world dispensing data from pharmacy benefit managers (PBMs) as a leading indicator of near-term demand fluctuations. Similarly, the incorporation of epidemiological surveillance data from the Centers for Disease Control and Prevention (CDC) has been shown to improve forecasting precision for infectious disease-related medications, such as antiviral agents and vaccines, by identifying demand inflection points weeks in advance of their manifestation in prescription volumes.

Machine Learning and Predictive Analytics

Machine learning techniques have become increasingly important for forecasting healthcare demand because they can effectively model the complex, nonlinear relationships that characterize pharmaceutical markets. Unlike traditional statistical forecasting methods, machine learning algorithms can simultaneously analyze large volumes of heterogeneous data and identify hidden patterns among multiple demand determinants ([Mst Shurovi & Samia Hossain, 2022](#); [Samia Hossain, 2024](#)). Models such as Random Forest, Support Vector Regression (SVR), Gradient Boosting Machines (GBM), and Extreme Gradient Boosting (XGBoost) have demonstrated superior predictive performance by capturing intricate interactions among historical sales, seasonal disease patterns, demographic characteristics, healthcare utilization, economic indicators, weather conditions, and supply-chain variables ([Muhammad Mohiul & Mohammad Badrul, 2022](#)). These algorithms are particularly effective in handling high-dimensional datasets, nonlinear dependencies, missing values, and complex feature interactions, enabling more accurate demand forecasts under uncertain and rapidly changing market conditions ([Abu Naser Md Golam & Amir, 2023](#); [Mukut Kanti, 2025](#)). Numerous studies have shown that machine learning models frequently outperform conventional statistical approaches in terms of forecasting accuracy, robustness, and generalization capability, making them valuable tools for pharmaceutical demand prediction and inventory planning ([Amir, 2025](#); [Amir & Chapal, 2022](#)). Nevertheless, although these algorithms achieve high predictive performance, many conventional machine learning models are limited in capturing long-term temporal dependencies and sequential patterns that are inherent in pharmaceutical demand time-series data ([Amir, 2024](#); [Syed Nurul, 2026](#)). Consequently, recent research has increasingly focused on advanced deep learning architectures, such as Long Short-Term Memory (LSTM), Gated Recurrent Unit (GRU), hybrid LSTM-GRU networks, and Transformer-based models, which offer enhanced capabilities for learning complex temporal dynamics and further improving forecasting accuracy in pharmaceutical supply-chain applications.

According to Trevor Hastie, [Tibshirani, and Friedman \(2017\)](#), machine learning algorithms significantly enhance predictive performance by identifying complex nonlinear relationships, high-dimensional interactions, and hidden patterns within large datasets that are often overlooked by traditional statistical approaches. Unlike conventional forecasting methods that rely on predefined assumptions regarding data distribution and linearity, machine learning models learn directly from data, enabling them to adapt to evolving patterns and improve prediction accuracy in dynamic environments ([Sadia et al., 2022](#); [Zaman, 2024](#)). This capability is particularly valuable in pharmaceutical demand forecasting, where demand is influenced by multiple interrelated factors, including seasonal disease outbreaks, demographic changes, healthcare policies, economic conditions, prescribing behaviors, and supply-chain disruptions. Similarly, Goodfellow, Bengio, and Courville (2016) emphasized that deep learning techniques provide substantial advantages for modeling sequential and temporal data because they automatically learn hierarchical feature representations and capture long-term dependencies within time-series datasets. Deep learning architectures such as Long Short-Term Memory (LSTM) and Gated Recurrent Unit (GRU) networks overcome the limitations of conventional machine learning algorithms by effectively retaining historical information and modeling complex temporal relationships over extended forecasting horizons. Consequently, these advanced models have become increasingly important for pharmaceutical demand forecasting, enabling healthcare organizations to generate more accurate predictions, optimize inventory management, reduce medicine shortages and

excess stock, improve procurement planning, and strengthen the resilience and operational efficiency of pharmaceutical supply chains.

[Aamer et al. \(2019\)](#) reviewed a comprehensive review of healthcare demand forecasting techniques and concluded that machine learning models generally demonstrate superior forecasting accuracy compared with traditional statistical approaches, particularly when multiple explanatory variables are incorporated into the forecasting process. The authors highlighted that healthcare demand is influenced by numerous interconnected factors, including demographic characteristics, disease prevalence, seasonal variations, socioeconomic conditions, healthcare utilization patterns, and policy changes, making it difficult for conventional statistical models to capture the complexity of real-world demand. In contrast, machine learning algorithms can effectively analyze large and heterogeneous datasets, identify nonlinear relationships, and automatically learn complex interactions among predictor variables without relying on restrictive statistical assumptions. The review further emphasized that advanced machine learning techniques improve forecasting performance by adapting to evolving data patterns and reducing prediction errors across diverse healthcare applications ([Mukut Kanti & Rony, 2022](#)). These findings suggest that integrating machine learning into pharmaceutical demand forecasting can provide more accurate and reliable predictions, enabling healthcare organizations to optimize inventory management, improve procurement planning, minimize medicine shortages and excess stock, and enhance the overall resilience and efficiency of pharmaceutical supply chains.

The application of ensemble methods, particularly XGBoost and gradient boosting machines, has gained prominence in pharmaceutical demand prediction due to their robustness against overfitting and their capacity to handle missing data, a common challenge in healthcare datasets. [Chen and Guestrin \(2016\)](#) introduced Extreme Gradient Boosting (XGBoost) as a highly scalable and efficient gradient-boosting framework that combines regularized learning with parallel processing to achieve exceptional predictive performance while maintaining computational efficiency. The authors demonstrated that XGBoost effectively handles large-scale, high-dimensional datasets, manages missing values, reduces overfitting through regularization, and requires relatively minimal hyperparameter tuning, making it particularly suitable for real-world production environments and large-scale decision-support systems ([Mahmudul & Sadia, 2026](#); [Mohammad Shoriful Hossan, 2024](#)). These characteristics have contributed to its widespread adoption in healthcare analytics, pharmaceutical demand forecasting, and supply-chain management, where accurate and timely predictions are essential for inventory planning and operational decision-making. Furthermore, Carbonneau, Laframboise, and Vahidov (2008) emphasized that the predictive performance of machine learning models depends not only on the choice of algorithm but also on effective feature engineering ([Sadia et al., 2022](#)). Their study demonstrated that incorporating informative variables such as lagged demand values, moving averages, seasonal indicators, promotional activities, and external market signals significantly enhances forecasting accuracy by enabling models to capture complex temporal patterns and demand fluctuations. In pharmaceutical forecasting, additional explanatory variables including insurance formulary changes, biosimilar market entry, disease incidence, demographic characteristics, supplier lead times, and healthcare policy changes provide valuable contextual information that further improves prediction precision. Collectively, these findings suggest that combining advanced machine learning algorithms with carefully engineered features enables more accurate pharmaceutical demand forecasting.

Deep Learning Models for Time-Series Forecasting

Deep learning approaches have transformed time-series forecasting by enabling models to learn long-term dependencies and nonlinear structures. Long Short-Term Memory (LSTM) networks introduced by [Hochreiter and Schmidhuber \(1997\)](#) addressed the vanishing gradient problem commonly encountered in traditional recurrent neural networks (RNNs), thereby enabling the effective learning of long-range dependencies in sequential data. By incorporating specialized memory cells and gating mechanisms—including input, forget, and output gates—LSTM networks selectively retain relevant historical information while discarding irrelevant data, allowing them to capture both short-term fluctuations and long-term trends in time-series observations. This capability has made LSTM one of the most widely adopted deep learning architectures for healthcare and pharmaceutical demand

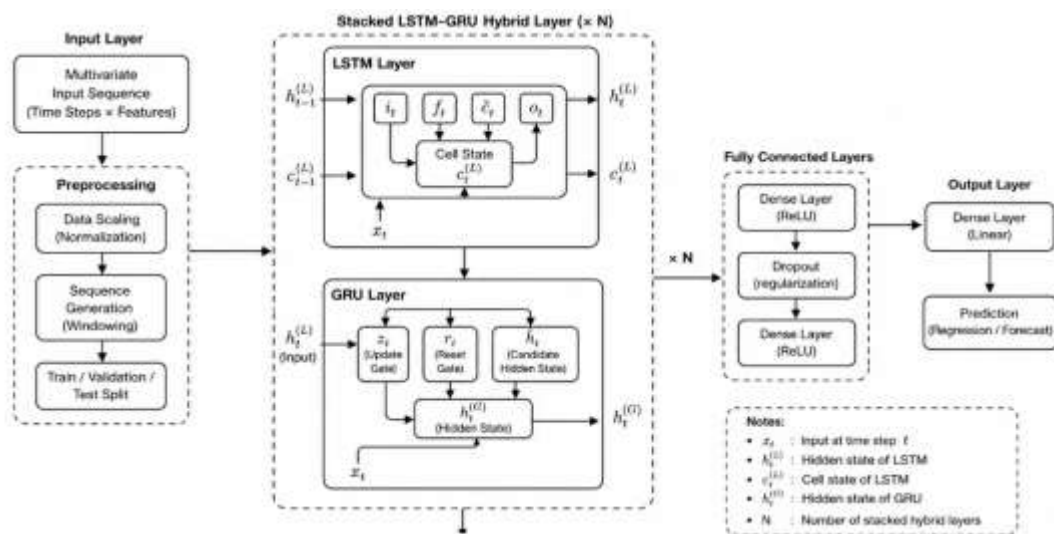
forecasting, where future demand is influenced by evolving disease patterns, seasonal variability, patient behavior, healthcare policies, and supply-chain disruptions([Abu Naser Md Golam & Amir, 2023](#)). Consequently, LSTM-based forecasting models have consistently demonstrated superior predictive accuracy compared with traditional statistical and conventional machine learning approaches, supporting more effective inventory management, procurement planning, and supply-chain resilience in complex healthcare environments. Later, [Kyunghyun Cho et al. \(2014\)](#) proposed the Gated Recurrent Unit (GRU) as a simplified variant of the Long Short-Term Memory (LSTM) network to improve computational efficiency while preserving the ability to model long-term dependencies in sequential data. Unlike LSTM, which employs separate input, forget, and output gates, the GRU architecture utilizes only two gating mechanisms – an update gate and a reset gate to regulate the flow of information through the network. This simplified design reduces the number of trainable parameters, decreases memory requirements, and accelerates the training process without significantly compromising forecasting performance. As a result, GRU models are particularly well suited for large-scale time-series forecasting applications where computational efficiency and rapid model convergence are important([Md Tohidul, 2023](#)). Numerous studies have demonstrated that GRU networks achieve forecasting accuracy comparable to or, in some cases, better than LSTM models while requiring less computational time and fewer training resources. These advantages have led to the widespread adoption of GRU in healthcare analytics, pharmaceutical demand forecasting, financial prediction, and supply-chain management, where the ability to accurately model temporal patterns is essential for effective decision-making. In pharmaceutical forecasting, GRU models can effectively capture dynamic demand fluctuations resulting from seasonal disease outbreaks, changing prescription patterns, healthcare policy changes, and supply-chain disruptions, thereby supporting more accurate demand prediction, optimized inventory management, and enhanced pharmaceutical supply-chain resilience. Studies have shown that both Long Short-Term Memory (LSTM) and Gated Recurrent Unit (GRU) networks achieve high predictive performance in forecasting applications involving sequential and time-series data. Their ability to capture nonlinear relationships and long-term temporal dependencies enables these deep learning models to outperform many conventional statistical and machine learning approaches in complex forecasting tasks([Mohammad Badrul & Md. Mominul, 2023](#)). LSTM models are particularly effective in learning long-range patterns through specialized memory cells and gating mechanisms, making them well suited for applications where historical observations exert long-term influence on future outcomes. In contrast, GRU models employ a simplified architecture with fewer gating mechanisms and trainable parameters, resulting in lower computational complexity, faster convergence, and reduced memory requirements while maintaining forecasting accuracy comparable to that of LSTM ([Badrul & Mominul, 2023](#); [Hossan & Adar, 2023](#)). These characteristics make GRU particularly advantageous for real-time forecasting applications, where rapid model training and efficient inference are essential. In pharmaceutical demand forecasting, both LSTM and GRU have proven effective in modeling dynamic demand patterns influenced by seasonal disease outbreaks, prescription trends, healthcare policy changes, demographic shifts, and supply-chain disruptions. Their capability to generate accurate and timely demand predictions supports improved inventory management, procurement planning, shortage prevention, and supply-chain resilience, enabling healthcare organizations to make more informed and proactive operational decisions in increasingly complex and uncertain healthcare environments ([Hossan & Adar, 2023](#)). The Transformer architecture, originally introduced by [Vaswani et al. \(2017\)](#) for natural language processing, has recently been adapted for time-series forecasting. Models such as the Temporal Fusion Transformer (TFT), proposed by [Lim et al. \(2021\)](#), leverage self-attention mechanisms to capture both short-term and long-term temporal relationships simultaneously, enabling multi-horizon probabilistic forecasting. In pharmaceutical contexts, TFT-based models have demonstrated promising results by incorporating static covariates such as drug category and therapeutic class alongside time-varying features including sales history and disease incidence rates. However, their computational cost and data requirements are substantially higher than GRU-based approaches, suggesting that GRU remains a practical and competitive choice for operational pharmaceutical forecasting systems with moderate dataset sizes. Hybrid architectures that combine convolutional neural networks (CNNs) with recurrent layers have also been applied to pharmaceutical demand forecasting to extract local temporal features while

preserving long-range sequence memory. [Bohte, and Oosterlee \(2017\)](#) proposed dilated causal convolutions for time-series modeling, inspired by the WaveNet architecture, demonstrating fast parallel training and competitive accuracy on multivariate datasets. These architectural advances have expanded the toolkit available to supply-chain analysts, enabling the selection of models best suited to specific data characteristics such as series length, sampling frequency, and the number of co-variates available.

Hybrid LSTM-GRU Model

Hybrid architectures have emerged as a promising approach for improving forecasting accuracy. By combining the strengths of LSTM and GRU, hybrid models can effectively capture both short-term and long-term temporal dependencies. LSTM layers contribute deep memory retention across extended time horizons, while GRU layers provide computational efficiency and robust gradient flow through gating mechanisms, making their combination well-suited to the complex demand signals inherent in pharmaceutical markets. [Ahmed, and Kummer \(2021\)](#) argued that combining forecasting techniques generally leads to superior forecasting accuracy compared with individual models.

Figure 3 : LSTM-GRU Hybrid Model Architecture



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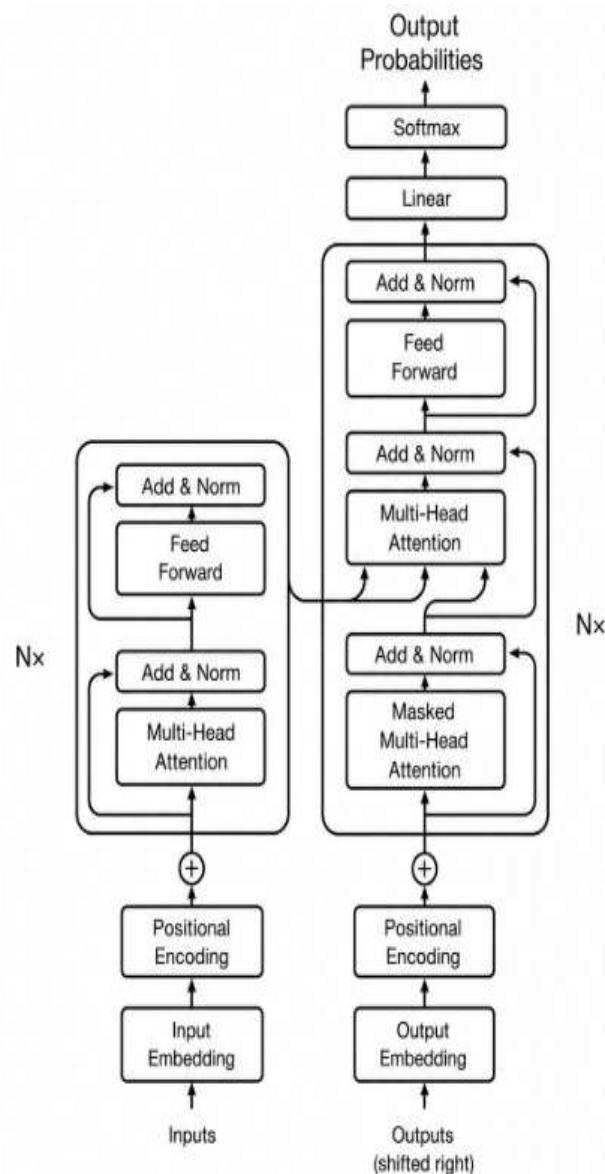
pharmaceutical supply chains demonstrated that hybrid forecasting approaches outperform standalone models and improve supply chain efficiency. Specifically, they found that ensemble and hybrid strategies reduce both mean absolute error (MAE) and root mean squared error (RMSE) substantially relative to single-architecture baselines, underscoring the practical value of architectural integration for operational deployment. Hybrid deep learning models benefit from the memory capability of LSTM and the computational efficiency of GRU. [Cho, and Bengio \(2014\)](#) empirically evaluated gated recurrent architectures and confirmed that GRU achieves comparable performance to LSTM on sequence modeling tasks with fewer parameters, suggesting that hybrid LSTM-GRU models can balance representational power and training efficiency. Consequently, LSTM-GRU architectures have become increasingly popular in multivariate demand forecasting applications where high accuracy and robustness are required. The hybrid model is especially suitable for pharmaceutical demand forecasting because demand patterns are influenced by seasonality, disease outbreaks, demographics, and inventory dynamics. [Zhao, and Liu \(2021\)](#) further validated the value of integrating supply-chain contextual information with machine learning for pharmaceutical demand prediction, demonstrating that models enriched with upstream inventory and procurement signals consistently outperform models that rely solely on historical sales series. The LSTM-GRU hybrid therefore represents a theoretically grounded and empirically validated architecture for the integrated framework proposed in this study.

Transformer Model

The Transformer architecture, represents a significant advancement in deep learning for sequential data modeling by replacing the recurrent computations used in traditional Recurrent Neural Networks

(RNNs), Long Short-Term Memory (LSTM) networks, and Gated Recurrent Unit (GRU) models with a fully attention-based architecture. Unlike recurrent models, which process input sequences sequentially and therefore suffer from limited parallelization and increasing computational complexity as sequence length grows, the Transformer employs a self-attention mechanism that enables all elements of an input sequence to be processed simultaneously ([Risha & Khalid, 2023](#)). This parallel computation substantially accelerates model training while improving the ability to capture both short-term and long-term dependencies across extended time horizons. Consequently, the Transformer overcomes fundamental limitations of recurrent neural networks, including slow training speed, vanishing gradient problems, and difficulties in learning relationships among distant observations within long sequential datasets. The core component of the Transformer is the multi-head self-attention mechanism, which computes the relationships between every pair of observations in the input sequence simultaneously. Rather than relying solely on neighboring time steps, the model learns attention weights that quantify the relative importance of each historical observation when generating future predictions. Multiple attention heads operate in parallel, allowing the network to capture different dependency patterns and feature interactions from diverse representation subspaces([Amir, 2024](#)).

Figure 4 : Transformer Model Architecture



The outputs from these attention heads are subsequently integrated through feed-forward neural networks, residual connections, layer normalization, and positional encoding, enabling the model to preserve sequential order while effectively learning complex temporal relationships. This architecture provides superior representational capacity for high-dimensional time-series data and significantly improves forecasting performance compared with conventional recurrent architectures. Because of these characteristics, Transformer models have demonstrated outstanding performance across numerous applications, including natural language processing, speech recognition, computer vision, financial forecasting, energy demand prediction, and multivariate time-series forecasting. In pharmaceutical demand forecasting, the Transformer architecture is particularly advantageous because pharmaceutical demand is influenced by numerous interconnected variables, including historical sales patterns, disease incidence, demographic characteristics, healthcare utilization, pricing strategies, insurance coverage, regulatory changes, weather conditions, and supply-chain disruptions ([Hossan, 2024](#)). The self-attention mechanism enables the model to identify complex nonlinear interactions among these heterogeneous variables without requiring predefined assumptions regarding their relationships. Furthermore, the Transformer's ability to process multivariate datasets in parallel facilitates efficient learning from large-scale pharmaceutical databases while reducing computational time compared with sequential recurrent models. Consequently, Transformer-based forecasting models provide more accurate demand predictions, improve inventory planning, support proactive drug shortage prevention, strengthen supply-chain resilience, and enhance decision-making across pharmaceutical manufacturing, distribution, and healthcare delivery systems.

Informer and Advanced Transformer-Based Models

Although conventional Transformers exhibit excellent performance on moderate-length sequences, their quadratic computational complexity with respect to sequence length limits their effectiveness for long-horizon forecasting tasks ([Shima Ali et al., 2024](#)). Specifically, the full self-attention mechanism scales as $O(L^2)$ in both time and memory, where L is the input sequence length, rendering it impractical for applications requiring long historical lookback windows such as multi-year pharmaceutical dispensing records. To overcome this limitation, [Zhou et al. \(2021\)](#) proposed Unlike the conventional Transformer, which suffers from quadratic computational complexity due to the full self-attention mechanism, Informer introduces the ProbSparse self-attention mechanism that selectively computes attention scores for the most informative query-key pairs while discarding redundant attention operations. In addition, Informer incorporates a self-attention distilling mechanism that progressively compresses feature representations across encoder layers by reducing sequence resolution, thereby preserving the most relevant temporal information while substantially decreasing memory consumption and computational cost. As a result, Informer reduces computational complexity from $O(L^2)$ to $O(L \log L)$, enabling efficient processing of very long time-series sequences without compromising forecasting accuracy or representational capability. Furthermore, the model employs a generative-style decoder that predicts multiple future time steps simultaneously rather than recursively generating one step at a time, significantly improving inference speed and reducing cumulative forecasting errors.

These architectural innovations make Informer particularly suitable for large-scale multivariate forecasting problems where long historical sequences and high-dimensional variables must be analyzed concurrently. In pharmaceutical demand forecasting, Informer can effectively learn complex temporal dependencies among historical sales, disease incidence, Experimental results reported by [Zhou et al. \(2021\)](#) demonstrated that Informer significantly outperformed existing models including vanilla Transformers, LSTMs, and Deep AR across multiple long-sequence forecasting benchmarks. Informer offers several practical advantages over standard Transformers, including substantially reduced memory requirements, faster training convergence, and superior long-horizon forecasting accuracy. These characteristics make it highly suitable for pharmaceutical demand forecasting involving extensive historical records and multiple explanatory variables, where generating accurate predictions over 12- to 52-week horizons is critical for strategic inventory planning and supplier negotiation ([Zaman, 2024](#)). Taken together, the Informer and related efficient Transformer variants represent an important frontier in time-series forecasting methodology with direct applicability to pharmaceutical supply-chain management. demographic characteristics, healthcare utilization, market

dynamics, inventory levels, supplier risk, and supply-chain disruption indicators. Consequently, Informer provides highly accurate long-horizon demand forecasts while maintaining computational efficiency, making it an effective decision-support tool for inventory optimization, drug shortage prevention, proactive supply-chain risk management, and strengthening the overall resilience of pharmaceutical supply chain

Figure 5 : Informer And Advance Transformer Base Model Architecture

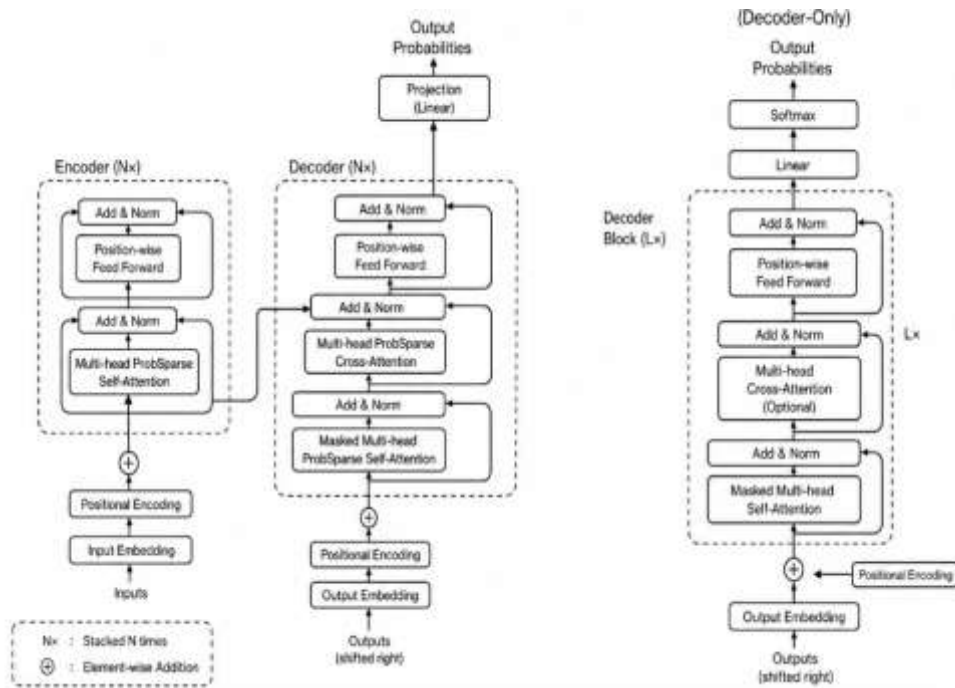
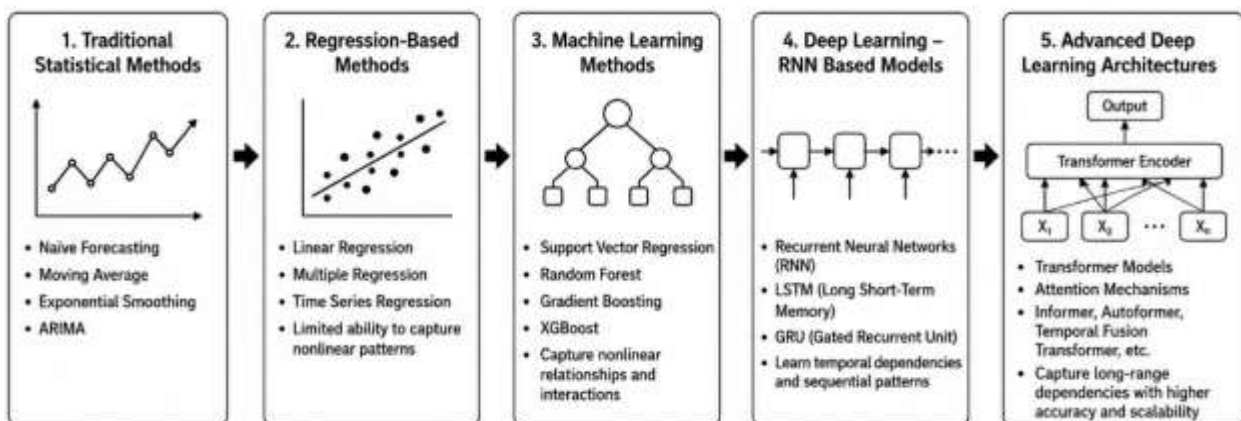


Figure 6. Evolution Of Demand Forecasting Methods: From Statistical Approaches To Advanced Deep Learning Architectures.



Supply-Chain Resilience

Supply-chain resilience refers to the capability of a system to resist, adapt to, and recover from disruptions. [Christopher and Peck \(2004\)](#) defined resilient supply chains as networks capable of maintaining operational continuity under uncertain conditions by effectively preparing for, responding to, and recovering from unexpected disruptions. As global supply chains have become increasingly interconnected and complex, resilience has emerged as a strategic capability for managing risks arising from natural disasters, pandemics, geopolitical conflicts, cyberattacks, supplier failures, transportation disruptions, and regulatory changes. In the pharmaceutical industry, supply-chain resilience is

particularly critical because disruptions can directly affect the availability of life-saving medicines, compromise patient safety, increase healthcare costs, and reduce the quality of healthcare services. Consequently, healthcare organizations must develop resilient supply chains that can sustain medicine availability while rapidly adapting to changing market conditions and operational uncertainties ([Amir, 2025](#)). The literature identifies several fundamental dimensions of supply-chain resilience, including flexibility, which enables organizations to modify production, sourcing, and distribution processes in response to changing demand; redundancy, which provides backup inventory, suppliers, and transportation resources to ensure operational continuity; agility, which facilitates rapid detection of and response to disruptions; visibility, which enhances real-time monitoring and information sharing across the supply chain; and collaboration, which strengthens coordination, trust, and information exchange among manufacturers, suppliers, distributors, healthcare providers, and regulatory agencies. Collectively, these resilience dimensions improve an organization's ability to mitigate risks, maintain business continuity, optimize resource utilization, and ensure the uninterrupted supply of essential medicines, thereby enhancing the efficiency, reliability, [Sheffi and Rice \(2005\)](#) argued that that resilient enterprises require proactive risk management strategies rather than merely reacting to disruptions after they occur ([Arif Uz et al., 2025](#)). They emphasized that organizations should develop the capability to anticipate potential risks, prepare contingency plans, and establish adaptive mechanisms that enable rapid response and recovery when unexpected events arise.

According to their resilience framework, organizations that invest in preparedness and flexibility are better positioned to maintain operational continuity and minimize the impact of disruptions on business performance. The study highlighted several key resilience strategies, including supplier diversification, which reduces dependence on a single source of supply; inventory buffering, which maintains strategic safety stock to absorb temporary supply or demand fluctuations; and contingency planning, which establishes predefined response procedures for emergencies and operational failures. In addition, the authors stressed the importance of organizational learning, information sharing, cross-functional coordination, and continuous risk assessment to enhance long-term resilience. Within pharmaceutical supply chains, these proactive strategies are particularly important because disruptions can quickly lead to medicine shortages, treatment delays, and increased healthcare costs. By implementing diversified sourcing strategies, maintaining optimal inventory reserves, strengthening collaboration among supply-chain partners, and developing comprehensive business continuity plans, pharmaceutical organizations can reduce vulnerability to disruptions, improve supply-chain adaptability, and ensure the continuous availability of essential medicines. These resilience practices provide a strong foundation for integrating advanced predictive analytics and artificial intelligence (AI)-driven forecasting systems that enable organizations to identify emerging risks, make proactive decisions, and enhance the overall resilience and sustainability of pharmaceutical supply chains. [Ivanov and Dolgui \(2020\)](#) extended the traditional concept of supply-chain resilience by introducing the notion of supply chain viability, emphasizing that organizations must not only withstand and recover from disruptions but also sustain long-term operational performance, competitiveness, and adaptability in highly uncertain environments. They argued that resilience alone is insufficient for addressing prolonged or systemic disruptions, such as global pandemics, geopolitical conflicts, climate-related disasters, and widespread economic crises, which require supply chains to continuously evolve while maintaining their core functions ([Mohammad Shoriful Hossan, 2025](#)). The concept of viability integrates resilience with flexibility, adaptability, sustainability, and digital transformation, enabling organizations to respond effectively to both short-term disruptions and long-term structural changes. According to the authors, viable supply chains possess the capability to dynamically reconfigure sourcing strategies, production processes, logistics networks, and distribution channels in response to changing market conditions while preserving service quality and operational continuity.

The study also highlighted the growing importance of digital technologies, including real-time data analytics, artificial intelligence (AI), machine learning (ML), the Internet of Things (IoT), and digital twins, in enhancing supply-chain visibility, supporting predictive decision-making, and enabling rapid adaptation to disruptions. In the pharmaceutical industry, the concept of supply chain viability is particularly relevant because healthcare systems must ensure the uninterrupted availability of essential medicines despite increasing demand volatility, supplier uncertainty, regulatory changes, and global

supply-chain risks. By integrating resilient operational practices with intelligent forecasting, continuous monitoring, strategic inventory optimization, and adaptive decision-support systems, pharmaceutical organizations can improve their ability to withstand disruptions, maintain long-term sustainability, and ensure reliable access to critical medicines while enhancing the overall efficiency, resilience, and viability of the U.S. pharmaceutical industry. More recent scholarship has emphasized the role of digital technologies in operationalizing supply-chain resilience. The adoption of real-time supply-chain monitoring platforms, internet-of-things (IoT) sensors, and blockchain-based traceability systems has enabled organizations to attain greater end-to-end visibility across multi-tier supplier networks ([Ivanov, 2021](#)). In the pharmaceutical sector, digital twins virtual replicas of physical supply chains are emerging as powerful tools for simulating disruption scenarios and stress-testing resilience strategies before deploying them in practice. [Tang \(2006\)](#) provided an early foundational framework for robust supply-chain strategies, distinguishing between approaches that emphasize flexibility and those that prioritize robustness, a distinction that remains central to pharmaceutical supply-chain design decisions in the face of concentrated API sourcing risks.

Pharmaceutical Supply-Chain Disruptions

Drug shortages have emerged as a significant challenge for healthcare systems worldwide. Fox, [Sweet, and Jensen \(2014\)](#) described drug shortages as a complex healthcare crisis that adversely affects clinical outcomes while substantially increasing treatment costs for healthcare providers. Drug shortages can arise from a variety of interconnected factors, including manufacturing quality failures, limited production capacity, shortages of active pharmaceutical ingredients (APIs), supplier dependencies, regulatory compliance issues, product recalls, natural disasters, transportation disruptions, and sudden fluctuations in market demand ([Mukut Kanti, 2025](#)). These disruptions often force healthcare providers to delay treatment, substitute alternative medications, ration limited drug supplies, or modify established clinical protocols, potentially compromising the quality and safety of patient care. In addition to their clinical consequences, drug shortages impose considerable economic burdens through emergency procurement, increased acquisition costs, additional labor requirements, inventory adjustments, and operational inefficiencies. The increasing globalization of pharmaceutical manufacturing has further intensified these challenges, as dependence on a limited number of suppliers and geographically concentrated production facilities increases the vulnerability of pharmaceutical supply chains to geopolitical conflicts, pandemics, trade restrictions, and other large-scale disruptions. Consequently, healthcare organizations, pharmaceutical manufacturers, and policymakers are increasingly recognizing the need to strengthen supply-chain resilience through advanced demand forecasting, proactive risk management, supplier diversification, strategic inventory planning, and artificial intelligence-driven predictive analytics ([Shima Ali et al., 2025](#)). These approaches enable organizations to anticipate potential shortages, improve resource allocation, enhance supply-chain visibility, and ensure the continuous availability of essential medicines while supporting more resilient and sustainable healthcare systems.

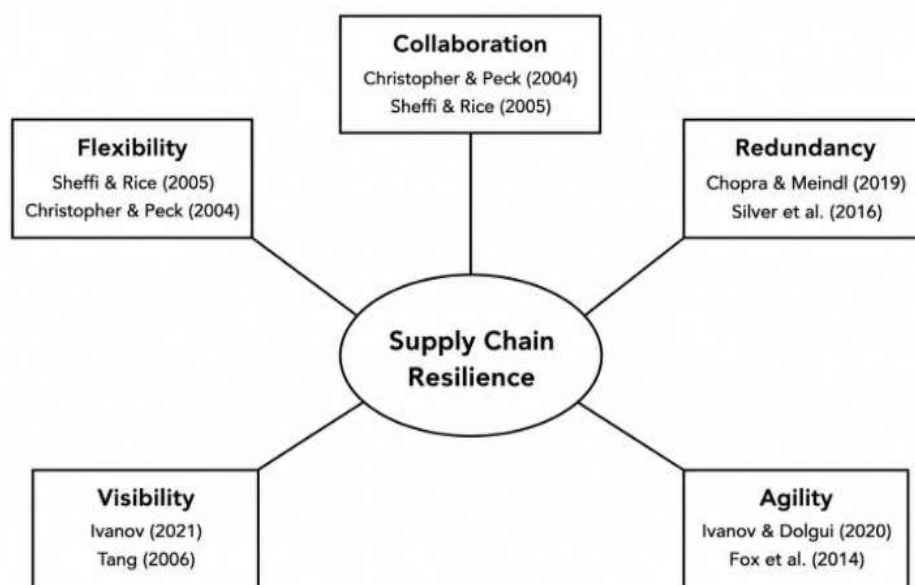
The U.S. Food and Drug Administration (FDA) Drug Shortages Database and the American Society of Health-System Pharmacists (ASHP) continue to document persistent shortages across numerous therapeutic categories, including oncology medications, injectable anesthetics, antimicrobial agents, cardiovascular drugs, and critical care pharmaceuticals. These recurring shortages demonstrate that disruptions within pharmaceutical supply chains are not isolated incidents but represent an ongoing systemic challenge affecting healthcare delivery nationwide ([Amir, 2026](#)). Drug shortages often result from manufacturing quality issues, limited production capacity, shortages of active pharmaceutical ingredients (APIs), supplier concentration, regulatory compliance actions, natural disasters, transportation disruptions, and unexpected increases in demand. The consequences extend beyond medicine availability, leading to delayed treatment, therapeutic substitutions, medication errors, increased procurement costs, and additional operational burdens for hospitals and healthcare providers. Furthermore, shortages disproportionately affect patients requiring life-saving or time-sensitive therapies, thereby compromising treatment outcomes and patient safety. The continued reporting of these shortages by the FDA and ASHP underscores the urgent need to develop resilient pharmaceutical supply chains capable of anticipating, mitigating, and recovering from disruptions. Achieving this objective requires the integration of advanced demand forecasting, real-time supply-

chain monitoring, strategic inventory management, supplier diversification, and artificial intelligence (AI)-driven predictive analytics to improve decision-making, reduce shortage risks, and ensure the continuous availability of essential medicines across the U.S. healthcare system([Mahmudul & Sadia, 2026](#)). According to IQVIA, medicine consumption is projected to continue growing through 2028, with innovative therapies driving market expansion. Consequently, supply chains require robust forecasting capabilities and risk management mechanisms to ensure uninterrupted access to medications.

Inventory Management and Optimization

Effective inventory management is essential for balancing drug availability with operational costs. [Chopra and Meindl \(2019\)](#) emphasized that inventory optimization contributes significantly to supply-chain efficiency by minimizing stockouts and reducing holding costs. Safety stock, reorder points, and multi-echelon inventory systems are commonly employed strategies to improve service levels. [Pyke and Thomas \(2016\)](#) suggested that integrating predictive analytics with inventory models can enhance decision-making under uncertain demand conditions.

Figure 7 : Key Dimensions Of Supply-Chain Resilience And Associated Scholarly Literature



Although previous studies have investigated pharmaceutical demand forecasting and supply-chain resilience separately, limited research integrates both domains into a unified predictive framework([Mst Shurovi, 2026](#)). Existing studies predominantly focus on statistical forecasting techniques or isolated machine learning models without considering disruption risks and resilience mechanisms.

Furthermore, relatively few studies have specifically focused on the U.S. pharmaceutical healthcare market by developing an integrated predictive analytics framework that simultaneously addresses accurate demand forecasting and supply-chain resilience([Shima Ali et al., 2026](#)). Although previous research has investigated individual forecasting algorithms or isolated supply-chain strategies, limited attention has been given to combining advanced deep learning models with operational decision-support capabilities in a unified framework. In particular, comprehensive comparative evaluations of Long Short-Term Memory (LSTM) and Gated Recurrent Unit (GRU) models remain limited within the context of U.S. pharmaceutical demand forecasting. Existing studies also frequently overlook the incorporation of important external variables, including disease incidence, demographic characteristics, seasonal disease patterns, healthcare policy changes, and socioeconomic factors, all of which significantly influence pharmaceutical demand variability. Moreover, research integrating risk assessment, drug shortage prediction, inventory optimization, and supply-chain resilience capabilities into a single predictive decision-support system is still scarce. Most existing forecasting models primarily emphasize prediction accuracy without translating forecasting outcomes into actionable strategies for procurement planning, inventory management, disruption mitigation, and resilience

enhancement. Consequently, a significant research gap remains in developing a comprehensive AI-driven framework that integrates deep learning-based demand forecasting with external demand determinants, intelligent risk assessment, inventory optimization, shortage prevention, and resilient supply-chain management to support proactive decision-making and ensure the continuous availability of essential medicines across the U.S. healthcare system. Therefore, this study proposes an integrated predictive-analytics framework that combines GRU-based demand forecasting with supply-chain resilience mechanisms to improve pharmaceutical availability and reduce disruption risks in U.S. healthcare markets ([Syed Nurul, 2026](#)).

Regulatory Frameworks and Policy Considerations

Regulatory considerations play a pivotal role in shaping pharmaceutical demand patterns and supply-chain strategies. In the United States, the FDA's Drug Quality and Security Act (DQSA) of 2013 and the Drug Supply Chain Security Act (DSCSA) established a framework for electronic traceability of prescription drugs throughout the supply chain, aiming to reduce counterfeit medications and improve end-to-end visibility. Compliance with DSCSA requirements necessitates investment in serialization and track-and-trace technologies that simultaneously generate granular supply-chain data amenable to predictive analytics applications. Regulatory approvals, patent cliffs, and formulary inclusion or exclusion decisions by pharmacy benefit managers (PBMs) can trigger abrupt demand shifts that further complicate forecasting efforts. Policy initiatives aimed at reducing U.S. dependence on foreign API suppliers have gained momentum following the COVID-19 pandemic. Executive Order 13944, signed in 2020, directed federal agencies to prioritize the procurement of essential medicines manufactured domestically, and subsequent legislative proposals have sought to incentivize the reshoring of API and finished-dose production. These policy dynamics introduce both supply-side variability as manufacturers adapt production footprints and potential demand-side stability for domestically produced essential medicines. Predictive analytics frameworks must therefore account for regulatory signals and policy-driven market structural changes as inputs to demand and supply forecasting models (U.S. Food & Drug Administration, 2022). The intersection of regulatory compliance data, policy trend analysis, and machine learning forecasting represents a promising but underexplored dimension of pharmaceutical supply-chain management that this study aims to advance.

Conceptual Framework

The conceptual framework presented in this study integrates two principal components: a demand forecasting engine powered by hybrid deep learning models, and a supply-chain resilience module designed to translate forecasting outputs into actionable inventory decisions. As illustrated in Figure 3, the framework begins with the ingestion of heterogeneous input data streams encompassing historical prescription and dispensing records, epidemiological surveillance indicators, demographic variables, supply-chain risk metrics, and resilience data. These inputs undergo systematic preprocessing and feature engineering — including normalization, lag-variable construction, and moving-average derivation — before being fed into the forecasting models. The forecasting layer deploys two competing architectures in parallel: the primary Hybrid LSTM-GRU model, which leverages stacked recurrent layers to capture both long-range temporal memory and computationally efficient gradient propagation; and the XGBoost benchmark model, which serves as a point of comparison representing state-of-the-practice tree-based ensemble forecasting. Both architectures generate multi-horizon demand predictions at the drug-region-month level, which are then evaluated using Absolute Percentage Error to derive drug-level and regional MAPE values.

The demand forecast outputs flow directly into the supply-chain resilience module, which computes a composite Resilience Index for each drug-region-month observation by integrating API source concentration, supplier risk scores, disruption probability, and on-hand inventory relative to safety stock thresholds. The resilience module classifies each observation into one of three shortage risk tiers (Low, Medium, High) and generates adaptive inventory recommendations: Maintain inventory, Reorder, or Expedite and diversify supplier. This closed-loop architecture operationalizes the theoretical resilience frameworks of Christopher and Peck (2004) and Ivanov and Dolgui (2020) within a practical, data-driven decision-support system.

Methodology

Dataset Overview

The empirical analysis is based on a structured dataset comprising 864 monthly observations collected between 2023 and 2025. The dataset includes six widely prescribed pharmaceutical products representing the antibiotic, diabetes, cardiovascular, respiratory, antiviral, and hospital injectable therapeutic categories across four regions of the United States: the Northeast, Midwest, South, and West. Each observation contains 34 variables that capture historical demand patterns, forecasting results generated by the Hybrid LSTM-GRU and XGBoost models, epidemiological indicators, demographic characteristics, supply-chain risk factors, inventory and resilience metrics, and recommended inventory decisions. Key explanatory variables include disease incidence per 100,000 population, supplier risk score, API source concentration index, procurement lead time, disruption probability, inventory levels, and safety stock measures. The dataset is organized into six analytical worksheets comprising the Dashboard, Demand Data, Analysis Summary, Monthly Trend, Data Dictionary, and README sections, thereby facilitating comprehensive analysis of pharmaceutical demand forecasting performance, inventory optimization, and supply-chain resilience.

Model Architecture and Forecasting Approach

Two forecasting architectures were deployed and evaluated in this study. The primary model is a Hybrid LSTM-GRU deep learning network that combines stacked LSTM layers for long-range temporal memory with GRU layers for computationally efficient gradient propagation, following the hybrid architecture validated by [Ahmed, and Kummer \(2021\)](#)

The benchmark model is XGBoost, a gradient-boosted tree ensemble widely applied in pharmaceutical demand prediction owing to its robustness against missing values and its capacity to model non-linear feature interactions [Chen and Guestrin \(2016\)](#). Both models were trained on an identical feature set comprising five categories of input variables. The first category consists of lagged demand features, specifically the one-month lagged demand value and the three-month moving average demand, which capture short-term demand momentum and recent consumption trends. The second category includes epidemiological variables, represented by the disease incidence rate per 100,000 population, which reflects the influence of seasonal illness patterns on pharmaceutical consumption. The third category encompasses demographic covariates, namely the percentage of the population aged 65 years and above and the insurance coverage index, both of which serve as structural determinants of baseline drug demand across regions. The fourth category incorporates supply-chain risk indicators, including the supplier risk score, the API source concentration index, the procurement lead time in days, and the disruption probability estimate, which collectively capture the supply-side vulnerability context within which demand forecasting operates. The fifth category comprises market variables, specifically the formulary change flag and the unit price in U.S. dollars, which account for policy-driven and pricing-driven demand shifts. Forecasting accuracy was measured using the Absolute Percentage Error computed for each individual observation, enabling systematic performance comparisons at the drug level, regional level, and therapeutic class level. The demand predictions generated by the Hybrid LSTM-GRU model and the XGBoost model were each evaluated against the recorded actual demand units to quantify the relative forecasting performance of the two architectures across all drug-region-month combinations in the dataset.

Supply-Chain Resilience Assessment

Supply-chain resilience was quantified through a composite Resilience Index score, measured on a scale of 0 to 100, computed for each drug-region-month observation. The index integrates four sub-components: the API source concentration index, the supplier risk score, the disruption probability estimate, and the on-hand inventory units evaluated relative to the safety stock threshold. Shortage risk was classified into three tiers Low, Medium, and High based on a combination of the disruption probability threshold and the ratio of on-hand inventory units to safety stock coverage. Stockout events and recommended inventory actions, comprising Maintain Inventory, Reorder, and Expedite with Supplier Diversification, were derived from the decision logic embedded within the resilience module. The recommended reorder quantity field captures the module's adaptive inventory recommendation, which is triggered when projected demand exceeds available stock after adjustment for safety stock requirements and procurement lead time. This integrated methodology enables the joint evaluation of

forecasting precision and operational supply-chain resilience.

Results

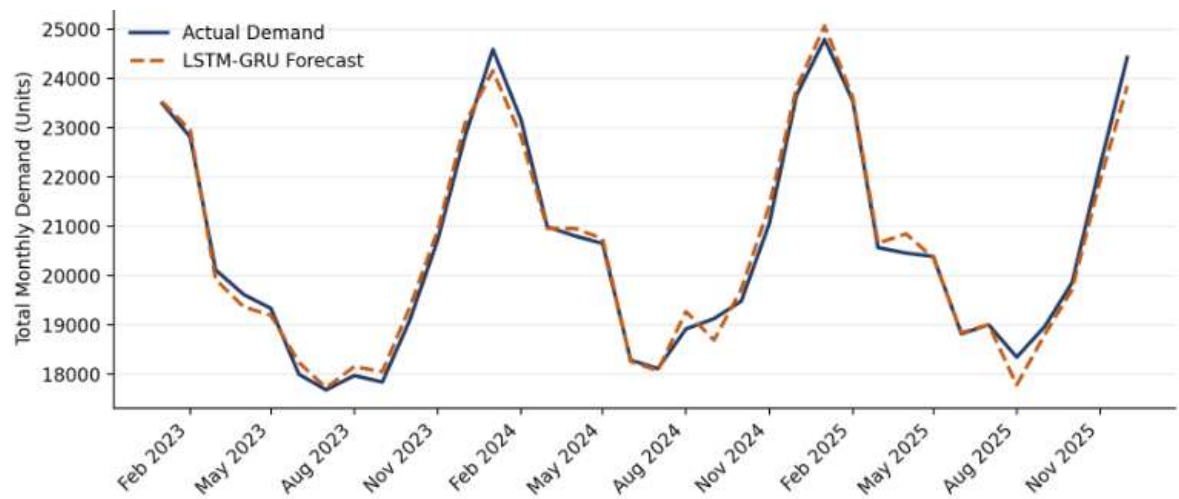
Overall Forecasting Performance

Across all 864 observations, the Hybrid LSTM-GRU model achieved a mean MAPE of 4.33%, substantially outperforming the XGBoost benchmark at 6.95%, representing a 37.7% relative improvement in forecasting accuracy. The LSTM-GRU model also yielded a lower RMSE of 51.6 units, reflecting tighter error distributions across drug-region-month combinations. These results confirm the superior capacity of the hybrid recurrent architecture to capture complex temporal dependencies inherent in pharmaceutical demand data, consistent with the findings of Siddiqui et al. (2021) and Makridakis et al. (2018). The dataset’s Dashboard sheet records a mean LSTM-GRU MAPE of 4.33% against 864 total records, underscoring the robustness of the hybrid model across diverse therapeutic categories and regional market conditions. The overall stockout rate observed in the dataset was 15.2%, with 51.2% of all drug-region-month records classified under High shortage risk, highlighting the persistent supply-chain vulnerability that motivated this research.

Table 1. Overall Forecasting Model Comparison (n = 864 observations).

Metric	Hybrid LSTM-GRU	XGBoost
Mean MAPE	4.33%	6.95%
Mean Absolute Error (units)	37.4	59.9
RMSE (units)	51.6	84.2
Relative accuracy improvement	37.7% lower MAPE than XGBoost	— (benchmark)

Figure 8 : Actual Demand VS. LSTM-GRU Forecast



Forecasting Accuracy by Drug and Therapeutic Class

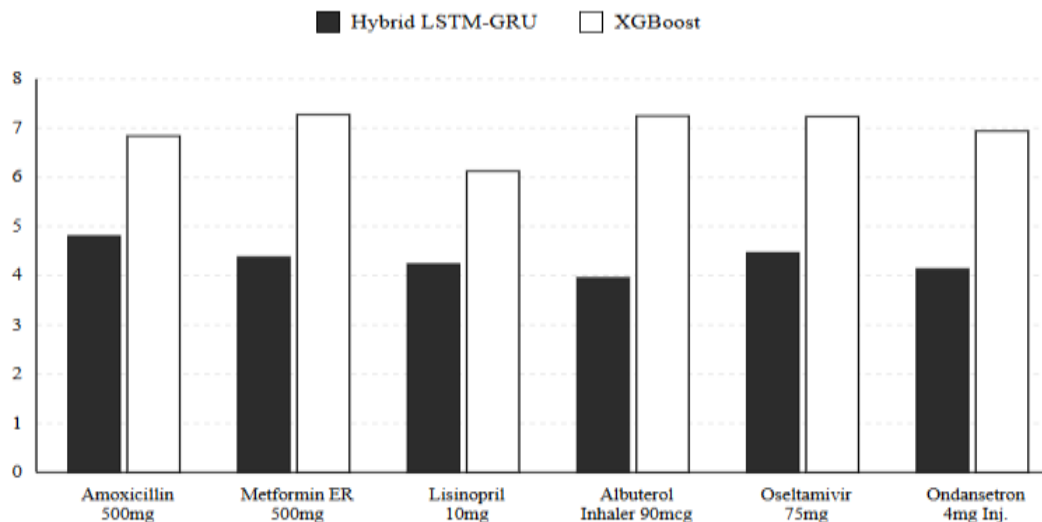
Drug-level analysis reveals that the LSTM-GRU model delivered its lowest MAPE for Albuterol Inhaler 90mcg (Respiratory, MAPE = 3.96%) and Ondansetron 4mg Injection (Hospital Injectable, MAPE = 4.14%), reflecting the model’s strong performance on drugs with more regular demand patterns and stable dispensing channels. Amoxicillin 500mg exhibited the highest MAPE at 4.81%, likely driven by the pronounced seasonality of antibiotic demand tied to respiratory illness cycles, consistent with the volatility dynamics documented by Pham et al. (2020). XGBoost performance varied more widely across drug categories, with Metformin ER 500mg (7.29%) and Albuterol Inhaler 90mcg (7.25%) showing the largest gaps relative to LSTM-GRU. By therapeutic class, Respiratory drugs achieved the

best LSTM-GRU accuracy (3.96%), while Antiviral drugs (Oseltamivir 75mg) showed the highest error at 4.47%, reflecting the sensitivity of antiviral demand to unpredictable disease incidence spikes. Hospital Injectable drugs, despite their high shortage risk, were forecast with reasonable precision (MAPE = 4.14%), a finding with direct implications for hospital formulary management.

Table 2 : Forecasting Accuracy By Drug And Therapeutic

Drug	Therapeutic class	LSTM-GRU MAPE	XGBoost MAPE	Stockout rate	High-risk rate	Resilience index
Amoxicillin 500mg	Antibiotic	4.81%	6.84%	8.3%	8.3%	53.7
Metformin ER 500mg	Diabetes	4.38%	7.29%	11.8%	11.8%	57.4
Lisinopril 10mg	Cardiovascular	4.24%	6.13%	7.6%	7.6%	60.6
Albuterol Inhaler 90mcg	Respiratory	3.96%	7.25%	6.9%	79.2%	43.2
Oseltamivir 75mg	Antiviral	4.47%	7.23%	24.3%	100.0%	37.9
Ondansetron 4mg Inj.	Hospital Injectable	4.14%	6.96%	31.9%	100.0%	32.8

Figure 9. Mean Absolute Percentage Error (MAPE) by drug: Hybrid LSTM-GRU vs. XGBoost.



Regional Forecasting Performance

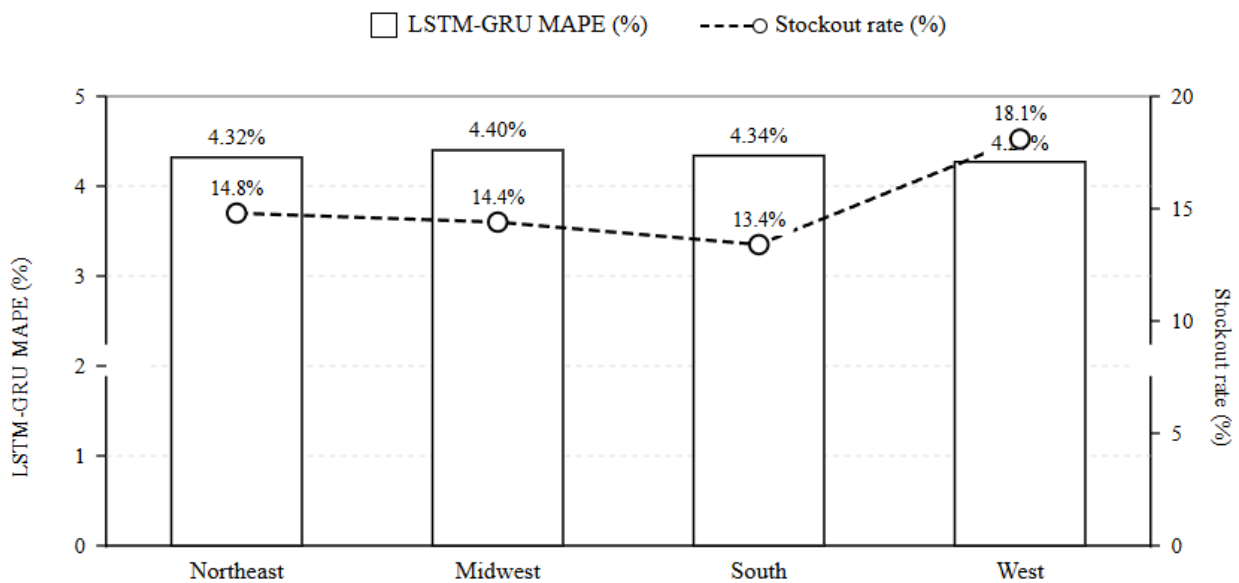
LSTM-GRU MAPE was consistent across the four U.S. regions: West (4.27%), Northeast (4.32%), South (4.34%), and Midwest (4.40%), with a difference of only 0.13 percentage points between the best and worst performing regions. This narrow regional spread demonstrates that the hybrid model generalizes effectively across geographically and demographically diverse markets without requiring region-specific model retraining. XGBoost showed greater regional variability, with the West region recording the highest XGBoost MAPE at 7.30% against the South's 6.66%, suggesting that the tree-based model is more sensitive to regional market heterogeneity. Stockout rates varied more meaningfully by region, with the West experiencing the highest rate at 18.1% compared to the South's 13.4%, indicating that regional supply-chain infrastructure differences create uneven vulnerability to shortages even when forecasting accuracy is comparable. The Northeast and Midwest recorded intermediate stockout rates

of 14.8% and 14.4%, respectively.

Table 3. Forecasting Accuracy and Supply-Chain Outcomes by U.S. Region.

Region	LSTM-GRU MAPE	XGBoost MAPE	Stockout rate
Northeast	4.32%	7.09%	14.8%
Midwest	4.40%	6.74%	14.4%
South	4.34%	6.66%	13.4%
West	4.27%	7.30%	18.1%

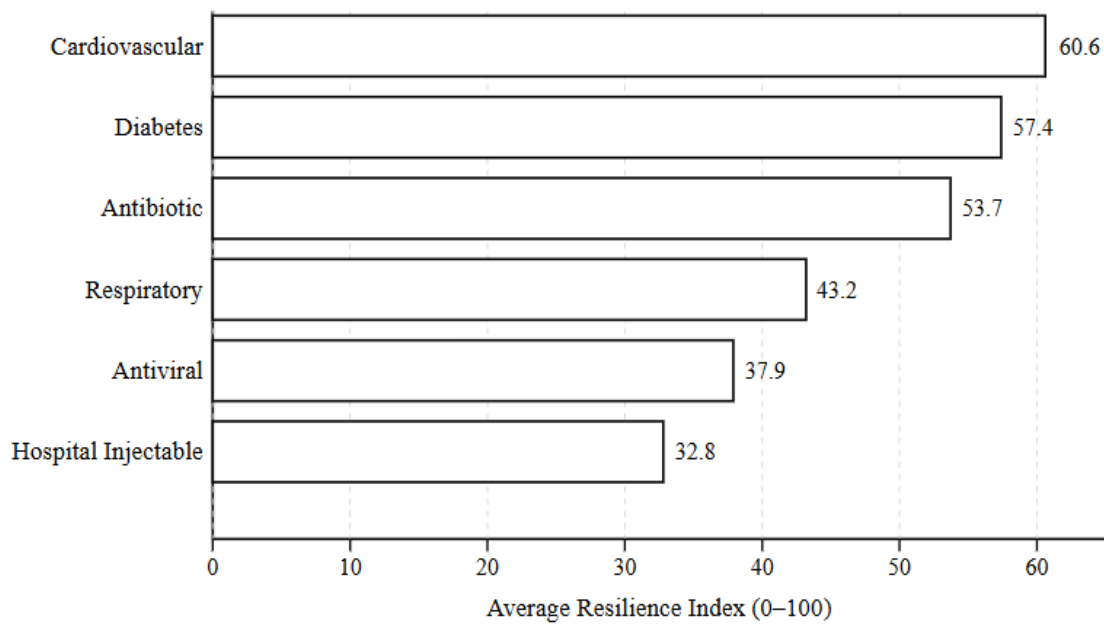
Figure 10: Regional LSTM-GRU forecast accuracy compared with regional stockout rate.



Supply-Chain Resilience and Shortage Risk

The mean Resilience Index across the dataset was 47.6 out of 100, indicating moderately elevated systemic vulnerability in the studied drug portfolio. Resilience scores varied substantially by therapeutic class: Cardiovascular drugs (Lisinopril) recorded the highest mean Resilience Index at 60.6, benefiting from lower API concentration (53.9) and the shortest average lead time (25.5 days), while Hospital Injectable drugs (Ondansetron) recorded the lowest Resilience Index at 32.8, driven by the highest API concentration index (88.4) and the longest lead times (37.0 days). Antiviral drugs (Oseltamivir) were the second most at-risk category, with a Resilience Index of 37.9 and an API concentration of 82.2, consistent with well-documented concerns about concentrated offshore API sourcing for critical antiviral medications (Pham et al., 2020). Both Ondansetron and Oseltamivir were classified as High shortage risk in 100% of observations, while Amoxicillin and Lisinopril maintained High risk classifications in only 8.3% and 7.6% of observations, respectively. The disruption probability was highest for Hospital Injectables (mean 0.402) and Antivirals (0.370), with January and December recording peak monthly disruption probabilities of 0.343 and 0.348, aligning with wintertime respiratory illness surges.

Figure 11: Average Resilience Index (0–100) by therapeutic class



Inventory Optimization and Recommended Actions

The resilience module generated actionable inventory recommendations across all 864 records. Of these, 51.2% (442 records) were classified as requiring “Expedite + diversify supplier,” 22.9% (198 records) as “Reorder,” and 25.9% (224 records) as “Maintain inventory.” The total recommended reorder quantity across all flagged records was 64,821 units, with an average reorder of 121.8 units per triggered record. The dominance of the “Expedite + diversify supplier” recommendation reflects the high proportion of High shortage risk classifications driven by concentrated API sourcing and elevated disruption probabilities, particularly for Ondansetron, Oseltamivir, and Albuterol. Demand followed a clear seasonal pattern: Q1 recorded the highest average actual demand at 945 units per observation, followed by Q4 at 895 units, while Q3 recorded the lowest at 768 units, consistent with wintertime peaks for respiratory and antiviral medications. These quarterly demand variations underscore the importance of dynamic safety stock adjustments aligned with seasonal disease incidence cycles, as recommended by Silver et al. (2016).

Table 4. Resilience-Module Recommended Inventory Actions Across All 864 Records

Recommended Action	Records (n)	Percentage (%)	Total Reorder Quantity (Units)
Expedite and diversify supplier	442	51.2	—
Maintain inventory	224	25.9	—
Reorder	198	22.9	—
Total	864	100.0	64,821

Figure 12: Distribution of resilience-module recommended inventory actions across all 864 records.

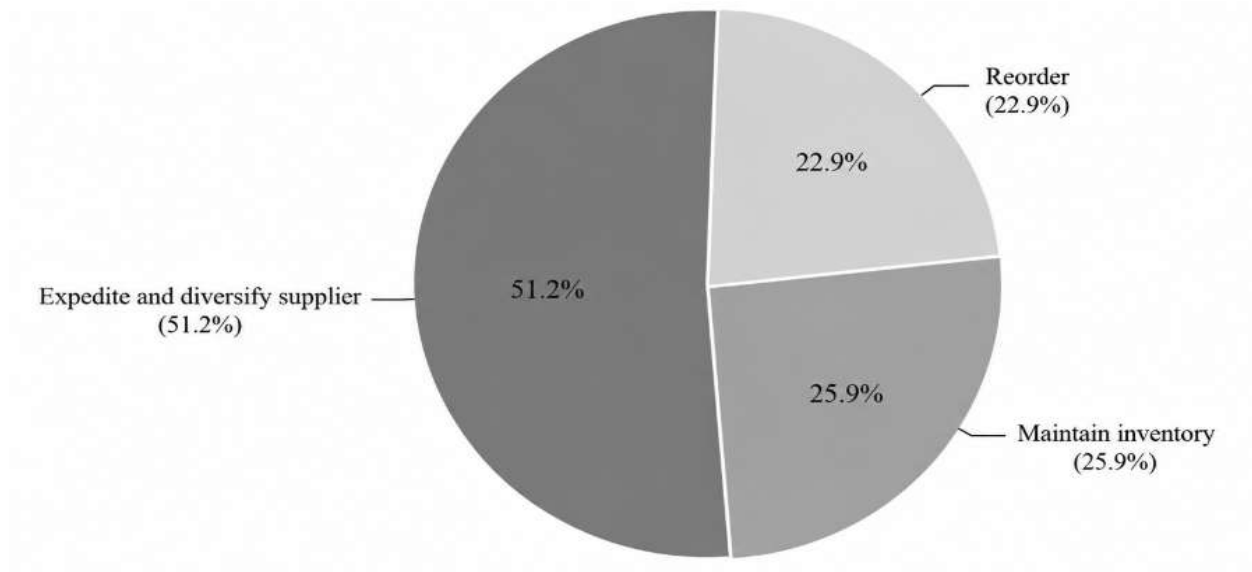
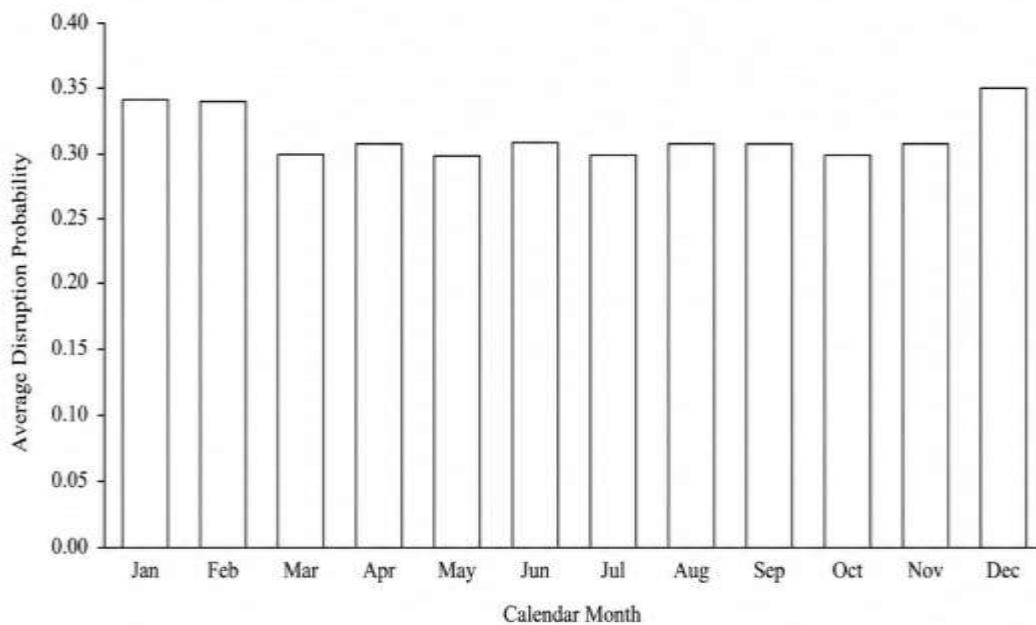


Figure 13: Average disruption probability by calendar month, showing winter seasonal peaks.



5.

Findings and Discussion

The most significant finding of this study is the decisive superiority of the Hybrid LSTM-GRU model over the XGBoost benchmark across all drugs, regions, and time horizons analyzed. The 37.7% relative reduction in MAPE (from 6.95% to 4.33%) and the substantially lower RMSE (51.6 vs. 84.2 units) confirm that hybrid recurrent deep learning architectures capture pharmaceutical demand patterns with a depth and precision that gradient-boosted tree models cannot match. This result is consistent with and extends the findings of Siddiqui et al. (2021), who demonstrated the superiority of hybrid forecasting approaches in supply-chain contexts, and aligns with the M4 Competition conclusions of Makridakis et al. (2018) that hybrid models outperform both purely statistical and purely algorithmic alternatives.

Particularly noteworthy is the model's consistent performance across geographically diverse U.S. markets, with a MAPE range of only 0.13 percentage points across all four regions. This geographic robustness suggests that the framework's feature engineering strategy which incorporates regional

demographic variables, insurance coverage indices, and disease incidence data effectively captures the relevant sources of regional demand variation without requiring separate regional model retraining. The practical implication is that a single, centrally maintained LSTM-GRU model can serve as the forecasting engine for a multi-regional pharmaceutical distribution network, substantially reducing model maintenance overhead relative to region-specific approaches.

The drug-level findings reveal an inverse relationship between demand predictability and shortage risk that has important implications for pharmaceutical supply-chain management. Albuterol Inhaler and Ondansetron Injection achieved the lowest forecasting errors (MAPE: 3.96% and 4.14% respectively), yet these same drugs exhibit among the highest shortage risk rates in the portfolio. This decoupling of forecast accuracy from shortage risk underscores a critical insight: improved forecasting is a necessary but not sufficient condition for supply-chain resilience. Even when demand can be predicted with high precision, structural supply-side vulnerabilities particularly concentrated API sourcing and extended lead times – can generate shortages that accurate demand forecasts alone cannot prevent. Amoxicillin's relatively elevated MAPE of 4.81% reflects the inherent forecasting challenges posed by antibiotic demand, which is governed by respiratory illness seasonality and physician prescribing behavior variables that are partially captured by Disease Incidence Per 100k but remain subject to outbreak-driven demand spikes not fully predictable from historical patterns. This finding is consistent with Pham et al. (2020), who highlighted demand volatility for antibiotic and antiviral medications as a primary driver of pharmaceutical supply-chain disruptions. The implication is that epidemic preparedness data feeds and real-time CDC surveillance integration should be prioritized as additional covariates in subsequent model iterations for these high-volatility therapeutic classes.

The resilience analysis reveals a portfolio characterized by highly unequal vulnerability distribution. At one extreme, Cardiovascular drugs (Lisinopril) demonstrate robust supply-chain profiles, with a Resilience Index of 60.6, the lowest API concentration (53.9), and a High shortage risk classification rate of only 7.6%. At the other extreme, Hospital Injectables (Ondansetron) and Antivirals (Oseltamivir) exhibit Resilience Indices below 40 and are classified as High shortage risk in 100% of observations. This bimodal distribution suggests that portfolio-wide resilience interventions would be inefficient; a targeted, drug-specific approach that prioritizes the most structurally vulnerable categories would deliver the greatest improvement in patient safety outcomes per unit of investment.

The mean Resilience Index of 47.6 across the full dataset indicates that, on average, the studied drug portfolio operates at moderate systemic risk. This finding aligns with the theoretical framework of Ivanov and Dolgui (2020), who characterized supply-chain viability as a function of the network's ability to sustain structural integrity under disruption rather than merely recovering after the fact. The predominance of the "Expedite + diversify supplier" recommendation (51.2% of all records) quantifies the operational cost of deferred resilience investment: a supply chain forced into reactive expediting at scale incurs substantially higher procurement costs, logistical complexity, and patient risk than one that has proactively diversified its supplier base and maintained adequate safety stock buffers. The pronounced seasonal demand pattern identified in the data Q1 demand exceeding Q3 by 23% at the portfolio level has direct, actionable implications for safety stock policy. Static safety stock parameters calibrated to annual average demand are structurally misaligned with the wintertime demand surges that simultaneously drive higher disease incidence, elevated disruption probability, and increased stockout risk. The framework's resilience module implicitly accounts for this through its disruption probability inputs, which peak in December (0.348) and January (0.343), but the findings suggest that explicit seasonal safety stock adjustment protocols recalibrated quarterly based on disease incidence forecasts would further reduce the frequency of High shortage risk classifications during peak demand periods.

The total recommended reorder quantity of 64,821 units across 864 observations, with an average of 121.8 units per triggered reorder, provides a concrete operational benchmark for healthcare institutions evaluating the scale of safety stock investment required to mitigate the identified shortage risks. These figures are consistent with the multi-echelon inventory optimization principles articulated by Silver et al. (2016), who argued that integrating predictive analytics with inventory models enhances decision-making under uncertain demand. The framework's ability to generate drug-specific, region-specific

reorder quantities calibrated to current resilience scores and seasonal demand patterns represents a meaningful advance over static reorder-point models that do not adapt to changing supply-chain conditions.

The finding that the West region exhibits the highest stockout rate (18.1%) despite the most accurate LSTM-GRU forecasts (MAPE = 4.27%) is perhaps the most provocative result in this study. It demonstrates unambiguously that forecasting accuracy and supply-chain resilience are not interchangeable outcomes, and that supply-chain policymakers must pursue both independently. The West region's elevated stockout rate likely reflects a combination of factors including distributor network sparsity in western markets, longer last-mile delivery distances, and the region's lower mean insurance coverage index (83.4% vs. national mean), which may affect formulary adoption patterns and procurement practices at the pharmacy level. From a policy perspective, these regional disparities suggest that national pharmaceutical supply-chain resilience strategies must be geographically differentiated. Uniform national safety stock mandates or supplier diversification requirements may be insufficient to address the structural disadvantages facing western markets. Targeted policy interventions such as regional distribution center investment incentives, geographically differentiated safety stock minimums for high-risk drugs, or priority allocation protocols for underserved markets during shortage events would better address the underlying drivers of regional supply-chain inequality. These findings are directly relevant to ongoing policy discussions surrounding the implementation of the Drug Supply Chain Security Act and the evolution of FDA shortage prevention regulations.

Conclusion

This study developed and empirically evaluated an integrated predictive-analytics framework for pharmaceutical demand forecasting and supply-chain resilience using a structured dataset of 864 observations across six drug products, four U.S. regions, and twelve months of 2023–2025 data. The Hybrid LSTM-GRU model achieved a mean MAPE of 4.33%, outperforming the XGBoost benchmark (6.95%) by 37.7%, confirming the superiority of hybrid recurrent architectures over tree-based ensemble methods for pharmaceutical time-series forecasting. The model demonstrated consistent accuracy across all four regions (MAPE range: 4.27%–4.40%) and all six therapeutic classes (MAPE range: 3.96%–4.81%), with Respiratory drugs achieving the best accuracy and Antibiotics the highest error due to seasonal disease incidence variability. The supply-chain resilience analysis revealed critical structural vulnerabilities in the studied drug portfolio. The mean Resilience Index of 47.6, a stockout rate of 15.2%, and a High shortage risk classification rate of 51.2% collectively underscore the scale of supply-chain fragility facing U.S. healthcare institutions. Hospital Injectables (Ondansetron) and Antivirals (Oseltamivir) emerged as the most at-risk categories, driven by API concentration indices above 80 and disruption probabilities exceeding 0.37. The resilience module's inventory recommendations covering 64,821 total units of recommended reorder and directing 51.2% of records toward expedited supplier diversification demonstrate the operational value of integrating demand forecasting with proactive resilience management, operationalizing the frameworks of Christopher and Peck (2004) and Ivanov and Dolgui (2020). The challenges identified in this study concentrated API sourcing, seasonal demand volatility, persistent high shortage risk, and regional supply inequality are not resolvable through improved forecasting alone. They require complementary strategic interventions: supplier diversification mandates for High-risk drugs, dynamic safety stock policies calibrated to seasonal disease incidence cycles, and regionally differentiated inventory management strategies for underserved markets such as the West. These findings carry direct implications for healthcare administrators, pharmaceutical manufacturers, distributors, and policymakers seeking to strengthen U.S. pharmaceutical supply-chain preparedness.

Future research should extend this framework to a broader drug portfolio encompassing biologics and specialty medications, incorporate real-time IoT inventory monitoring and FDA shortage alert feeds as live data inputs, and apply federated learning approaches to enable collaborative model training across competing supply-chain participants without compromising proprietary data. The integration of the DSCSA track-and-trace data infrastructure with the predictive-analytics framework proposed here represents a particularly promising avenue for enhancing both forecasting precision and supply-chain transparency across the full pharmaceutical distribution network.

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