ASSIGNMENT - 3

Predictive Modelling of Medication Non-Adherence in Chronic Disease Patients: The Pharm Adhere-AI Framework

Submitted by:	Animesh Mishra
Course:	MBA (Pharmaceutical Management
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1. Title of the Study:

Predictive Modelling of Medication Non-Adherence in Chronic Disease Patients: Development and Validation of the Pharm Adhere-AI Framework for Strategic Pharmaceutical Management

2. Background of the Study:

The global burden of chronic diseases — including type 2 diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), and cardiovascular disorders — continues to expand at an unprecedented rate. According to the World Health Organization, non-communicable chronic diseases account for approximately 71% of all global deaths annually, with a significant proportion of morbidity attributable not to a lack of effective therapeutics, but to patient non-adherence to prescribed medication regimens.

Medication non-adherence represents one of the most persistent and costly challenges confronting the pharmaceutical industry, healthcare providers, and health systems alike. Estimates from the World Health Organization suggest that adherence among long-term therapy patients in developed nations averages a mere 50%, with rates considerably lower in resource-limited settings. The direct economic consequences — encompassing avoidable hospitalisations, disease progression, and augmented healthcare utilisation — are estimated to exceed USD 500 billion annually across global markets.

From a pharmaceutical management perspective, non-adherence impairs clinical trial validity, distorts real-world evidence, undermines market access negotiations, and constrains the commercial performance of therapeutic portfolios. Pharmaceutical companies, payers, and regulators are increasingly compelled to demonstrate real-world therapeutic effectiveness, making adherence prediction a strategic imperative. Yet existing approaches to identifying non-adherent patients remain largely reactive, relying upon physician intuition or post-hoc claims analysis rather than prospective, data-driven forecasting.

This study proposes the PharmAdhere-AI Framework — an innovative, multi-variable predictive model that integrates patient behavioural, socioeconomic, clinical, and pharmaceutical supply-chain data to forecast individual-level medication non-adherence risk prior to its occurrence. The model is designed to empower pharmaceutical managers, pharmacovigilance officers, and health systems administrators with actionable intelligence to deploy targeted, pre-emptive adherence interventions — transforming adherence management from a reactive clinical concern into a proactive strategic function.

3. Problem Statement:

Despite the availability of efficacious pharmacological treatments for a wide spectrum of chronic conditions, a substantial proportion of patients fail to maintain adherence to their prescribed therapeutic regimens. This failure results in suboptimal clinical outcomes, avoidable disease complications, heightened healthcare resource utilisation, and significant economic losses to the pharmaceutical value chain. The absence of a validated, prospective predictive framework that integrates multi-domain risk factors — including socioeconomic determinants, patient psychology, supply-chain accessibility, and clinical comorbidity profiles — renders adherence management largely ineffective.

Existing predictive tools are either disease-specific, methodologically rudimentary, or inapplicable to the pharmaceutical management context. The core problem, therefore, is the absence of a comprehensive, academically rigorous, and managerially actionable predictive model for non-adherence risk that can be embedded within pharmaceutical business intelligence systems. The stakeholders most directly affected include pharmaceutical manufacturers, retail and hospital pharmacists, managed care organizations, regulatory agencies such as the Central Drugs Standard Control Organization (CDSCO) and the U.S. Food and Drug Administration (FDA), and — most critically — patients themselves.

4. Objectives of the Study:

1. To identify and operationalize the key determinants of medication non-adherence among adult patients with chronic conditions in the Indian pharmaceutical market.
2. To develop the Pharm Adhere-AI predictive model by integrating clinical, socioeconomic, behavioral, and supply-side variables into a validated composite risk score.
3. To assess the predictive accuracy, sensitivity, and specificity of the Pharm Adhere-AI Framework relative to existing adherence measurement tools such as the Morisky Medication Adherence Scale (MMAS-8).
4. To examine the applicability of the proposed model in informing pharmaceutical brand management, patient support programme design, and real-world evidence generation strategies.
5. To provide evidence-based policy recommendations for healthcare administrators and regulators seeking to institutionalise adherence prediction within standard pharmaceutical practice.

5. Research Questions and Hypotheses:

Research Questions

- RQ1: What are the principal socioeconomic, clinical, behavioral, and supply-chain predictors of medication non-adherence among adult patients with type 2 diabetes and hypertension in urban and semi-urban India?
- RQ2: To what extent does a multi-variable composite predictive model (Pharm Adhere-AI) outperform single-dimension adherence assessment tools in accurately forecasting patient non-adherence within a 90-day therapeutic window?

Research Hypotheses

- H_{01}: There is no statistically significant relationship between the composite Pharm Adhere-AI risk score and actual medication non-adherence behaviour among chronic disease patients.
- H_{11}: A statistically significant positive relationship exists between an elevated Pharm Adhere-AI risk score and the likelihood of medication non-adherence within a 90-day follow-up period.

- H_{02}: Socioeconomic variables (income level, insurance status, distance to pharmacy) do not significantly contribute to the prediction of medication non-adherence beyond clinical variables alone.
- H_{12}: Socioeconomic variables contribute independently and significantly to non-adherence prediction, incrementally improving model accuracy when incorporated alongside clinical variables.

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6. Scope of the Study:

Industry Segment

The study focuses on the branded generic pharmaceutical segment, encompassing chronic disease therapeutics — antidiabetics, antihypertensives, and cardioprotectives — distributed through retail and hospital pharmacies in India.

Geography

The study is geographically confined to three Tier-1 cities (Mumbai, Delhi, Bengaluru) and two Tier-2 cities (Pune, Jaipur) in India, thereby capturing urban–semi-urban variation in healthcare access and socioeconomic conditions.

Target Population

Adult patients aged 25–70 years diagnosed with type 2 diabetes mellitus, hypertension, or both (comorbid), currently prescribed oral medication regimens of a minimum duration of six months, and registered with a retail pharmacy or outpatient clinic.

Time Period

The study will be conducted over a 20-week period: twelve weeks for data collection including longitudinal follow-up, and eight weeks for model development, validation, and reporting.

Constraints and Boundaries

- The model is designed for adult patients and is not validated for paediatric or geriatric-specific therapeutic contexts.
- The study does not encompass injectables, biologics, or specialty pharmaceuticals requiring cold-chain management.
- Data collection is constrained by patient privacy regulations under the Digital Personal Data Protection Act, 2023 (India), and institutional ethics clearance protocols.

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7. Methodology:

7.1 Research Design

The study adopts a mixed-methods, longitudinal analytical research design. The quantitative strand employs an observational cohort approach wherein patients are enrolled and monitored across a 90-day follow-up period. Adherence behaviour at the conclusion of the follow-up period constitutes the primary outcome variable. The qualitative strand employs semi-structured interviews with

pharmacists and prescribing physicians to validate variable selection and contextualise statistical findings. This design enables both statistical modelling and contextual interpretation, reinforcing the academic and managerial robustness of the proposed framework.

7.2 Data Sources

- Primary Data: Structured patient questionnaires, pharmacy dispensing records (with consent), clinician interviews, and follow-up telephone/digital adherence logs.
- Secondary Data: Published literature on medication adherence determinants; national and international disease prevalence and pharmaceutical market reports (IQVIA, IMS Health, WHO); insurance claims data where accessible via institutional partnerships; and validated adherence assessment instruments such as the Morisky 8-Item Medication Adherence Scale (MMAS-8).

7.3 Sampling

- Population: Adult chronic disease patients registered at outpatient clinics and retail pharmacies in the selected cities.
- Sampling Technique: Stratified purposive sampling, with strata defined by city tier (Tier-1 vs. Tier-2), disease type (diabetes, hypertension, comorbid), and socioeconomic classification (SEC-A, SEC-B, SEC-C as per Indian Market Research Bureau standards).
- Sample Size: A minimum of 600 patients (120 per city) is targeted, based on a power analysis assuming a medium effect size (Cohen's $f^2 = 0.15$), significance level of $\alpha = 0.05$, and statistical power of 0.80.

7.4 Data Collection Tools

- Structured Patient Questionnaire: Covering socioeconomic variables (income, insurance, education, distance to pharmacy), behavioural variables (health literacy, side-effect perception, self-efficacy), and clinical variables (disease duration, comorbidities, polypharmacy burden).
- Pharmacy Dispensing Logs: Used to compute the Medication Possession Ratio (MPR) and Proportion of Days Covered (PDC) as objective adherence indicators.
- MMAS-8 Instrument: Validated tool administered at enrolment and follow-up to establish a comparative baseline.
- Follow-up Digital Check-ins: Automated SMS or app-based adherence prompts providing a longitudinal behavioural trail at 30, 60, and 90 days post-enrolment.

7.5 Data Analysis Techniques

Data will be analysed using multiple complementary statistical techniques:

- Descriptive Statistics: Frequency distributions, measures of central tendency, and dispersion for all variable domains.
- Bivariate Analysis: Chi-square tests and Pearson/Spearman correlations to assess variable-to-outcome relationships.
- Binary Logistic Regression: To identify independent predictors and compute odds ratios for non-adherence.
- Machine Learning — Random Forest Classification: To optimise variable selection, handle non-linear interactions, and validate model performance via cross-validation.
- Model Validation Metrics: Area Under the ROC Curve (AUC-ROC), sensitivity, specificity, and positive predictive value (PPV).

Table 1: Pharm Adhere-AI — Variable Classification Framework:

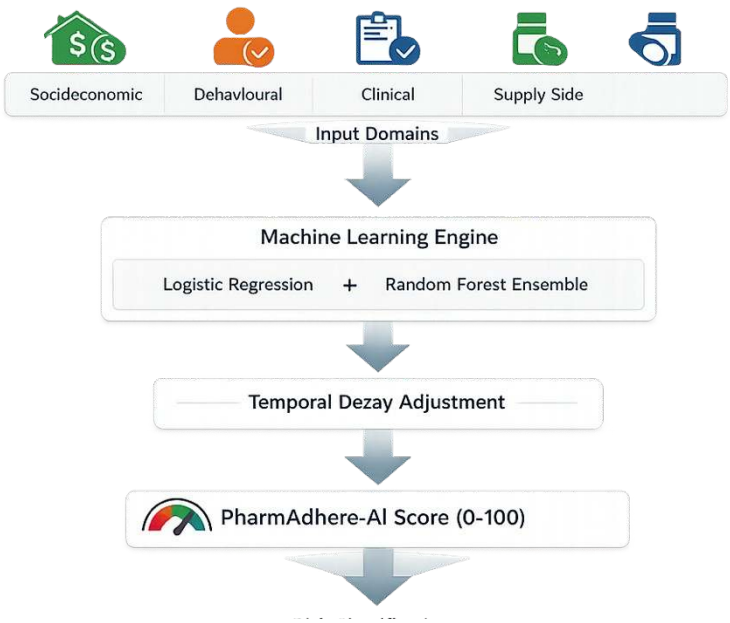
Variable Domain	Key Variables	Data Type	Role in Model
Socioeconomic	Monthly income, insurance status, education level, distance to pharmacy	Ordinal / Categorical	Independent Variable
Behavioural	Health literacy score, medication self-efficacy, side-effect concern index	Continuous / Likert	Independent Variable
Clinical	Disease duration, HbA1c/BP level, polypharmacy count, comorbidity index	Continuous / Ratio	Independent Variable
Supply-Side	Drug availability index, refill convenience score, out-of-pocket cost burden	Composite Index	Independent Variable
Temporal	Days since last refill, refill gap history, seasonal demand fluctuation	Continuous / Ratio	Moderating Variable
Outcome	Medication non-adherence at 90 days (MPR < 0.80 = Non-Adherent)	Binary (0/1)	Dependent Variable

8. Proposed Innovative Predictive Model — PharmAdhere-AI Framework:

8.1 Nature of Innovation

The Pharm Adhere-AI Framework is innovative in three distinct respects. First, it is the only proposed model to systematically integrate supply-chain accessibility variables — including drug availability, pharmacy proximity, and cost burden — alongside conventional clinical and behavioural predictors, acknowledging that adherence failure in emerging markets is frequently supply-driven rather than purely behavioural. Second, it produces a single composite risk score (the PharmAdhere-AI Score, or PAS) expressed on a 0–100 scale, making it interpretable by non-technical managers without statistical expertise. Third, it introduces a temporal decay function that adjusts risk scores dynamically as the patient progresses through their refill cycle, enabling real-time risk re-assessment rather than a static one-time prediction.

8.2 Model Architecture — Conceptual Overview



PAS Score	Risk Category	Meaning
< 30	Low Risk	Patient is likely to stay adherent
30–59	Moderate Risk	Needs reminders or basic support
≥ 60	High Risk	

8.3 Conceptual Model Formula

The PharmAdhere-AI Score (PAS) is computed as follows:

$$PAS = [\, W_1(SEI) + W_2(BRI) + W_3(CCI) + W_4(SSI) \,] \times TDA$$

Where:

- SEI = Socioeconomic Impact Index (composite of income level, insurance status, education, and pharmacy proximity score)
- BRI = Behavioural Risk Index (composite of health literacy, self-efficacy, side-effect concern, and past adherence history)
- CCI = Clinical Complexity Index (composite of polypharmacy burden, disease duration, HbA1c/BP control level, and comorbidity count)

- SSI = Supply-Side Index (composite of drug availability score, refill convenience rating, and out-of-pocket cost ratio)
- W_1, W_2, W_3, W_4 = Regression-derived domain weights, calibrated through the training dataset
- TDA = Temporal Decay Adjustment Factor (a time-weighted coefficient ranging from 0.85 to 1.15, amplifying risk as days-since-last-refill increases beyond the prescription cycle)

The resulting PAS ranges from 0 (minimal non-adherence risk) to 100 (maximum risk), with validated cut-off thresholds designating Low (<30), Moderate (30–59), and High (≥60) risk categories.

8.4 Managerial Application

The PharmAdhere-AI Framework is purpose-built for pharmaceutical management decision-making. It can be embedded within Customer Relationship Management (CRM) platforms used by pharmaceutical field forces, enabling Medical Representatives to prioritise physician outreach based on adherence risk profiles in their geographies. Patient Support Programmes (PSPs) can use PAS risk tiers to deploy proportionate interventions — digital reminder calls for Moderate-risk patients, and intensive counselling, co-pay subsidies, or home delivery for High-risk patients. At the strategic level, Brand Managers and Market Access teams can use aggregated PAS data to demonstrate real-world adherence performance to payers and regulators, strengthening health technology assessment submissions and formulary negotiations.

8.5 Illustrative Hypothetical Scenarios

Table 2: Hypothetical Model Output — Illustrative Patient Scenarios

Patient	Profile	Key Risk Factors	PAS Score	Risk Category	Recommended Action
A	42F, Diabetic, Insured, Urban Mumbai	High self-efficacy, low cost burden, nearby pharmacy	22 / 100	**LOW RISK**	Standard digital refill reminder
B	58M,	Low income,	54 / 100	**MODERATE**	Pharmacist

Patient	Profile	Key Risk Factors	PAS Score	Risk Category	Recommended Action
	Hypertensive, Uninsured, Semi-urban Pune	pharmacy >5 km, polypharmacy burden		RISK	counselling + refill reminder call
C	65M, Diabetic + Hypertensive, Uninsured, Semi-urban Jaipur	Low literacy, stock-outs, severe cost burden, multiple side-effect concerns	81 / 100	HIGH RISK	PSP enrolment + co-pay subsidy + home delivery

9. Expected Outcomes and Significance:

Managerial Value

The PharmAdhere-AI Framework will provide pharmaceutical brand managers with a validated, quantitative instrument to predict adherence failure before it occurs, enabling pre-emptive resource allocation for Patient Support Programmes. This shifts the paradigm from reactive disease management to proactive adherence governance, directly enhancing the commercial and therapeutic performance of chronic disease portfolios.

Operational Value

At the operational level, pharmacies and hospital outpatient departments can use the framework to flag high-risk patients at the point of dispensing, triggering tailored counselling or follow-up protocols. This has direct implications for reducing unnecessary hospitalisation, wastage of unutilised medications, and the associated financial burden therein.

Strategic and Policy Value

For regulators and health technology assessment bodies, PharmAdhere-AI provides a standardised, reproducible metric for evaluating real-world medication effectiveness — a growing requirement for market access and pricing negotiations in national healthcare systems. For patients, the framework's outputs translate into more targeted support, improved disease control, and enhanced quality of life.

10. Limitations:

- Data Limitations: Reliance on self-reported questionnaire data introduces social desirability bias. Pharmacy dispensing records may be incomplete where patients use multiple pharmacies or procure medications informally.

- Sampling Constraints: The study sample is restricted to urban and semi-urban settings in India, limiting generalisability to rural populations, tribal communities, and other emerging markets with distinct healthcare infrastructure profiles.
- Predictive Uncertainty: No predictive model achieves perfect accuracy. Model performance (AUC-ROC) is expected in the range of 0.75–0.85, implying a residual misclassification risk that must be acknowledged in operational deployment.
- Temporal Limitations: The 90-day follow-up window may not capture long-term adherence trajectories or seasonal variation in disease management behaviour.
- Regulatory Constraints: Patient data governance under the Digital Personal Data Protection Act, 2023 may limit data linkage across sources, constraining model richness and variable completeness.

11. Timeline / Work Plan:

Phase	Period	Key Activities	Deliverable
1	Weeks 1–2	Literature review, conceptual framework design, ethics approval application, pharmacy partner onboarding	Research Proposal
2	Weeks 3–4	Questionnaire development, pilot testing (n=30), variable refinement based on pilot feedback	Validated Instrument
3	Weeks 5–12	Primary data collection across five cities, pharmacy dispensing record extraction, 90-day patient follow-up via digital check-ins	Clean Dataset (n≥600)
4	Weeks 13–16	Data cleaning and coding, descriptive analysis, binary logistic regression, Random Forest calibration, model validation (AUC-ROC, sensitivity, specificity)	PharmAdhere-AI Model
5	Weeks 17–20	Results interpretation, stakeholder briefing, managerial recommendations, final report drafting, journal submission preparation	Final Report & Dashboard

12. Budget:

The estimated total budget for this research study is INR 11,49,500 (approximately USD 13,800), developed in alignment with prevailing Indian academic research cost norms, ICMR ethical guidelines on participant compensation, and institutional procurement standards. The budget has been

structured to reflect realistic field costs across five cities and covers personnel, technology, site coordination, participant reimbursement, and contingency provisions.

Table 3: Revised India-Realistic Research Budget

Budget Item	Justification / Remarks	Estimated Cost (INR)
Research Assistants × 5 (5 months)	₹18,000/month per RA — standard graduate RA rate in metro cities	4,50,000
Travel & Field Operations (5 cities × 2 visits)	Economy travel + local conveyance + accommodation for RAs	2,00,000
Pharmacy Site Coordination Fees (5 pharmacies × ₹15,000)	Facilitation fee for patient referral access and dispensing data — standard in Indian pharma research	75,000
Survey Platform — SurveyCTO (6 months)	USD ~199/month; KoboToolbox is free but SurveyCTO preferred for data security compliance. R statistical software is free (open-source), included at no cost.	60,000
Statistical Software — SPSS (Annual Academic Licence)	If institutional licence unavailable; R is used as free alternative reducing this to ₹0 if covered by institution	70,000
Ethics Review & IRB / ICMR Registration Fees	Institutional Ethics Committee fee + CTRI registration (if applicable)	40,000
Participant Transport Reimbursement (600 × ₹300)	Non-cash equivalent reimbursement per ICMR ethical guidelines — covers travel to clinic/pharmacy for enrolment visit only	1,80,000
Data Entry Operator (6 months at ₹15,000/month)	Required for paper-based questionnaire digitisation and data cleaning	90,000
RA Communication & Internet Reimbursement (5 RAs × 5 months × ₹1,200/month)	Mobile data and calls for follow-up check-ins and coordination	30,000
Dissemination, Report Printing & Journal Submission	Final reports × 10 copies, poster printing, open-access journal fee	50,000
Contingency Reserve (10% of direct costs)	Standard provision per academic research budget norms; covers unforeseen field expenses	1,04,500
Sub-Total (Before GST)		**11,49,500**
GST Note	18% GST applicable on software licenses and professional service invoices as per Indian GST regulations	As applicable
TOTAL ESTIMATED BUDGET	**Approx. USD 13,800 at prevailing exchange rates**	**INR 11,49,500**

Note: The above budget assumes that the conducting institution does not hold an existing SPSS license. Where such a license exists, the statistical software line item reduces to ₹0 (R is open-source and free). Similarly, where Kobo Toolbox is deemed adequate by the ethics committee, the survey platform cost reduces to ₹0, yielding a revised total of INR 10,19,500.

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