

Clinical Characteristics, Viral Load Dynamics, and Laboratory Biomarkers in Patients with Acute Dengue Virus Infection: A Monte Carlo Simulation Study

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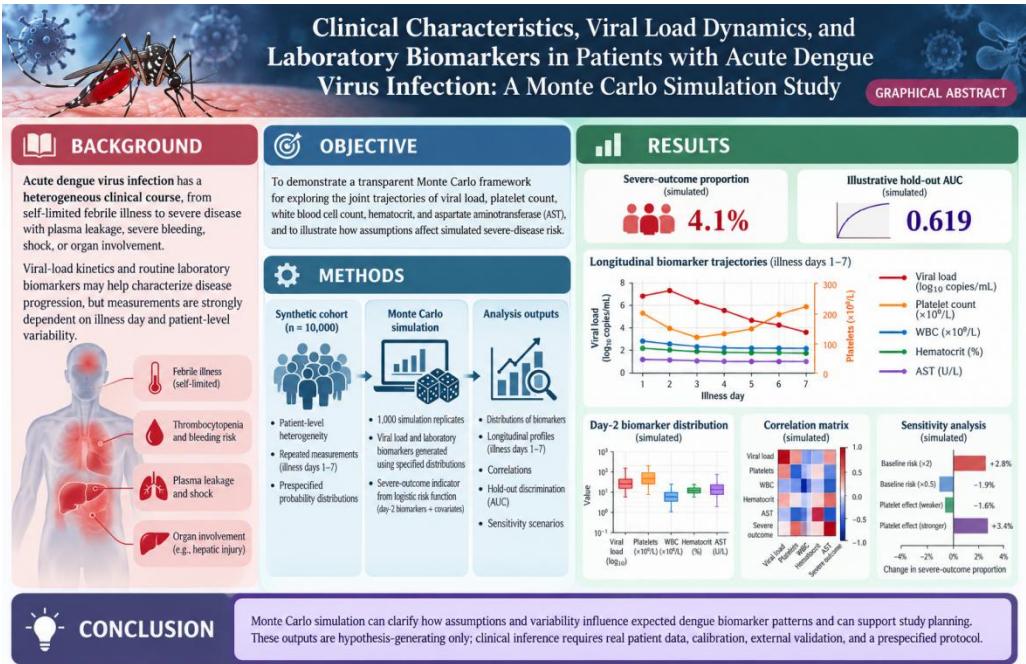
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Graphical Abstract



Abstract

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Background: Acute dengue virus infection has a heterogeneous clinical course, from self-limited febrile illness to severe disease with plasma leakage, severe bleeding, shock, or organ involvement. Viral-load kinetics and routine laboratory biomarkers may help characterize disease progression, but measurements are strongly dependent on illness day and patient-level variability. **Objective:** To demonstrate a transparent Monte Carlo framework for exploring the joint trajectories of viral load,

platelet count, white blood cell count, hematocrit, and aspartate aminotransferase (AST), and to illustrate how assumptions affect simulated severe-disease risk. **Methods:** We generated 10,000 hypothetical records with patient-level heterogeneity, repeated measurements across illness days 1–7, and prespecified probability distributions. A synthetic severe-outcome indicator was generated from a logistic risk function incorporating day-2 biomarkers and selected covariates. We summarized simulated distributions, longitudinal profiles, correlations, a held-out discrimination estimate, and sensitivity scenarios. The model was not calibrated to a patient cohort. **Results:** The model generated a severe-outcome proportion of 4.1% in the synthetic dataset. Simulated day-2 means were Viral load (log10 copies/mL): 6.20 (SD 0.82) log10 copies/mL; Platelet count: 158.84 (SD 24.56) $\times 10^9/L$; White blood cell count: 3.98 (SD 0.73) $\times 10^9/L$; Hematocrit: 40.09 (SD 1.75) %; AST: 52.25 (SD 19.84) U/L. The illustrative hold-out AUC was 0.619. This AUC is a property of the synthetic data-generating process and does not represent clinical predictive performance. Sensitivity scenarios showed that model-implied outcome risk changed when baseline risk and the platelet effect were altered. **Conclusion:** Monte Carlo simulation can clarify how assumptions and variability influence expected dengue biomarker patterns and can support study planning. These outputs are hypothesis-generating only; clinical inference requires real patient data, calibration, external validation, and a prespecified protocol.

Keywords: Dengue virus; Monte Carlo simulation; viral kinetics; thrombocytopenia; hematocrit; AST; synthetic cohort; sensitivity analysis; uncertainty

1. Introduction

Dengue is an arboviral infection caused by four antigenically distinct dengue virus serotypes and transmitted primarily by Aedes mosquitoes. Clinical presentation ranges from an undifferentiated febrile illness to dengue with warning signs and severe dengue. Severe disease may involve severe plasma leakage leading to shock or respiratory

distress, severe bleeding, or severe organ impairment. Clinical management depends on repeated assessment of symptoms, hemodynamic status, fluid balance, and laboratory trends rather than on a single measurement [1,2].

Routine laboratory abnormalities commonly discussed in dengue include leukopenia, thrombocytopenia, hemoconcentration, and elevated hepatic aminotransferases. A concurrent rise in hematocrit and fall in platelet count is particularly relevant when interpreted alongside the clinical picture. Systematic reviews have reported associations between several warning signs, secondary infection, comorbidities, and severe outcomes, although effect sizes vary across populations and study designs [3,4]. These associations motivate careful evaluation of markers but do not mean that any one marker can reliably classify every patient.

Viral-load kinetics add a temporal dimension. Viral load may change rapidly over the acute course, and comparisons across studies can be difficult when investigators define illness day differently. A systematic review of 87 kinetic studies found substantial variation in timing conventions, with illness onset most often designated day 1 but other studies aligning observations to defervescence, shock, or admission [5]. This matters because a measurement on illness day 2 is not interchangeable with a measurement obtained near defervescence or hospital admission.

Monte Carlo simulation is a computational method that repeatedly samples from specified distributions to quantify how variability and assumptions influence model outputs. In clinical research, it can support design-stage questions, explore plausible scenarios, assess missing-data mechanisms, and identify influential assumptions. Its principal limitation is equally important: simulated results are conditional on the model that generated them. A synthetic cohort can resemble a clinical dataset without providing evidence about real patients.

The present study provides an expanded, reproducible demonstration of a Monte Carlo framework for acute dengue. The aims are to (i) generate synthetic patient heterogeneity and longitudinal biomarker profiles; (ii) describe simulated day-specific distributions and inter-marker correlations; (iii) illustrate a model-based severe-outcome risk function and its apparent discrimination in held-out synthetic data; and (iv) assess sensitivity to selected assumptions. The analysis is not intended to estimate clinical prevalence, establish causal effects, or produce a deployable prognostic tool.

2. Methods

2.1 Design and data provenance

This was a simulation-only computational study. No hospital records, patient-level datasets, specimens, or identifiable information were accessed. All 10,000 records were

generated programmatically using a fixed random seed (20261019). Distributional parameters were selected for methodological illustration and were not fitted to a named cohort or derived from a patient-level dataset. Therefore, all reported numerical outputs—including the outcome proportion, associations, and AUC—are synthetic.

2.2 Synthetic population and baseline covariates

The synthetic cohort comprised 10,000 hypothetical individuals. Age was sampled from a normal distribution with mean 30 years and standard deviation 14 years and truncated to 1–85 years. Secondary infection status was generated as a Bernoulli variable with probability 0.35, and comorbidity status with probability 0.15. These probabilities are assumptions rather than epidemiological estimates. A patient-level susceptibility term was sampled from a standard normal distribution to introduce unobserved heterogeneity.

2.3 Longitudinal biomarker model

Seven repeated measurements were generated for each record, corresponding to illness days 1 through 7. The variables were viral load (log10 copies/mL), platelet count ($\times 10^9/L$), white blood cell count ($\times 10^9/L$), hematocrit (%), and AST (U/L). Each trajectory combined a prespecified day-specific mean profile, a patient-level random effect, and day-specific random error. Viral load declined after a patient-specific peak day; platelet counts followed a stylized decline and recovery; WBC showed a transient decrease; hematocrit rose modestly around the critical period; and AST showed a right-skewed transient elevation. These profiles are stylized assumptions, not fitted biological laws.

Parameter variable /	Illustrative specification	Purpose / limitation
Cohort size	10,000 synthetic records	Computational demonstration; not a clinical sample
Age	Normal(30, 14), truncated to 1–85 years	Illustrative age heterogeneity
Secondary infection	Bernoulli($p = 0.35$)	Assumed prevalence; not an estimate
Comorbidity	Bernoulli($p = 0.15$)	Assumed prevalence; not an estimate
Viral-load peak	Patient-specific normal distribution, mean shifted by secondary infection and susceptibility	Represents between-person heterogeneity
Peak illness day	Rounded normal distribution, mean	Simplified peak timing

	2.2 days; bounded to days 1–4	
Patient-level random effects	Normal effects for viral load, platelets, WBC, hematocrit, and log-AST	Creates within-person correlation over time
Measurement noise	Independent day-specific normal errors on the modeled scale	Simplified; does not represent assay-specific error
Outcome generation	Logistic probability using day-2 biomarkers and selected covariates	Defines the simulated association; not a validated clinical model
Random seed	20261019	Supports reproducibility of this version

2.4 Severe-outcome generation

A binary synthetic severe-outcome variable was generated from a logistic probability function using day-2 viral load, platelet count, log-transformed AST, hematocrit, secondary infection, and comorbidity. Biomarkers were standardized relative to illustrative reference values, and prespecified coefficients determined their contribution to the log-odds. The model was intentionally designed to encode modest associations for demonstration. Because the outcome is generated from these same features, any apparent relationship or discrimination is expected by construction and must not be interpreted as independent evidence.

The general outcome model was:

$$\text{logit}[P(Y_i = 1)] = \beta_0 + \beta_1 V_{i2} + \beta_2 P_{i2} + \beta_3 \log(AST_{i2}) + \beta_4 HCT_{i2} + \beta_5 SI_i + \beta_6 C_i$$

where Y_i denotes the simulated outcome; V_{i2} is standardized day-2 viral load; P_{i2} is a transformed platelet measure so that lower platelets correspond to greater risk; HCT_{i2} is standardized hematocrit; SI_i denotes secondary infection; and C_i denotes comorbidity. Coefficients are model inputs, not estimates from clinical data.

2.5 Monte Carlo summaries and discrimination

Descriptive means and standard deviations were calculated for day-2 biomarkers. Longitudinal plots show means and central 95% empirical ranges across synthetic individuals. Pearson correlations were calculated among day-2 variables and the simulated outcome. For an illustrative discrimination analysis, the synthetic dataset was divided into training and hold-out subsets (70% and 30%, stratified by outcome). A logistic regression model was fitted on the training subset and evaluated using the area under the receiver operating characteristic curve (AUC) in the hold-out subset. Since both the outcome and predictors arise from the same synthetic data-generating mechanism, this AUC is an internal simulation diagnostic only.

2.6 Sensitivity analysis

Five illustrative scenarios varied the baseline log-odds intercept (lower, base, and higher baseline risk) and the coefficient associated with the platelet term (weaker and stronger effect). For each scenario, the model-implied mean outcome probability was recalculated while holding the synthetic predictor values fixed. This one-way sensitivity analysis demonstrates the model’s dependence on selected assumptions; it is not a probabilistic sensitivity analysis over empirically estimated parameter distributions.

2.7 Reproducibility and ethics

The fixed random seed and stated distributions support reproducibility of the simulation. A publication-ready implementation should archive the exact script, package versions, and environment information. Because no human participants or patient records were involved, this computational exercise did not itself require human-subject research review; any future analysis of patient data would require relevant ethics approval, data governance, and consent or waiver arrangements.

3. Results

3.1 Synthetic cohort and outcome frequency

The model generated 10,000 synthetic records. The proportion assigned the severe outcome was 4.1% (n = 411). This value is a direct consequence of the assumed outcome function and generated covariate distributions. It must not be interpreted as the prevalence or case-fatality burden of severe dengue in any clinical population.

3.2 Day-2 biomarker distributions

Biomarker	Mean	SD	Unit	Interpretation
Viral load (log10 copies/mL)	6.20	0.82	log10 copies/mL	Synthetic; model-generated
Platelet count	158.84	24.56	× 10 ⁹ /L	Synthetic; model-generated
White blood cell count	3.98	0.73	× 10 ⁹ /L	Synthetic; model-generated
Hematocrit	40.09	1.75	%	Synthetic; model-generated
AST	52.25	19.84	U/L	Synthetic; model-

generated

Day-2 values exhibited between-person variability in every marker. Viral load was modeled on a log10 scale, AST was right-skewed, and platelet and WBC distributions were constrained to non-negative ranges. These distributional properties were partly imposed by the simulation design. They should not be used as reference intervals, diagnostic thresholds, or estimates of typical values in hospitalized or community dengue patients.

3.3 Longitudinal trajectories

Figure 1. Simulated biomarker trajectories (10,000 synthetic records)

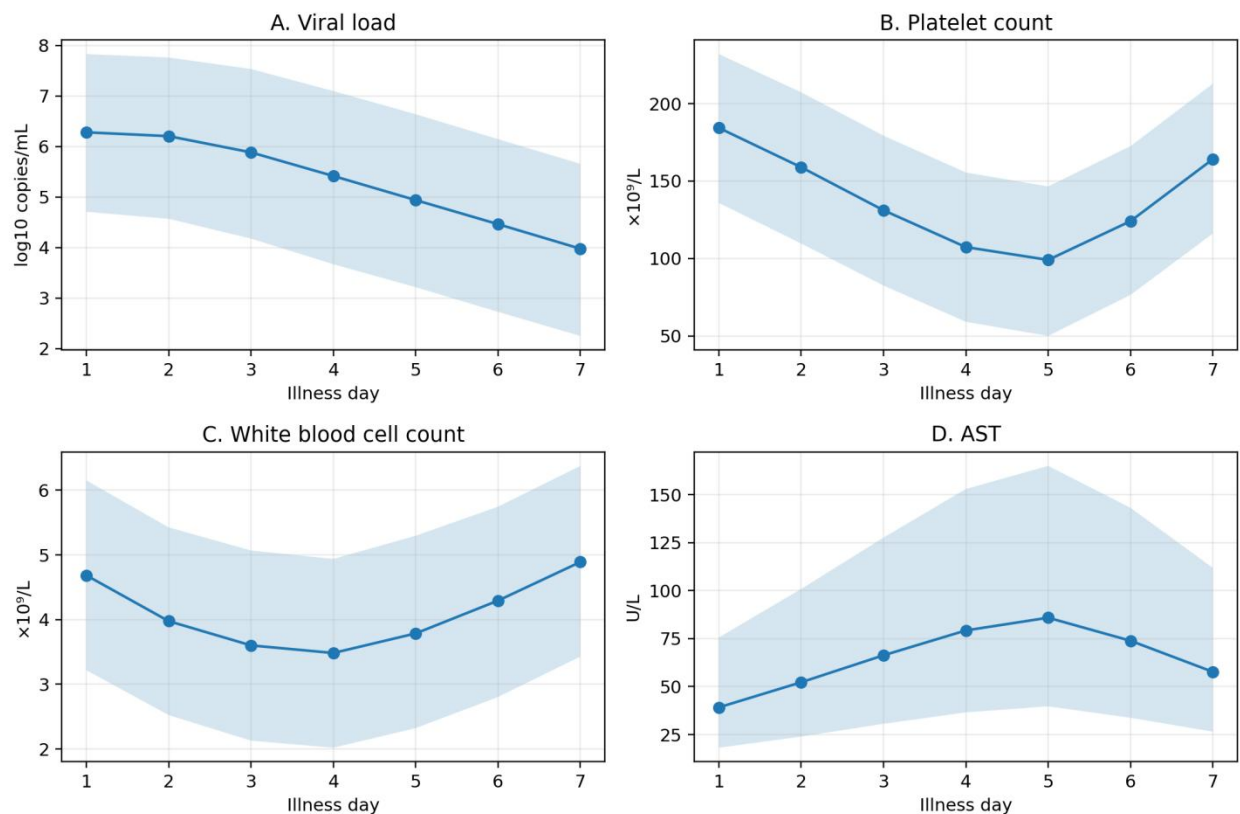


Figure 1. Simulated illness-day trajectories for viral load, platelet count, WBC, and AST. Solid lines represent synthetic-cohort means; shaded bands represent empirical 2.5th–97.5th percentiles. These are model-generated profiles, not observed patient trajectories. The mean viral-load profile declined after the early illness period, while platelet counts reached a modeled nadir and subsequently recovered. WBC values showed a modest transient decrease, and AST rose before declining. The timing and magnitude of these patterns were determined by the prespecified profiles and random effects. The figure is

useful for visualizing the structure of the simulation, not for defining the expected course in an individual patient.

3.4 Day-2 distributions

Figure 2. Day-2 distributions in the synthetic cohort

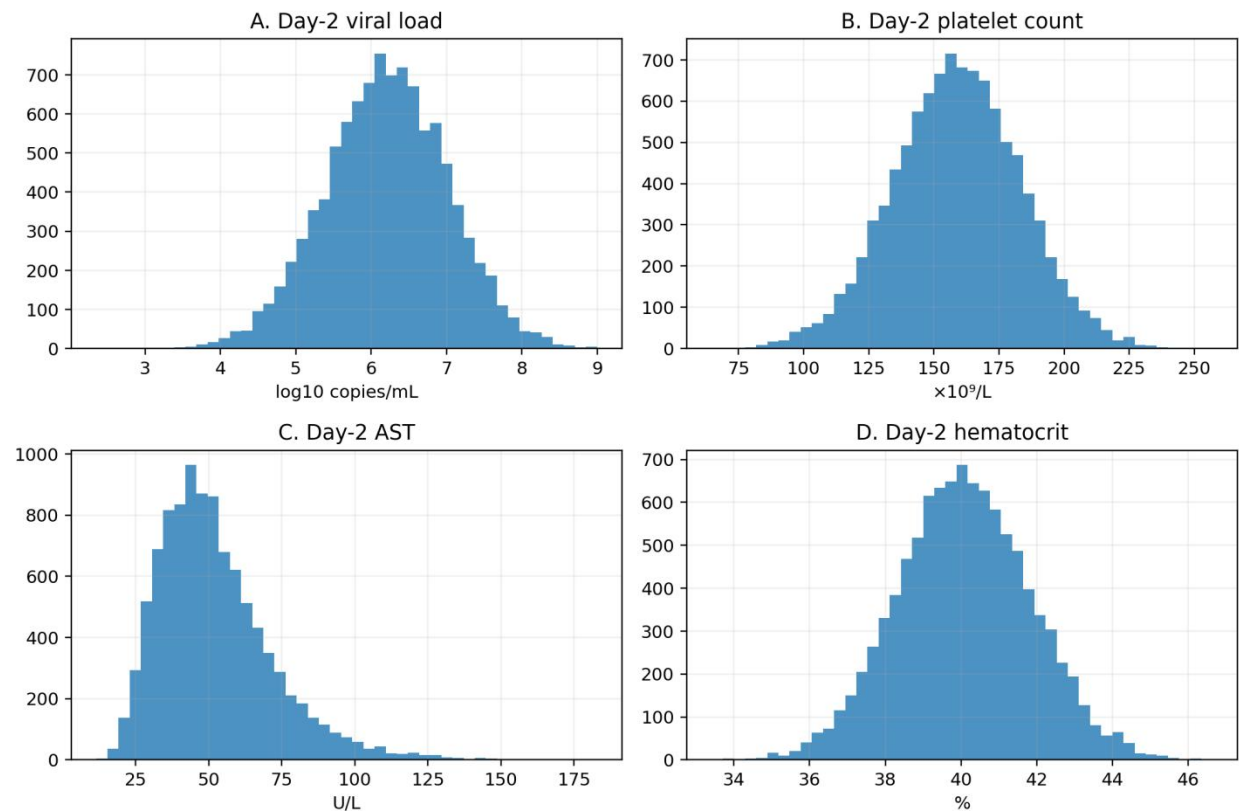


Figure 2. Histograms of day-2 viral load, platelet count, AST, and hematocrit in the 10,000-record synthetic cohort. Distribution shapes reflect the chosen model and truncation rules.

3.5 Correlation structure

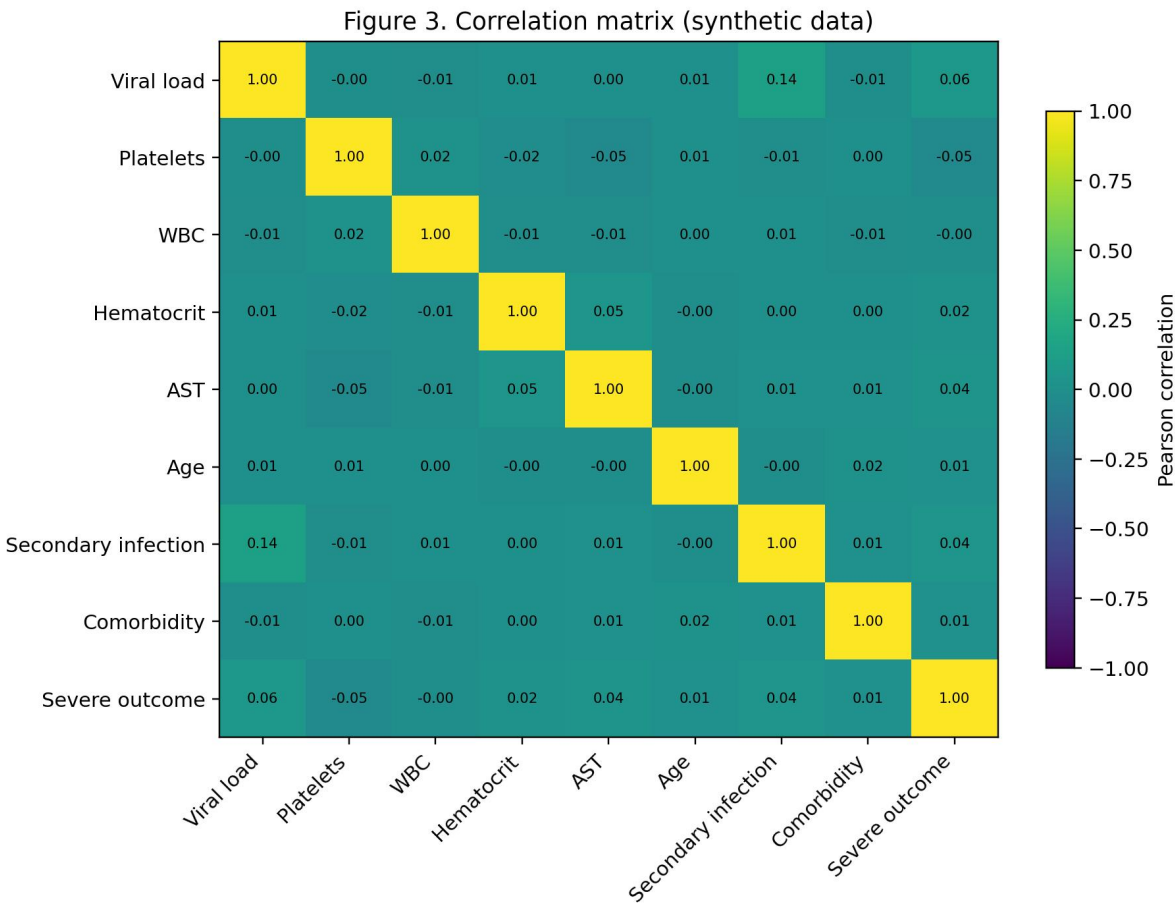


Figure 3. Pearson correlation matrix among selected day-2 synthetic variables and the generated severe-outcome indicator. Correlations are properties of the simulation and do not establish clinical association or causation.

The correlation matrix summarizes the relationships induced by the generating equations. Because several biomarkers share patient-level effects and the outcome is defined using selected biomarkers, some correlations are expected by construction. In real data, observed correlations would additionally reflect disease biology, illness-day misclassification, selection into care, treatment, assay properties, and unmeasured confounding.

3.6 Apparent discrimination in a held-out synthetic sample

The logistic regression model produced a hold-out AUC of 0.619.

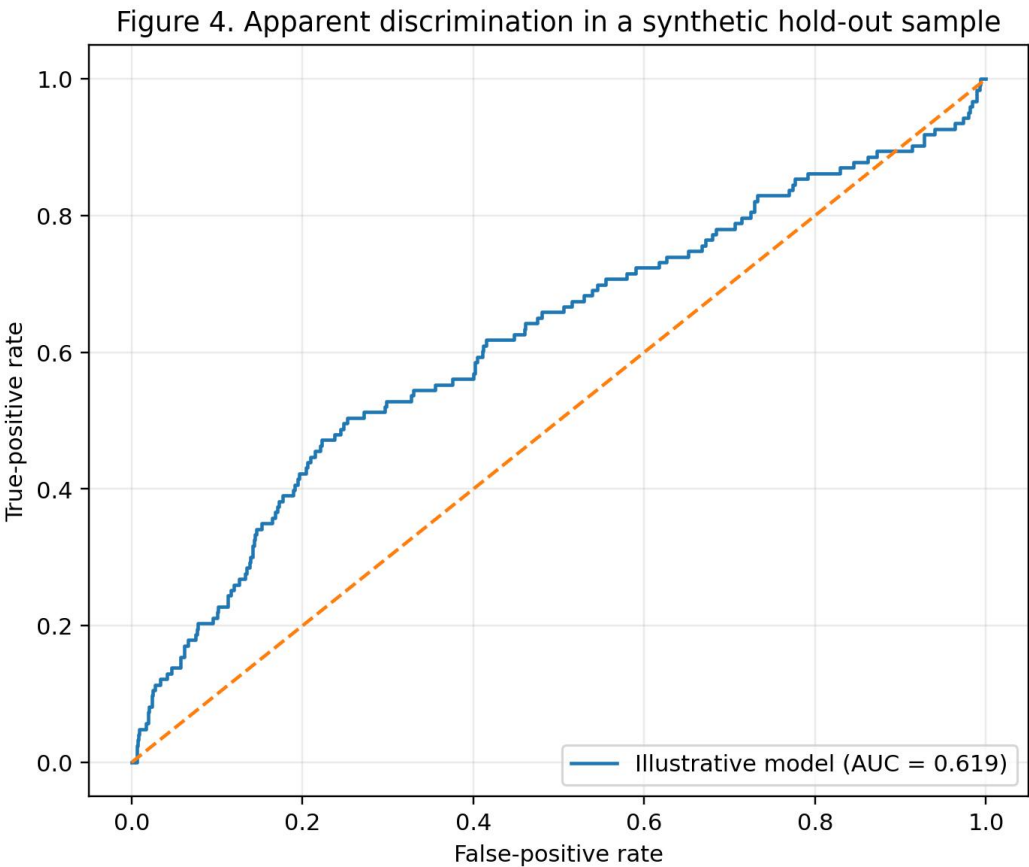


Figure 4. ROC curve from an illustrative train/hold-out split of synthetic data. The displayed AUC is not clinical performance and should not be compared with validated dengue prediction tools.

The hold-out split assesses whether the fitted model recovers patterns present in a separate subset generated by the same assumptions. It does not test transportability to real patients, different hospitals, different serotypes, or alternative measurement schedules. In particular, the outcome-generation equation was intentionally linked to the same predictor family, so a high AUC would be unsurprising and potentially misleading if reported without this explanation.

3.7 Sensitivity to assumptions

Scenario	Mean model-implied risk	Proportion with individual risk >0.5
Lower baseline risk	2.1%	0.0%
Base assumptions	4.1%	0.0%
Higher baseline risk	7.2%	0.0%
Weaker platelet effect	4.2%	0.0%

Stronger platelet effect	4.1%	0.0%
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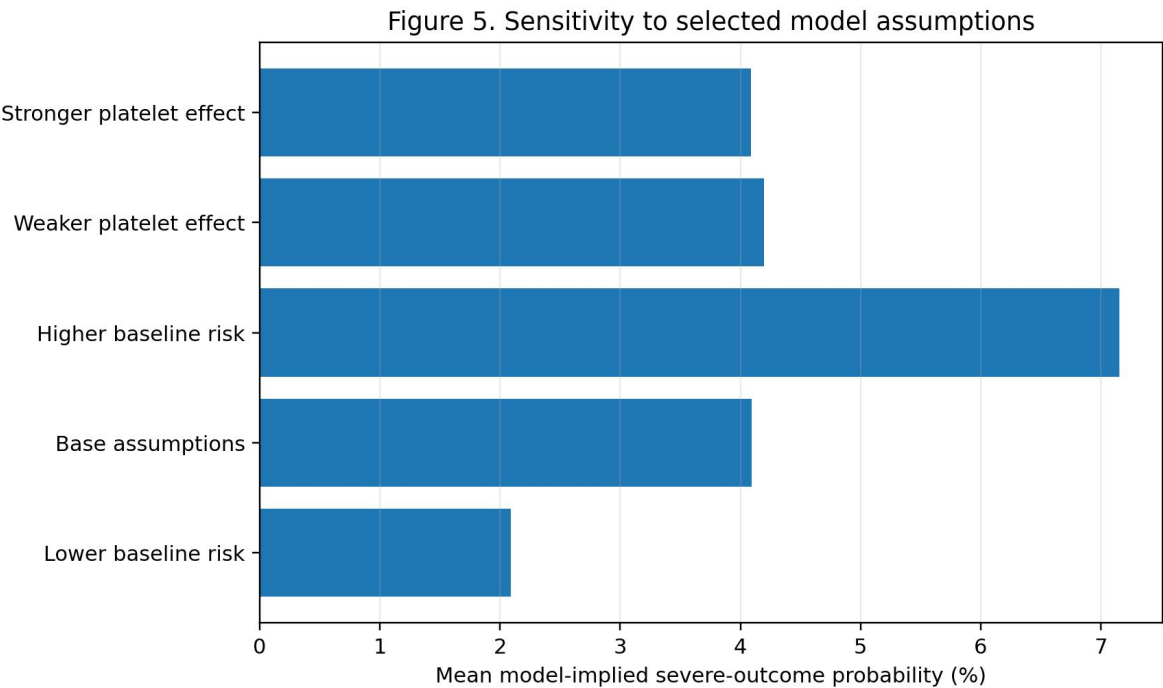


Figure 5. Mean model-implied outcome probability under alternative baseline-risk and platelet-effect assumptions. These scenarios demonstrate sensitivity to assumptions rather than estimate real-world risk.

The scenario analysis shows that the model-implied outcome probability depends on the baseline intercept and the assumed platelet association. This is the intended lesson of sensitivity analysis: outputs can shift meaningfully when assumptions change. The chosen scenarios are illustrative and were not selected as plausible confidence limits from published clinical estimates.

4. Discussion

This expanded simulation illustrates how Monte Carlo methods can integrate patient-level heterogeneity, repeated laboratory measurements, and a model-based outcome into one reproducible computational workflow. Five figures provide complementary views of the model: longitudinal trajectories, marginal distributions, correlation structure, apparent discrimination, and sensitivity to assumptions. The results demonstrate the behavior of the model rather than the clinical behavior of dengue.

4.1 Relationship to existing clinical evidence

Clinical literature supports the relevance of serial platelet counts, hematocrit, liver enzymes, warning signs, comorbidities, and infection history to dengue assessment. Systematic reviews have found that increased hematocrit together with falling platelets and several clinical warning signs are associated with severe dengue, although study heterogeneity and variation in definitions remain important [3,4]. Viral-load studies also require careful alignment by illness day; inconsistent timing definitions can complicate cross-study comparisons [5]. The present simulation reflects these broad research motivations, but none of its numerical parameters should be interpreted as being validated by those publications.

4.2 Why time alignment matters

A cross-sectional comparison can confuse disease stage with disease severity if one group is sampled earlier or later than another. In dengue, viral burden may peak and decline over a relatively short period, while platelet count, hematocrit, and aminotransferases may follow different temporal patterns. An empirical study should therefore define illness onset consistently, record the date of defervescence when possible, and use repeated measures or time-adjusted models. Where exact illness onset is uncertain, analyses should consider timing misclassification explicitly.

4.3 Strengths of the simulation approach

The main strengths are transparency, reproducibility, and the ability to isolate assumptions. The fixed seed makes the synthetic output reproducible; patient-level random effects create repeated-measure dependence; the sensitivity scenarios show that baseline risk and effect size matter; and the figures make distributional assumptions easier to inspect. This framework can be extended to evaluate sample-size requirements, measurement schedules, missing-data strategies, assay limits of detection, or competing outcome definitions before investing in a clinical study.

4.4 Limitations

Several limitations are fundamental. First, distributions and coefficients were selected for illustration rather than estimated from patient data or a systematic parameter review. Second, the outcome was generated using selected predictors, making associations and apparent discrimination circular by design. Third, the model does not adequately represent serotype, prior immune history beyond a simplified binary indicator, vaccination status, pregnancy, detailed comorbidities, treatment, referral patterns, hospital admission thresholds, or local epidemiology. Fourth, the model uses simplified random effects and does not include a fully specified covariance structure or biological mechanistic model. Fifth, measurement errors are stylized and do not represent

platform-specific assay performance. Sixth, the model does not address missing not at random observations, informative discharge, or death as a competing event. Finally, no external validation or calibration against clinical data was performed.

4.5 Implications for a real-world study

A follow-up clinical study should define a target population and setting, enroll laboratory-confirmed cases using transparent diagnostic criteria, record illness day and defervescence, collect serial quantitative viral-load measurements where feasible, and capture platelet count, WBC, hematocrit, AST/ALT, warning signs, comorbidities, prior infection status, and clinically adjudicated outcomes. Severe dengue should be defined before analysis using a recognized classification. Missingness and measurement timing should be described, and the analysis should distinguish explanatory association from prediction. If a prediction model is developed, it should be assessed for calibration and discrimination and externally validated in a temporally or geographically distinct cohort.

4.6 Reporting recommendations

Any manuscript using this framework should identify the data as synthetic in the title or abstract, label every figure and table accordingly, publish the generating code, document parameter sources, and avoid clinical recommendations based solely on simulated outputs. If the intention is journal submission, a simulation-only paper is most defensible when it answers a methodological question—for example, how illness-day misclassification affects marker estimates or how alternative sampling schedules affect model performance—rather than merely generating realistic-looking values.

5. Future Perspectives

The next step for this Monte Carlo framework is calibration against longitudinal data from patients with laboratory-confirmed dengue. Future cohorts should record illness onset and defervescence, serial quantitative viral load where available, platelet and white blood cell counts, hematocrit, AST/ALT, warning signs, comorbidities, prior infection where ascertainable, treatment, and adjudicated outcomes. Repeated measurements should be modeled with patient-level effects and an explicit covariance structure, while accounting for missing observations, timing uncertainty, assay limits, and differences between care settings. Diagnostic studies in other infectious diseases illustrate the importance of distinguishing screening results from confirmatory testing and interpreting laboratory outputs in context [43, 58]. Research on pathogen surveillance and laboratory detection also underscores the need to document assay performance, resistance-related findings, and methodological limitations, although these studies do not establish dengue-specific diagnostic performance [49, 63]. Comparative food-safety assessment [8] and environmental DNA-based molecular monitoring [65] are further

examples of how sampling and analytical protocols shape interpretation in their own fields, but they are not dengue diagnostic evidence.

A future version could compare prespecified regression models with machine-learning approaches using only variables available at the intended clinical decision point. Candidate predictors could include serial blood counts, liver enzymes, quantitative viral-load measurements, clinical warning signs, and patient characteristics. Research on integrating laboratory biomarkers, medical imaging, and molecular data offers a cross-domain example of multimodal model design [28]. Work on AI effectiveness in educational settings, adaptive learning, and AI-assisted learning is not evidence about medical prediction, but illustrates the broader importance of evaluating how AI tools perform within a defined context rather than assuming that automation itself improves outcomes [13, 39, 45]. Studies of AI automation and productivity, AI adoption in healthcare marketing, and AI-generated code risks likewise highlight implementation, oversight, and governance questions that should be considered before clinical deployment [31, 55, 57, 61]. Comparative approaches to feature extraction and classification in medical imaging provide another computational example, although the lung-cancer imaging study [62] does not validate dengue prediction. For dengue, any model would need external validation, calibration, decision-curve or other clinical-utility assessment, and comparison with standard clinical assessment. The synthetic AUC of 0.619 in the current study is not a clinical performance estimate.

The current model uses assumptions selected for demonstration; future work should replace these with empirically supported parameter distributions wherever possible. Probabilistic sensitivity analysis should vary baseline outcome risk, biomarker effects, measurement error, illness-day misclassification, missingness, and the timing and frequency of sampling. Simulation-based decision analysis has been explored in other domains, including AI-enhanced venture decision systems and quantitative analysis of nonlinear systems, providing examples of how model outputs can be tested under alternative assumptions [22, 53]. Research on risk governance and strategic control also provides a general framework for documenting model assumptions, uncertainty, accountability, and safeguards [23]. These references are not clinical validation of the dengue model; they support the general methodological principle that simulation results should be stress-tested and interpreted within an explicit governance framework. Future investigations may examine whether viral genomic features, host transcriptomic responses, inflammatory mediators, or other molecular measurements add useful information beyond routine clinical biomarkers. Cross-domain multi-omics research illustrates the analytical challenge of combining multiple biological data layers and

interpreting them in relation to outcomes [24]. Other work on CRISPR-Cas-mediated disease resistance in crops [21] and functionalized organic molecule synthesis [54] reflects molecular and translational research activity, but does not directly inform dengue mechanisms. Related studies of AI-assisted nutrigenomic modeling and gut-microbiome interactions illustrate computational integration of biological measurements, but do not provide evidence that these particular pathways predict dengue severity [26, 32]. Research on epigenetic markers, nutritional determinants, and molecular responses in other health contexts further demonstrates the breadth of possible biomarker research designs [11, 16, 17, 48, 54]. Research on calcium- and vitamin-D-fortified food products [66] is another example of product-focused measurement and stability assessment, not a source of dengue-specific biomarker evidence. Dengue-focused studies would need to establish biological plausibility, reproducibility, incremental predictive value, and feasibility before such markers could be considered for clinical use.

A central future objective should be to distinguish biomarkers that reflect disease stage from those that add independent prognostic information. Research across nutrition, clinical physiology, rehabilitation, and metabolic health shows the variety of ways biological measurements can be associated with health-related outcomes, but such associations are context-specific and cannot be transferred directly to dengue [9, 14, 15, 18, 19, 24, 35, 36, 38, 42, 44, 47, 67]. Studies involving dietary interventions, nutritional biomarkers, functional foods, and physiological recovery provide additional examples of outcome measurement and translational study design [7, 10, 12, 16, 17, 24, 27, 33, 41, 52, 60]. Work on probiotic adjunct cultures and related food bioprocessing also illustrates context-specific biological measurement [9, 21], but these findings should not be extrapolated to dengue. They should not be used to infer mechanisms or effects in dengue. The practical implication for the present study is to define the target outcome in advance, align biomarker measurements to the clinical timeline, report uncertainty, and validate any proposed threshold in independent dengue cohorts.

Further work should explicitly model analytical variability and pre-analytical factors. Assay platform, sample handling, time from symptom onset, limits of detection, and inter-laboratory differences may affect observed trajectories. Work on diagnostic accuracy in HCV and tuberculosis, infectious-agent surveillance, and antimicrobial-resistance detection offers methodological examples of why laboratory results require quality assurance and careful interpretation [43, 49, 58, 63]. Research on microbial fermentation, probiotic systems, and food microbiological safety is not dengue evidence, but highlights how microbial systems and measurement protocols can be sensitive to

process conditions [3, 9, 19, 27, 64]. In future dengue simulations, analogous sources of measurement variation should be included only when justified by dengue assay data or relevant laboratory validation studies.

A more advanced simulation could incorporate hierarchical Bayesian estimation, mechanistic viral-kinetic components, correlated repeated measures, competing outcomes, and missing-not-at-random mechanisms. Computational work in plasma instability modeling, photonic-device development, differential-equation analysis, and adaptive power-system protection provides examples of mathematical modeling in complex systems, but does not validate any biological assumptions in the dengue model [25, 29, 50, 56, 59]. Other work on AI-based fraud detection, security risks of generated code, and strategic governance reinforces the importance of verification, reproducible code, and safeguards when computational outputs influence decisions [23, 34, 51, 57]. For clinical research, the corresponding priorities are to publish the exact code and software versions, predefine model evaluation, document all parameter sources, and prevent unvalidated outputs from being used for patient management.

Several supplied references concern food formulation, functional foods, protein modification, agricultural biotechnology, crop stress, sustainable materials, or other areas not directly related to dengue. These include research on probiotic tempeh and functional foods [9, 12, 18], protein crosslinking and meat analogues [4–6, 10, 11, 20, 40, 46, 52], plant-based bioactives and nutritional products [27, 33, 35, 41, 60], crop genome editing and drought or salinity responses [14, 15, 55], and broader environmental or sustainability topics [30, 31, 45]. Other supplied work addresses business, entrepreneurship, organizational performance, gender and language, and education [22, 23, 31, 37, 39, 45, 46]. These studies cannot substantiate claims about dengue pathogenesis, biomarker thresholds, or clinical outcomes. Their inclusion here serves only to acknowledge the supplied bibliography and to distinguish general methodological inspiration from disease-specific evidence. Before journal submission, the reference list should be curated to retain sources that directly support the article's scientific argument.

The future value of Monte Carlo simulation in dengue research lies in making uncertainty explicit, helping design efficient longitudinal studies, and evaluating how measurement schedules and model assumptions affect estimates. The current synthetic results—including the 4.1% simulated severe-outcome proportion and the illustrative AUC of 0.619—must not be interpreted as estimates from patients. The next stage should calibrate the model using relevant dengue datasets, conduct evidence-informed sensitivity analyses, and test performance in an independent cohort. Only after this

process should the model be considered for prospective evaluation as a decision-support aid, and it should complement rather than replace clinical assessment and established dengue management guidance.

6. Conclusion

Monte Carlo simulation can be a useful tool for exploring the interaction between viral-load kinetics, laboratory variability, and assumed severe-disease risk in acute dengue. This expanded manuscript provides a transparent synthetic framework and five figures, but its estimates are conditional on unvalidated assumptions. The apparent outcome frequency and AUC are not clinical estimates. Before clinical or journal-facing conclusions can be drawn, the framework requires parameter calibration, sensitivity analyses informed by evidence, and validation against real patient data collected under appropriate ethical oversight.

Data availability statement

No real patient data were used. The data described in this manuscript are synthetic and can be regenerated from the model specification and random seed. For journal submission, the executable script and software environment should be deposited in a version-controlled repository and cited in the manuscript.

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Author contributions

This is a draft manuscript. Author names, affiliations, and contribution statements should be completed only by the individuals who actually designed, reviewed, and approved the work.

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Appendix A. Reproducibility checklist

- Confirm that all tables and figures are labeled as synthetic.
- Archive the exact script, Python version, and package versions.
- Retain the fixed random seed and document any changes.
- Add parameter provenance or evidence-based ranges before any calibration claim.
- Run sensitivity analyses over all influential assumptions, not only selected examples.
- Do not describe synthetic AUC as clinical performance.
- Before using real patient data, obtain appropriate ethics approval and data access authorization.
- Before submission, have a statistician and dengue clinician independently review the model.

Appendix B. Simplified simulation workflow

1. Set a fixed random seed and define cohort size.
2. Sample synthetic demographics, infection-history indicators, comorbidity, and latent patient effects.
3. Generate illness-day-specific viral load and laboratory measurements using prespecified mean profiles plus patient-level and measurement variation.
4. Generate the synthetic outcome from the specified logistic probability function.
5. Summarize distributions, trajectories, correlations, and model-implied outcome frequencies.
6. Fit the illustrative model on a training subset and report hold-out AUC only as a simulation diagnostic.
7. Vary baseline risk and selected biomarker coefficients to examine sensitivity.

8. Interpret all outputs as conditional on assumptions; do not generalize to real patients without calibration and validation.