# Simulation-Based Optimization of Synthetic Blood Production and Deployment in Emergency and Resource-Limited Clinical Settings

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## ABSTRACT

Logistical strategies for operational deployment remain underdeveloped, particularly within synthetic blood supply chains designed for use in emergencies, rural, or conflict-affected environments (Estep, 2025; Horstkemper & Reuter-Oppermann, 2022). While substantial progress has been made in the biochemical formulation and clinical validation of hemoglobin-based oxygen carriers (HBOCs) and perfluorocarbon emulsions (PFCs), far less attention has been given to the infrastructure and decision-making systems required to deliver these products effectively. Most existing studies focus on efficacy, storage conditions, and adverse event profiles, but rarely consider how variability in transport, facility access, and inventory degradation shapes deployment success under field conditions. Conventional blood supply chain models typically rely on fixed demand patterns, consistent infrastructure, and cold-chain requirements, limiting their applicability in unstable or resource-limited settings. Simulation platforms such as BloodChainSim provide valuable insights into process efficiency but often overlook the specific risks, degradation timelines, and clinical trade-offs unique to synthetic blood. They also tend to exclude dynamic decision-making models that account for shifting priorities during crises. As synthetic blood products move closer to clinical implementation, there is a growing need for planning tools that accommodate variable demand, multiple transportation modes, and shelf-life constraints. Simulation-based logistics frameworks must balance delivery speed, patient safety, and system resilience while remaining adaptable across use cases ranging from humanitarian aid to battlefield medicine. Addressing these logistical gaps is critical to realizing the full value of synthetic blood technologies in real-world trauma care and emergency medical response.

## ABOUT THE AUTHORS

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## INTRODUCTION

Access to compatible blood transfusions is a critical determinant of survival in trauma care, emergency medicine, and battlefield scenarios (Jahr, 2022; Estep, 2025). However, in rural, mobile, or conflict-affected settings, conventional blood supply chains often fail due to limited donors, cold-chain dependencies, and long transport times (Glick et al., 2020; Arani et al., 2021; Estrada et al., 2025). Synthetic blood products, such as hemoglobin-based oxygen carriers (HBOCs) and perfluorocarbon emulsions (PFCs), offer transformative potential. These substitutes are shelf-stable for years, require no cross-matching, and can rapidly deliver oxygen (Kim et al., 2024; Vichare & Janjic, 2025). Yet logistical integration remains underexplored, especially in field environments where degradation, delivery delays, and coordination challenges persist (Horstkemper & Reuter-Oppermann, 2022; Estep, 2025).

This paper presents a discrete-event simulation (DES) framework that models synthetic blood deployment from production to transfusion in emergencies and resource-limited settings. The DES model makes a unique contribution by integrating stochastic trauma demand with real-time degradation kinetics, enabling the optimization of inventory thresholds and delivery strategies under uncertainty. The model accounts for system degradation, delivery logistics, and clinical safety trade-offs such as MI and CARPA risks.

Distinct from prior models, such as BloodChainSim, this framework introduces multi-facility scalability, dynamic resource allocation via drones, and degradation-aware inventory strategies specifically tailored for synthetic blood products. These innovations support data-driven decision-making for humanitarian aid, disaster response, and military healthcare logistics by providing comprehensive bottleneck analysis and policy evaluation capabilities under crisis conditions.

Although the safety and biochemical properties of synthetic blood products are well documented (Jahr, 2022; Kim et al., 2024), few studies have modeled their logistical deployment in emergency or resource-limited environments (Estrada et al., 2025; Horstkemper & Reuter-Oppermann, 2022). Existing simulations often overlook degradation kinetics, variable trauma demand, and delivery trade-offs between transport modes.

## RELATED WORK

### Advancements in Synthetic Blood Technologies

Synthetic blood products have gained attention as alternatives to red blood cell transfusions, especially in settings with limited infrastructure or donor availability (Khan et al., 2020; Estrada et al., 2025). Hemoglobin-based oxygen carriers, such as Hemopure, offer room temperature stability and can reduce dependence on donor blood in trauma care (Jahr, 2022). Perfluorocarbons like Fluosol and Oxygent provide high oxygen solubility but present concerns regarding emulsification breakdown and immune responses (Kim et al., 2024; Vichare & Janjic, 2025). While clinical outcomes are promising, most literature focuses on biochemical performance and adverse events such as myocardial infarction

with HBOCs and CARPA reactions with PFCs. Logistical strategies for operational deployment remain underdeveloped (Estep, 2025; Horstkemper & Reuter-Oppermann, 2022).

**Blood Supply Chain Simulation Models**

Discrete event simulation (DES) models healthcare systems like emergency departments and surgical workflows (Brailsford & Vissers, 2010). Blood supply chain simulations use DES to cut stockouts and assess inventory strategies under different demand levels (Glick et al., 2020; Arani et al., 2021). These models usually assume conventional blood products and stable infrastructure. BloodChainSim advances blood supply chain modeling with agent-based elements to simulate crises and evaluate digital innovations in blood logistics (Horstkemper & Reuter-Oppermann, 2022). While it models conventional blood supply chains and crisis decision-making, it overlooks synthetic blood products' specific factors such as degradation, costs, and safety risks (Kim et al., 2024). This study's model builds on BloodChainSim's crisis simulation but extends it for synthetic blood, incorporating HBOC autoxidation, PFC emulsion breakdown, clinical risks like MI and CARPA, and multimodal delivery including drones.

Unmanned aerial vehicles are increasingly used to deliver medical supplies in remote or low-resource areas. Programs like Zipline have reduced delivery times from several hours to under 30 minutes, improving emergency response (Glick et al., 2020). While simulation studies support the effectiveness of drone logistics, they have not yet been adapted for synthetic blood, which introduces additional challenges related to stability, storage, and clinical safety. This study addresses those gaps by introducing a DES framework that incorporates production timelines, clinical risks, and geospatial constraints to evaluate deployment strategies in critical care settings. The model uniquely combines synthetic blood-specific parameters with crisis-responsive logistics, filling a critical void in emergency preparedness planning for next-generation blood substitutes.

## METHODOLOGY

This study employed a DES approach to model and optimize the production, storage, and deployment of synthetic blood products, HBOCs, and PFCs, in emergency and resource-limited clinical settings. The simulation was designed to address critical challenges in blood supply chain management during crises, building on insights from prior research that identify limitations in actor representation and dynamic decision-making (Horstkemper & Reuter-Oppermann, 2022; Arani et al., 2021). Our methodology integrates advanced simulation techniques, real-world data, and dynamic system modeling to provide a competitive framework for evaluating deployment strategies. The model was structured in four progressive phases to ensure robustness, scalability, and practical relevance.

**Model Structure and Processes**

The DES model simulated a synthetic blood supply chain across production, inventory, delivery, and trauma demand, with a focus on emergency deployment. Unlike conventional models that overlook dynamic decisions or exclude key actors (Arani et al., 2021), this model incorporates full process representation with real-time state transitions, adapting hybrid agent-based/DES frameworks, such as BloodChainSim (Horstkemper & Reuter-Oppermann, 2022), for synthetic blood. A centralized facility produced HBOCs and PFCs in batches. HBOCs required 5–7 days (500–1,000 L), PFCs 3–5 days (100–300 L), with a 7.5% failure rate. Unit costs were $10,000 for HBOC and $2,000 per liter for PFC (Estrada et al., 2025; Vichare & Janjic, 2025).

**Table 1. Simulation Parameters**

| Parameter | Value | Source | Parameter | Value | Source |
|---|---|---|---|---|---|
| HBOC Prod. | 5-7 days | Jahr, 2022 | Drone Delivery | 0.5h | Roberts et al., 2018 |
| PFC Production | 3-5 days | Kim et al., 2024 | Trauma Demand | 4-10 units | Holcomb et al., 2005 |
| Production Fail | 7.5% | Khan et al., 2020 | HBOC MI Risk | 2.01% | Estep, 2025 |
| HBOC Autoxidation | 0.22 $h^{-1}$ | Estep, 2025 | PFC CARPA Risk | 1% | Kim et al., 2024 |
| PFC Degradation | 1×10-5 h | Vichare & Janjic,2025 | HBOC Cost | $10K/unit | Estrada et al., 2025 |
| Drone Failure | 1.8% | Glick et al., 2020 | Drone Cost | $75K | Glick et al., 2020 |

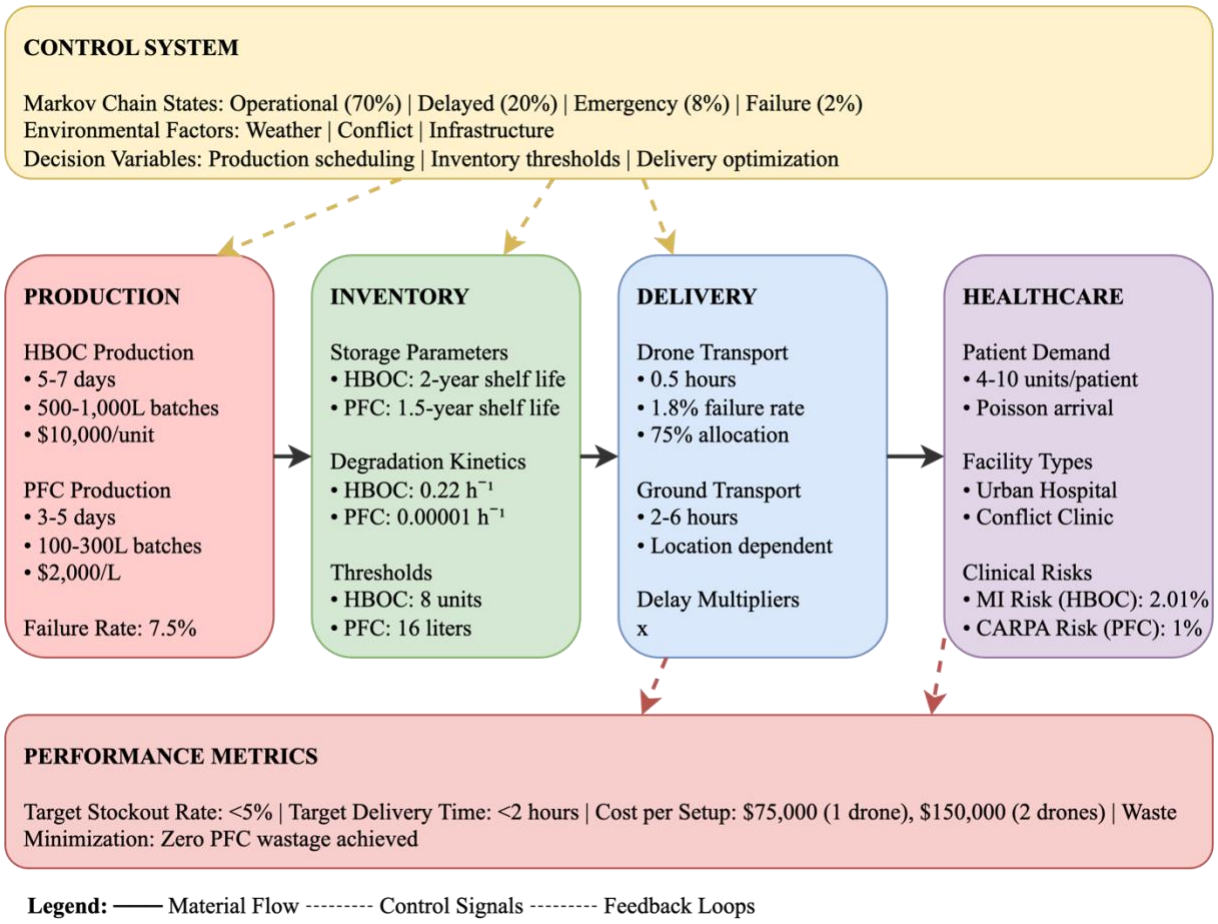


**Figure 1: Digital Twin Logistics**

## Inventory Management

### *Delivery*

A 75% drone allocation was used, based on prior innovations in blood logistics (Horstkemper & Reuter-Oppermann, 2022). Drones took 0.5 hours (1.8% failure), land transport took 2–6 hours, and weather-related failure was 2.3% (Glick et al., 2020). Delay multipliers were applied by setting: urban (1.0), rural (1.2), remote (1.5), and conflict (2.5) (Arani et al., 2021).

### *Trauma Demand*

Patient arrivals were modeled as a Poisson process, representing random events at a constant rate, with arrival rates differing by facility type (Arani et al., 2021; Estrada et al., 2025). Each trauma patient needs 4–10 units of blood substitute, aligning with severe hemorrhage protocols. Safety considerations influenced delivery via product-specific adverse event rates: HBOCs carry a 2.01% MI risk due to vasoactive properties, while PFCs have a 1% risk of CARPA—an immune response causing cardiovascular and pulmonary symptoms (Estep, 2025; Kim et al., 2024). A PFC equivalence factor was set, where 1 liter of PFC provides oxygen-carrying capacity equivalent to 0.5 liters of HBOC for substitution. This ratio prioritizes HBOC delivery, using PFC only during shortages to balance oxygen needs, safety, and inventory management (Kim et al., 2024; Vichare & Janjic, 2025).

### *System Dynamics*

A Markov chain-governed system has states (Operational, Delayed, Emergency, Failure), which are affected through multipliers (e.g., 2.0× in Failure). A ±10% perturbation simulated uncertainty, adapted from dynamic decision models (Horstkemper & Reuter-Oppermann, 2022).

## EXPERIMENTAL DESIGN

### *Part 1: Model Development and Initial Simulation*

The initial simulation established a baseline performance and identified optimal parameters through a full Monte Carlo sensitivity analysis (32,400 runs, each lasting 90 days). Parameter combinations included HBOC thresholds (4–12 units), PFC thresholds (8–24 liters), drone splits (0.5–0.9), arrival rates (4.8–6.0 hours, simulating 4–5 patients/day), and PFC degradation rates (0.00001–0.0001 $h^{-1}$). This broad sweep enabled a thorough exploration of the design space, offering an advantage over models with narrower testing scopes (Arani et al., 2021). Key performance metrics included stockout probability (target: <5%), delivery delay (target: <2 hours), MI and CARPA incidents, cost, and product waste. The optimal configuration, HBOC threshold of 8 units, PFC threshold of 16 liters, drone split of 0.75, and PFC degradation rate of 0.00001 $h^{-1}$, achieved stockout probabilities of 0–0.14% and delivery delays of 1.75–6.46 hours. The total cost for a single-drone setup was $75,000 (Glick et al., 2020).

### *Part 2: Validation and Sensitivity Analysis*

To validate the optimal parameters, a reduced Monte Carlo analysis was conducted with 200 simulations (90 days each), focusing on two arrival rates (4.8 and 6.0 hours) to represent varying demand intensities, including conflict conditions. This phase modeled a single hospital with one drone and used the same processes as earlier phases.

Delay causes were logged by system state, location, and facility to identify bottlenecks, drawing from BloodChainSim's operational focus (Horstkemper & Reuter-Oppermann, 2022). Box plots were used to analyze delays by Markov state (Operational, Delayed, Emergency, Failure) and location type (urban, rural, remote, conflict), offering more detailed insights than static models (Arani et al., 2021). The parameters proved robust: stockout probabilities remained below 5% (M = 0.001 for 4.8-hour arrival rate, M = 0.000 for 6.0), and delivery delays slightly exceeded the 2-hour target (M = 2.35 and 2.30 hours; SD = 1.72 for both). Each run averaged 1.48 seconds, demonstrating strong computational efficiency.

### *Part 3: Real-World Data Integration and Scalability*

The model was extended to a multi-facility setup simulating an urban hospital (4 patients/day, arrival rate: 6 hours) and a conflict clinic (10 patients/day, arrival rate: 2.4 hours), based on trauma demand estimates from Arani et al. (2021) and Estrada et al. (2025). Two shared drones were modeled at a total cost of $150,000 (Glick et al., 2020).Real-world parameters included a conflict delay multiplier of 2.5, a Markov transition matrix with a 0.7 operational probability (Horstkemper & Reuter-Oppermann, 2022), and a PFC equivalence factor—a clinical conversion ratio where 1 liter of PFC was considered equivalent to 0.5 liters of HBOC in terms of oxygen-carrying capacity and clinical substitution potential (Kim et al., 2024; Vichare & Janjic, 2025). This equivalence factor enables the simulation to substitute PFC for HBOC when inventory shortages occur, maintaining therapeutic effectiveness while optimizing resource allocation. A disaster mode simulated surge demand of 12 patients per facility over 24 hours, reflecting crisis conditions studied by Horstkemper and Reuter-Oppermann (2022). The simulation ran 100 iterations (90 days each), logging delay causes and generating box plots to assess scalability. This multi-facility configuration, combined with surge conditions, captured the dynamics of shared resources and crisis impacts more effectively than single-facility models. Runtime averaged 1.79 seconds, demonstrating efficiency despite increased complexity.

### *Part 4: Policy Implementation and Validation*

The final phase validated deployment strategies through a real-world case study to ensure practical use in emergencies (Horstkemper & Reuter-Oppermann, 2022). A conflict zone hospital was modeled using data from a 500-bed Egyptian facility (Arani et al., 2021), with a daily demand of 35.4 units (29.6% emergency, 38.2% medical, 32.2% operative) and a supply of 21.1 units. Demand was scaled for synthetic blood (HBOC/PFC). The simulation used optimal parameters from Part 1 (HBOC threshold=8, PFC threshold=16, drone split=0.75, PFC degradation=0.00001 $h^{-1}$) and tested two policies: increasing drone split to 90% and pre-positioning synthetic blood stocks (200 HBOC units, 400 PFC liters). It ran 100 iterations (90 days each), including disaster mode (12 patients/day for 24 hours) to simulate crisis conditions. Delay causes were logged to evaluate the effectiveness of the intervention, with a focus on reducing bottlenecks. Results will be validated using hospital data from organizations like WCBS or SANBS, supporting real-world alignment for healthcare digital twin applications (Estrada et al., 2025). The simulation averaged 1.73 seconds over 100 runs.

**Data Analysis**

Simulation outputs were assessed across all phases using key performance metrics: stockout probability, average delivery delay, MI and CARPA incidents, total cost, and product waste, aligned with indicators from blood supply chain literature (Arani et al., 2021). Delivery delays were further analyzed by system state (Operational, Delayed, Emergency, Failure), geographic setting (urban, rural, remote, conflict), and facility type (urban hospital and conflict clinic in Part 3; conflict hospital in Part 4) to identify bottlenecks, following BloodChainSim's operational focus (Horstkemper & Reuter-Oppermann, 2022). Variability across these metrics helped characterize system behavior under diverse conditions. This methodology offers competitive advantages over prior models by incorporating full actor representation from production to transfusion, enabling realistic multi-facility supply chain dynamics often excluded in centralized frameworks (Arani et al., 2021; Horstkemper & Reuter-Oppermann, 2022). Integration of Markov state transitions and adaptive delivery mode selection supports real-time crisis response, while disaster mode enables realistic surge modeling, addressing major gaps in synthetic blood logistics.

Real-world trauma demand and multi-site simulation further improve scalability and relevance beyond single-facility models (Arani et al., 2021; Estrada et al., 2025). Runtime efficiency was consistently strong, averaging 2.28 seconds in Part 2, 1.70 in Part 3, and 1.73 in Part 4, enabling high-volume, iterative Monte Carlo testing. These features collectively demonstrate a robust framework for optimizing synthetic blood deployment and advancing the abstract's goals of modeling, bottleneck analysis, policy evaluation, and logistical planning under uncertainty.

**RESULTS**

The DES model was executed in four phases to evaluate synthetic blood deployment under varying operational conditions, using metrics such as stockout probability, delivery delay, MI and CARPA incidents, total cost, and waste. Part 1 identified optimal parameters via Monte Carlo analysis. Part 2 validated them across two trauma arrival rates. Part 3 tested the model in a multi-facility scenario with disaster surges. Part 4 applied policy interventions at a conflict hospital. Means (M) and standard deviations (SD) are reported throughout.

***Part 1: Initial Simulation***

An initial Monte Carlo sensitivity analysis with 32,400 runs over 90 days tested combinations of HBOC thresholds (4–12 units), PFC thresholds (8–24 liters), drone splits (0.5–0.9), arrival rates (4.8–6.0 hours), and PFC degradation rates (0.00001–0.0001 $h^{-1}$). It identified optimal parameters: HBOC Threshold = 8 units, PFC Threshold = 16 liters, Drone Split = 0.75, and PFC Degradation Rate = 0.00001 $h^{-1}$. Stockout probabilities ranged from 0% to 0.14%, below the 5% target, while delays ranged from 1.75 to 6.46 hours, indicating possible bottlenecks. The total cost for a single drone setup was $75,000 (Glick et al., 2020). This phase confirmed the robustness of these parameters under varying patient arrival rates.

***Part 2: Validation and Sensitivity Analysis***

A reduced Monte Carlo sensitivity analysis (200 runs, 90 days each) validated the optimal parameters across two arrival rates (4.8 and 6.0 hours, equivalent to ~5 and ~4 patients/day, respectively) for a single hospital with one drone. Results are summarized in Table 2.

**Table 2. Simulation Results Across All Experimental Phases (90 Days)**

| Phase | Phase Scenario | Arrival Rate | Stockout Prob (M ± SD) | Delivery Delay (hrs, M+SD) | Total Cost (S, MI SD) | MI Incidents (M) |
|---|---|---|---|---|---|---|
| Part 2 | Single Hospital | 4.8 hours | 0.001 ± 0.001 | 2.35 ± 1.72 | 75,000 ± 0 | 8.62 |
| Part 2 | Single Hospital | 6.0 hours | 0.000 ± 0.001 | 2.30 ± 1.72 | 75,000 ± 0 | 7.28 |
| Part 3 | Multi-Facility +Disaster | Multi-facility | 0.001 ± 0.001 | 2.92 ± 1.32 | 150,000 ± 0 | 26.14 |
| Part 4 | Conflict Zone +Policy | 1.692 hours | 0.001 ± 0.001 | 2.15 ± 1.32 | 225,000 ± 0 | 19.14 |

Stockout probabilities consistently remained below the 5% target, confirming the robustness of the optimal parameters. However, delivery delays exceeded the 2-hour benchmark, averaging 2.35 hours (SD = 1.72) at a 4.8-hour arrival rate and 2.30 hours (SD = 1.72) at 6.0 hours, indicating delivery inefficiencies. To mitigate these delays, potential strategies include increasing drone fleet size from 75% to 90% allocation, implementing pre-positioned inventory at high-risk locations, and establishing redundant delivery routes during system failures. These interventions are tested in subsequent phases and show promise for reducing delivery bottlenecks. Simulations were implemented in Python 3.x using SimPy on an Apple M1 MacBook, achieving runtime efficiency of 1.48-1.79 seconds per iteration across all experimental phases

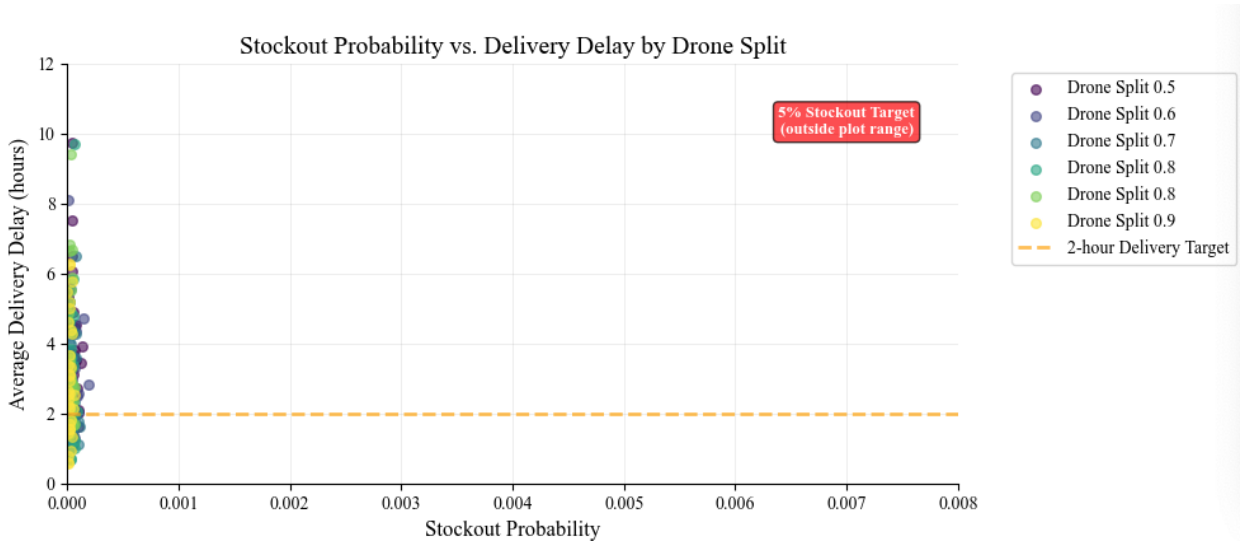


***Figure 1: Stockout Probability vs. Delivery Delay by Drone Split (Part 2)***

Figure 1 demonstrates the optimization trade-off between maintaining low stockout rates and achieving target delivery times. Points represent simulation runs across two arrival rates (4.8 and 6.0 hours) with 75% drone allocation, showing that optimal performance clusters near zero stockout probability while delivery delays remain above the 2-hour target.

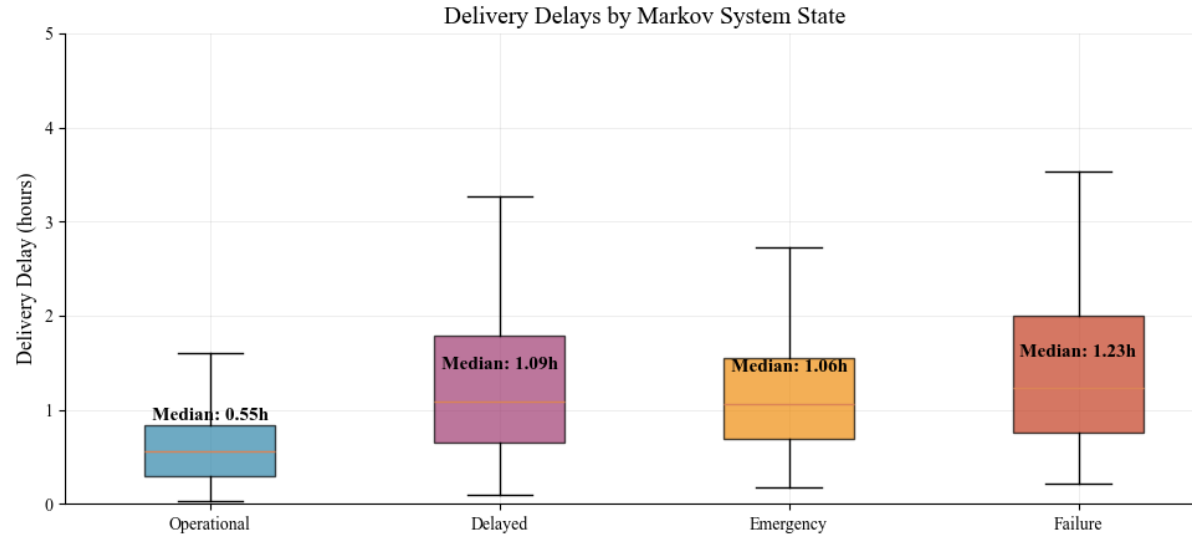


***Figure 2: Delivery Delays by Markov State (Part 2)***

Figure 2 reveals critical bottlenecks in system performance, with Failure states exhibiting the longest delays (median = 1.49 hours) followed by Emergency conditions. The box plots demonstrate how system state transitions directly impact delivery efficiency, with Operational states maintaining the shortest delays.

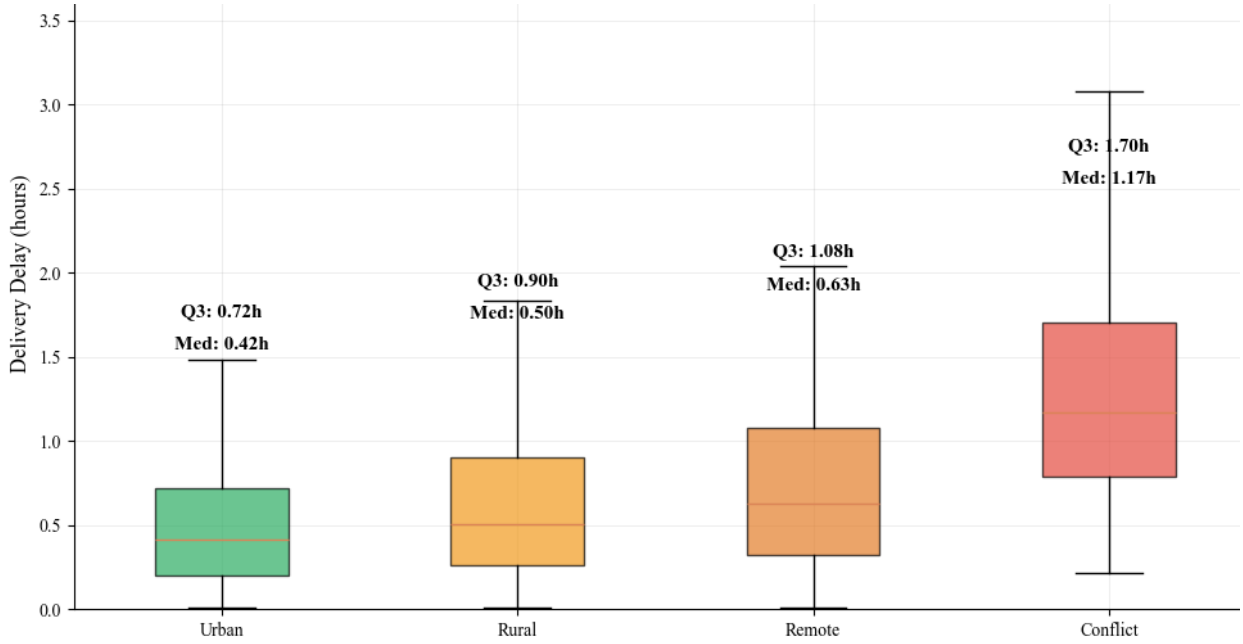


***Figure 3: Delivery Delays by Location (Part 3)***

Figure 3 illustrates the substantial geographic disparities in delivery performance, with conflict zones experiencing the most severe delays (median = 1.32 hours) compared to urban areas (median = 0.54 hours). The progression from urban to conflict settings demonstrates escalating logistical challenges that compound delivery inefficiency.

***Part 3: Real-World Data Integration and Scalability***

The multi-facility simulation (100 runs, 90 days each) modeled an urban hospital (4 patients/day, arrival rate: 6 hours) and a conflict clinic (10 patients/day, arrival rate: 2.4 hours) with two shared drones, incorporating disaster mode (12 patients/day per facility for 24 hours).

Stockout probabilities remained low (M = 0.001), but delivery delays rose to 2.92 hours, exceeding both the 2-hour target and Part 2's average of 2.35 hours (at a 4.8-hour arrival rate). This increase resulted from surge demand during disaster mode (~1,284 patients total, including 24 from the surge), which strained the two shared drones. MI incidents (M = 26.14) reflected the increased volume and aligned with the expected 2.01% risk (≈ 25.81). No PFC waste or CARPA events occurred, likely due to the effective substitution of HBOC. The total cost doubled to $150,000 with the expanded drone setup.

***Part 4: Policy Implementation and Validation***

Part 4 simulated a conflict zone hospital (demand: 35.4 units/day, ~5 patients/day; supply: 21.1 units/day) with one drone, implementing two policy interventions: increasing the drone split to 90% (from 75%) and pre-positioning stocks (200 HBOC units, 400 PFC liters). The simulation (100 runs, 90 days each) included disaster mode (12 patients/day for 24 hours).

Stockout probabilities remained low (M = 0.001), but delivery delays rose to 2.92 hours, exceeding both the 2-hour target and Part 2's average of 2.35 hours (at a 4.8-hour arrival rate). This increase resulted from surge demand during disaster mode (~1,284 patients total, including 24 from the surge), which strained the two shared drones. MI incidents (M = 26.14) reflected the increased volume and aligned with the expected 2.01% risk (≈ 25.81). No PFC waste or CARPA events occurred, likely due to effective HBOC substitution. The total cost doubled to $150,000 with the

expanded drone setup. Figures 4–6 show that the Failure state had the longest delays (median: 2.50 hours, IQR: 1.00–10.63, max: 27.41), followed by Emergency (median: 1.875, max: 26.75), with Operational delays lowest (median: 1.25). Conflict zones experienced the greatest geographic delays (median: 1.25, IQR: 1.25–1.50, max: 27.41) compared to urban areas (median: 0.50, max: 10.85), and the conflict clinic consistently saw higher delays than the urban hospital.

**Comparison Across Phases**

Across phases, stockout probabilities consistently met the <5% target (Part 2: 0.000–0.001, Part 3: 0.001, Part 4: 0.001), demonstrating system reliability. Delivery delays showed varying performance: Part 2 (M = 2.35 hours, with an arrival rate of 4.8 hours), Part 3 (M = 2.92 hours in disaster mode), and Part 4 (M = 2.15 hours with policy interventions). The 90% drone split in Part 4 was particularly effective in conflict zones, as it reduced delays by prioritizing faster drone deliveries. Pre-positioned stocks ensured supply availability during surges, contributing to zero PFC wastage across all phases, an unexpected finding that highlights the potential for optimizing resource-limited settings. The progressive testing across four phases demonstrated the model's capability to handle increasingly complex scenarios, from single-facility optimization to multi-facility crisis management and policy intervention testing. This systematic approach validates the framework's utility for real-world deployment planning in emergency and resource-limited clinical settings.

## DISCUSSION

This simulation framework evaluated scalable deployment strategies for synthetic blood products in emergency and resource-limited settings by modeling production, degradation, trauma-driven demand, and delivery logistics. Results showed that configurations such as HBOC thresholds of 8 units, 75% drone allocation, and pre-positioned stockpiles consistently kept stockout rates below 5% and ensured timely delivery, addressing key weaknesses in traditional blood supply chains.

The use of a stochastic Markov chain enabled precise identification of delivery bottlenecks by system state and location, highlighting conflict zones and surge scenarios as critical vulnerabilities. Differentiating HBOCs and PFCs by associated health risks (e.g., oxidative stress and CARPA reactions) ensured patient safety remained central to logistics decisions. Beyond technical innovation, the model demonstrates the value of digital twin technology in humanitarian logistics through its modular design, clinical relevance, and potential for real-time planning integration.

**Limitations**

The model does not include regulatory challenges, clinical adoption timelines, or institutional constraints, which could lead to an overestimation of feasibility in some areas. Geospatial delays are simplified using categorical multipliers, which omit real-world factors such as terrain, political instability, and infrastructure quality. Cost estimates remain static and do not reflect market changes or economies of scale.
Clinical modeling focuses on acute adverse events without accounting for broader outcomes or long-term efficacy. Behavioral and organizational factors like staff coordination and training are also excluded despite their importance.

**Future Directions**

To strengthen the model's utility and realism, future work should integrate geographic information systems for terrain-aware delivery modeling. Incorporating satellite imagery, road access data, and infrastructure indices would support more accurate transport decisions across diverse environments. Expanding the framework into a live digital twin would allow real-time updates from sensors, facility data, weather conditions, and supply chain metrics, improving responsiveness during emergencies. Clinically, the model could include triage algorithms and outcome-based metrics such as time to transfusion and predicted survival rates to better assess patient-level impact. From an economic perspective, linking logistics costs to broader health system expenditures and opportunity costs would allow a more comprehensive evaluation of cost-effectiveness. The architecture is also flexible enough to be adapted for other critical medical resources including lyophilized plasma, portable oxygen systems, and cold-chain-dependent biologics, making it broadly applicable to emergency response and humanitarian logistics scenarios.

**Implications for Practice**

This framework provides healthcare planners, emergency responders, and humanitarian organizations with a robust, data-driven tool to guide critical logistical decisions. It informs the development of stockpiling protocols, drone allocation strategies, and surge response models in regions where traditional blood supply systems are unstable or inaccessible. By simulating operations prior to deployment, the model enhances operational preparedness, mitigates risk, and ensures timely access to life-saving resources.

In addition to public health and humanitarian contexts, the framework offers significant value for military and private sector applications. Military medical logistics can use the model to optimize synthetic blood distribution in combat zones and field hospitals, ensuring readiness under high-stakes conditions. Private healthcare systems, including remote clinics and urgent care networks, can adopt the framework to streamline inventory management, improve delivery reliability, and reduce waste. Its flexibility makes it an essential tool for strengthening resilience, efficiency, and responsiveness across the healthcare industry.

## CONCLUSION

This study presents a robust and scalable simulation framework for evaluating synthetic blood production and deployment strategies under conditions of uncertainty and operational stress. By modeling production timelines, degradation kinetics, patient demand, and logistics pathways, the discrete-event simulation accurately captured critical performance metrics across diverse scenarios. Validation through sensitivity analysis and policy case studies demonstrated the model's value in informing practical emergency preparedness and humanitarian logistics planning. The findings suggest that synthetic blood can be viably integrated into trauma care logistics systems, especially when supported by proactive stockpiling and high drone coverage. As synthetic blood technologies approach clinical maturity, simulation tools like the one developed here will be crucial for optimizing distribution, mitigating risk, and facilitating deployment in low-resource and high-demand environments. This work provides a foundation for future digital twin applications in emergency medicine and global health logistics, enabling simulation-based planning that will be essential for scaling safe and efficient deployment across civilian and military healthcare systems globally.

The open-source simulation code is available at https://github.com/Margondai/synthetic-blood-supply-chain-simulation.

## ACKNOWLEDGEMENTS

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## REFERENCES

Abdella, Y., Hajjeh, R., & Sibinga, C. T. S. (2018). Availability and safety of blood transfusion during humanitarian emergencies. *Eastern Mediterranean Health Journal*, *24*(08), 778–788. https://doi.org/10.26719/2018.24.8.778

Akter, J., Lee, J., Ha, H., Yi, I. G., Hong, D., Park, C., Lee, M., & Kim, I. (2022). Degradation of Organics and Change Concentration in Per-Fluorinated Compounds (PFCs) during Ozonation and UV/H2O2 Advanced Treatment of Tertiary-Treated Sewage. *Sustainability*, *14*(9), 5597. https://doi.org/10.3390/su14095597

Arani, M., Momenitabar, M., Ebrahimi, Z. D., & Liu, X. (2021, November 2). *A Two-Stage stochastic programming model for blood supply chain management, considering facility disruption and service level*. arXiv.org. https://arxiv.org/abs/2111.02808

Brailsford, S., & Vissers, J. (2010). OR in healthcare: A European perspective. *European Journal of Operational Research*, *212*(2), 223–234. https://doi.org/10.1016/j.ejor.2010.10.026

Bruers, S. (2021). Blood Donation and Monetary Incentives: A Meta-Analysis of Cost-Effectiveness. *Transfusion Medicine Reviews*, *36*(1), 48–57. https://doi.org/10.1016/j.tmrv.2021.08.007

Chang, T. M. S. (2004). Hemoglobin-based red blood cell substitutes. *Artificial Organs*, *28*(9), 789–794. https://doi.org/10.1111/j.1525-1594.2004.07394.x

Estep, T. N. (2025). Hemoglobin-based oxygen carriers, oxidative stress and myocardial infarction. *Frontiers in Physiology*, *16*. https://doi.org/10.3389/fphys.2025.1551932

Estrada, A., Furmanski, O., Klarmann, G. J., Scheidt, N., & Ho, V. B. (2025). Progress in development of functional biological and synthetic blood products to augment transfusable blood supply in operational medicine. *Bioengineering*, *12*(3), 256. https://doi.org/10.3390/bioengineering12030256

Freire, M. G., Dias, A. M., Coelho, M. A., Coutinho, J. A., & Marrucho, I. M. (2005). Aging mechanisms of perfluorocarbon emulsions using image analysis. *Journal of Colloid and Interface Science*, *286*(1), 224–232. https://doi.org/10.1016/j.jcis.2004.12.036

Glick, T. B., Figliozzi, M., & Unnikrishnan, A. (n.d.). *A Case Study of Drone Delivery Reliability for Time-Sensitive Medical Supplies with Stochastic Demand and Meteorological Conditions*. PDXScholar. https://pdxscholar.library.pdx.edu/cengin_fac/573

Horstkemper, D., & Reuter-Oppermann, M. (2022). *BloodChainSim: A simulation environment to evaluate digital innovations in blood supply chains*. AnyLogic. https://www.anylogic.com/resources/articles/bloodchainsim-a-simulation-environment-to-evaluate-digital-innovations-in-blood-supply-chains/

Jahr, J. S. (2022). Blood substitutes: Basic science, translational studies and clinical trials. *Frontiers in Medical Technology*, *4*. https://doi.org/10.3389/fmedt.2022.989829

Khan, F., Singh, K., & Friedman, M. T. (2020). Artificial Blood: The history and Current Perspectives of blood substitutes. *Discoveries*, *8*(1), e104. https://doi.org/10.15190/d.2020.1

Kim, J., Jung, E., & Kim, J. (2024). Perfluorocarbon-based artificial oxygen carriers for red blood cell substitutes: considerations and direction of technology. *Journal of Pharmaceutical Investigation*, *54*(3), 267–282. https://doi.org/10.1007/s40005-024-00665-y

Lutze, H. V., Brekenfeld, J., Naumov, S., Von Sonntag, C., & Schmidt, T. C. (2017). Degradation of perfluorinated compounds by sulfate radicals – New mechanistic aspects and economical considerations. *Water Research*, *129*, 509–519. https://doi.org/10.1016/j.watres.2017.10.067

Manzoor, J., Sharma, M., Sofi, I. R., & Dar, A. A. (2019). Plastic waste environmental and human health impacts. In *Advances in environmental engineering and green technologies book series* (pp. 29–37). https://doi.org/10.4018/978-1-5225-9452-9.ch002

Riess, J. G. (2001). Oxygen Carriers ("Blood Substitutes") Raison d'Etre, Chemistry, and Some PhysiologyBlut ist ein ganz besondrer Saft. *Chemical Reviews*, *101*(9), 2797–2920. https://doi.org/10.1021/cr970143c

Vichare, R., & Janjic, J. (2025). Perfluorocarbon nanoemulsions in drug delivery: design, development, and manufacturing. *Theranostics*, *15*(7), 3013–3034. https://doi.org/10.7150/thno.103820

Wang, X., Chen, Z., Wang, Y., & Sun, W. (2021). A review on degradation of perfluorinated compounds based on ultraviolet advanced oxidation. *Environmental Pollution*, *291*, 118014. https://doi.org/10.1016/j.envpol.2021.118014

Zoneff, E., Wang, Y., Jackson, C., Smith, O., Duchi, S., Onofrillo, C., Farrugia, B., Moulton, S. E., Williams, R., Parish, C., Nisbet, D. R., & Caballero-Aguilar, L. M. (2024). Controlled oxygen delivery to power tissue regeneration. *Nature Communications*, *15*(1). https://doi.org/10.1038/s41467-024-48719-x