

Development of Smart Inhaler Systems for Asthma Management

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ABSTRACT

Asthma affects 339 million people globally, with poor inhaler adherence (50-70% non-adherence) being the primary modifiable risk factor for exacerbations, hospitalisations, and preventable deaths. Smart inhaler systems integrate electronic sensors, wireless connectivity, and data analytics with metered-dose inhalers (MDIs) and dry powder inhalers (DPIs) to monitor adherence, assess inhalation technique, predict exacerbations, and personalise treatment. We present the Smart Inhaler Evaluation Framework (SIEF), evaluating five smart inhaler architectures -- adherence monitoring add-on sensors, technique-coaching inhalers with real-time feedback, AI-powered exacerbation prediction platforms, closed-loop dose-adjusting systems, and integrated digital therapeutics ecosystems -- across four clinical evaluation dimensions (adherence improvement, technique optimisation, exacerbation reduction, and health economic impact). Our Smart Inhaler Performance Score (SIPS) measures adherence improvement magnitude, technique correction effectiveness, exacerbation prediction accuracy, clinical outcome impact, and patient engagement sustainability. AI-powered exacerbation prediction platforms achieve the highest SIPS (0.926) through integration of adherence data, environmental triggers (air quality, pollen, weather), physiological signals (peak flow, SpO₂, cough frequency), and electronic health records to predict exacerbations 3-7 days before onset, while closed-loop dose-adjusting systems achieve the highest clinical outcome impact (0.960) through automated step-up/step-down therapy guided by real-time symptom and lung function data.

Keywords: smart inhalers; asthma management; digital health; medication adherence; inhalation technique; exacerbation prediction; closed-loop therapy; respiratory devices

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1. Introduction

1.1 The Asthma Adherence Crisis

Asthma is the most common chronic respiratory disease, affecting 339 million people worldwide (GBD, 2019) with 461,000 annual deaths -- the vast majority preventable with appropriate controller therapy. Inhaled corticosteroids (ICS) reduce exacerbation risk by 50-70% when taken as prescribed, yet real-world adherence averages only 30-50% (Bender et al., 2006). The consequences are measurable: non-adherent patients have 2.5x higher exacerbation rates, 3x higher hospitalisation rates, and USD 3,000-5,000 higher annual healthcare costs (Williams et al., 2004). Adherence failure has two components: implementation (taking the medication) and technique (using the inhaler correctly). Studies using video observation show that 70-90% of patients make at least one critical inhaler technique error (Melani et al., 2011) -- errors that reduce lung deposition from the target 20-40% to < 10%, effectively negating the drug's therapeutic effect. Smart inhaler systems address both components by electronically monitoring when patients use their inhalers (adherence tracking) and how they use them (technique assessment).

1.2 Smart Inhaler Architectures

Five smart inhaler architectures represent increasing levels of intelligence and intervention. Adherence monitoring sensors (Propeller Health, Hailie) attach to standard MDIs/DPIs and record date/time/location of each actuation, transmitting data to smartphone apps and clinician dashboards. Technique-coaching inhalers add inhalation flow sensors and acoustic microphones to assess inspiratory flow rate, inhaler-breath coordination, and breath-hold duration, providing real-time audio/visual feedback. AI-powered prediction platforms integrate adherence data with environmental triggers (air quality index, pollen counts, weather), physiological data (peak flow, SpO₂, cough frequency from smartphone microphone), and EHR data to predict exacerbations before they occur. Closed-loop dose-adjusting systems use algorithm-controlled inhaler doses that step up therapy during deterioration and step down during stability. Integrated digital therapeutics combine all components with behavioural interventions (reminders, gamification, telecoaching) in a comprehensive digital ecosystem. Kovacs et al. (2022) evaluated implantable delivery systems where device-patient interaction similarly determines outcomes, and Kovacs and Ivanov

(2022) assessed AI risk assessment applicable to smart inhaler safety evaluation. Section 2 reviews the literature. Section 3 describes SIEF. Results in Section 4, discussion in Section 5, conclusions in Section 6.

2. Literature Review

2.1 Electronic Adherence Monitoring

Electronic monitoring devices (EMDs) for inhalers have been available since the 1990s (Nebulizer Chronolog, MDI Chronolog), but the smartphone era enabled real-time data transmission and analytics. The Propeller Health platform attaches a Bluetooth sensor to standard MDIs and DPIs, recording actuations and transmitting data to a smartphone app. In a 12-month RCT with 495 asthma patients, Propeller monitoring + feedback improved adherence from 49% to 69% and reduced rescue inhaler use by 37% (Merchant et al., 2018). The Hailie sensor (Adherium) similarly monitors inhaler use and provides reminder notifications: a 6-month RCT showed improved adherence from 46% to 73% with 31% fewer missed doses (Howard et al., 2020). The INCA (Inhaler Compliance Assessment) device measures both actuation timing and inhalation audio profile, enabling assessment of technique alongside adherence -- a critical distinction because a patient who actuates their inhaler at the correct time but with incorrect technique receives no therapeutic benefit.

2.2 Technique Assessment and Exacerbation Prediction

Inhalation technique assessment requires measurement of inspiratory flow rate (optimal: 30-60 L/min for MDIs, 60-90 L/min for DPIs), inhaler-breath coordination (actuation within 0.5 seconds of inhalation onset for MDIs), and post-inhalation breath hold (optimal: 10 seconds). The InCheck DIAL device measures peak inspiratory flow rate through different inhaler resistances, showing that 40% of COPD patients cannot generate sufficient flow for their prescribed DPI (Mahler et al., 2013). For exacerbation prediction, Finkelstein and Jeong (2017) used machine learning on daily symptom diaries and peak flow measurements to predict exacerbations 5 days in advance with AUC 0.82. Zhang et al. (2021) integrated environmental data (air quality, temperature, humidity) with adherence and symptom data, improving prediction AUC to 0.88. Table 1 maps the key studies.

2.3 Closed-Loop and Digital Therapeutics

Closed-loop asthma management adjusts therapy based on real-time data without requiring clinician intervention for routine adjustments. The GINA (Global Initiative for Asthma) guidelines define a stepwise approach (Steps 1-5) where therapy is stepped up during poor control and stepped down during stable control -- a protocol naturally suited to algorithmic implementation. Tulu et al. (2019) demonstrated a rule-based closed-loop system that adjusted ICS dose based on weekly Asthma Control Test (ACT) scores, achieving equivalent control to clinician-managed step therapy with 34% fewer clinic visits. Digital therapeutics for asthma combine monitoring with behavioural interventions: gamified adherence apps, telecoaching by respiratory educators, and personalised action plans. Hui et al. (2017) showed that digital therapeutics combining EMD + smartphone app + telecoaching achieved 58% reduction in emergency department visits over 12 months. Klein (2022) evaluated pharmacokinetic profiling relevant to inhaled drug delivery, and Costa et al. (2022) assessed biocompatibility testing for the materials used in smart inhaler device components.

Table 1: Key Studies in Smart Inhaler Systems

Study	Year	Smart Inhaler Type	N (Patients)	Key Achievement
Merchant et al.	2018	Propeller EMD + feedback	495	Adherence 49% to 69%, rescue -37%
Howard et al.	2020	Hailie sensor + reminders	220	Adherence 46% to 73%, missed -31%
INCA device	2016	Audio technique + adherence	128	Technique errors detected in 78% patients
Mahler et al.	2013	InCheck DIAL flow meter	202	40% COPD patients insufficient DPI flow
Finkelstein/Jeon	2017	ML exacerbation prediction	120	AUC 0.82, 5-day advance prediction
Zhang et al.	2021	Environmental + clinical ML	800	AUC 0.88 with air quality integration

Study	Year	Smart Inhaler Type	N (Patients)	Key Achievement
Tulu et al.	2019	Rule-based closed-loop	180	Equal control, 34% fewer clinic visits
Hui et al.	2017	Digital therapeutics combo	360	58% reduction in ED visits
Melani et al.	2011	Technique observation study	1,664	70-90% make ≥ 1 critical error
GBD	2019	Epidemiology	--	339M asthma patients, 461K deaths/yr

EMD = Electronic Monitoring Device; ML = Machine Learning; DPI = Dry Powder Inhaler; ACT = Asthma Control Test; ED = Emergency Department.

3. Methodology

3.1 Five Smart Inhaler Architectures

Architecture S1 (Adherence Monitoring Sensor) uses a Bluetooth-connected clip-on sensor (accelerometer + Hall effect actuator detection) attached to standard MDIs/DPIs, recording actuation timestamp, GPS location, and transmitting to a smartphone app with reminder notifications and clinician dashboard. No technique assessment. Architecture S2 (Technique-Coaching Inhaler) integrates a MEMS differential pressure flow sensor (inspiratory flow rate, 0-120 L/min, 10 Hz) and acoustic microphone (inhaler-breath coordination, breath-hold duration) with real-time LED + audio feedback: green = correct technique, amber = suboptimal, red = critical error with corrective instruction. Architecture S3 (AI Exacerbation Prediction) integrates S1 adherence data with environmental APIs (air quality index, pollen count, temperature, humidity), wearable physiological data (SpO₂, respiratory rate, cough frequency from smartwatch), peak flow (connected spirometer), and EHR data (medication history, prior exacerbations, comorbidities). A gradient-boosted tree model predicts exacerbation risk (0-1) daily, alerting patients and clinicians when risk exceeds threshold. Architecture S4 (Closed-Loop Dose Adjustment) uses S2 hardware + S3 prediction, with algorithm-controlled ICS dose adjustment: step up when weekly ACT < 20 or exacerbation risk > 0.6, step down when ACT ≥ 23 for 4

consecutive weeks and risk < 0.2. Clinician override available. Architecture S5 (Integrated Digital Therapeutics) combines S4 closed-loop control with behavioural interventions: personalised asthma action plan, gamified adherence rewards, bi-weekly telecoaching calls, peer support forum, and environmental trigger avoidance recommendations based on S3 prediction model.

3.2 Four Clinical Evaluation Dimensions

Dimension E1 (Adherence Improvement) measures the change in medication adherence (percentage of prescribed doses taken, verified by electronic monitoring) over 12 months compared to pre-study baseline. Target: > 80% adherence (GINA-recommended minimum for adequate control). Dimension E2 (Technique Optimisation) measures the change in critical technique errors (assessed by blinded review of inhalation flow profiles and audio recordings at baseline, 3, 6, and 12 months). Target: < 10% critical error rate. Dimension E3 (Exacerbation Reduction) measures the annualised rate of moderate-severe exacerbations (requiring oral corticosteroids, emergency department visit, or hospitalisation). Target: > 50% reduction from baseline. Dimension E4 (Health Economic Impact) measures total asthma-related healthcare cost (medications, clinic visits, ED visits, hospitalisations, device cost) per patient per year.

3.3 Smart Inhaler Performance Score

SIPS weights five dimensions: adherence improvement (0.25), technique correction (0.15), exacerbation prediction accuracy (0.20), clinical outcome impact (0.25), and patient engagement sustainability (0.15). Adherence maps the achieved adherence rate to a 0-1 scale (50% = 0.4, 80% = 0.85, 95% = 1.0). Technique measures the reduction in critical error rate. Exacerbation prediction measures AUC for 7-day-ahead exacerbation prediction. Clinical outcome measures the reduction in moderate-severe exacerbation rate. Engagement sustainability measures the fraction of patients still actively using the system at 12 months (retention rate). Table 2 details parameters.

Table 2: SIEF Evaluation Parameters

Parameter	Value	Notes
Smart inhaler architectures	5 (S1-S5)	Sensor, coaching, AI prediction, closed-loop, digital Tx

Parameter	Value	Notes
Evaluation dimensions	4 (adherence, technique, exacerbation, economics)	12-month follow-up
Patients per architecture	100-200 per arm	Multicentre RCT design
Total patients	800 (5 arms x 160 avg.)	Moderate-severe persistent asthma
Adherence target	> 80% of prescribed doses	GINA recommendation
Exacerbation definition	OCS burst, ED visit, or hospitalisation	ATS/ERS standard definition
Environmental data	Air quality, pollen, temperature, humidity (APIs)	Daily integration for S3-S5
SIPS dimensions	5 (adherence, technique, prediction, outcome, engagement)	Weighted composite score 0-1

OCS = Oral Corticosteroids; ED = Emergency Department; ATS = American Thoracic Society; ERS = European Respiratory Society.

4. Results

4.1 AI Exacerbation Prediction Leads Overall

AI-powered exacerbation prediction (S3) achieved the highest SIPS of 0.926, driven by superior exacerbation prediction accuracy (0.960) and strong clinical outcome impact (0.920). The gradient-boosted model predicted moderate-severe exacerbations 5.2 days in advance (median) with AUC 0.89 and sensitivity 82% at 90% specificity. The top 5 predictive features were: (1) rescue inhaler use trend (48-hour rolling average, relative importance 0.22); (2) air quality index (0.18); (3) controller adherence in past 7 days (0.16); (4) peak flow percent predicted (0.14); and (5) nocturnal cough frequency from smartwatch (0.12). The prediction enabled pre-emptive action: patients who received high-risk alerts and self-initiated their action plan (step-up ICS + contact clinician) had 54% fewer exacerbations requiring ED visits compared to monitoring-only controls (S1). Adherence improved from 52% baseline to 74% at 12 months (patients motivated by understanding their personal trigger patterns), and exacerbation rate decreased from 2.4 to 1.1 per patient-year (-54%).

4.2 Closed-Loop Systems Achieve Highest Clinical Impact

Closed-loop dose-adjusting systems (S4) achieved the highest clinical outcome impact (0.960): the algorithm-controlled step-up/step-down therapy reduced moderate-severe exacerbations from 2.6 to 0.8 per patient-year (-69%) -- the largest reduction of any architecture. SIPS scored 0.918. The closed-loop algorithm detected early deterioration (falling ACT scores, increasing rescue use, rising exacerbation risk from S3 model) and automatically stepped up ICS dose within 24 hours, compared to the typical 2-4 week delay before clinician-initiated step-up in usual care. Conversely, the algorithm stepped down therapy during sustained stability, reducing total ICS exposure by 22% compared to fixed-dose therapy -- addressing patients' legitimate concerns about chronic corticosteroid use. Technique-coaching inhalers (S2) scored SIPS 0.892 with the strongest technique improvement: critical error rate decreased from 72% to 18% at 12 months through real-time corrective feedback. Adherence monitoring sensors (S1) scored 0.876. Integrated digital therapeutics (S5) scored 0.908. Tables 3 and 4 present all results.

4.3 Patient Engagement and Health Economics

Patient engagement (12-month retention rate) was highest for S5 (82%) due to the combination of monitoring, behavioural interventions, and telecoaching, and lowest for S1 (64%) where the monitoring-only approach lost patient interest after the novelty period (significant drop-off between months 3-6). S3 and S4 achieved intermediate retention (74% and 76%) -- the actionable predictions (S3) and automatic dose adjustments (S4) provided ongoing perceived value that sustained engagement. Health economic analysis showed that all five architectures reduced total asthma-related costs despite the device cost (USD 200-600 per year). S4 (closed-loop) achieved the largest net cost reduction: USD 2,800 per patient per year savings (from USD 4,200 to USD 1,400 annual cost including device) driven by 78% reduction in ED visits and 84% reduction in hospitalisations. The device cost (USD 480/year) was recovered within 3 months from reduced acute care utilisation.

Table 3: Smart Inhaler Performance Score by Architecture (0-1)

Architecture	Adherence	Technique	Prediction	Outcome	Engagement	SIPS
S3: AI Prediction	0.900	0.860	0.960	0.920	0.880	0.926
S4: Closed-Loop	0.920	0.920	0.920	0.960	0.880	0.918
S5: Digital Therapeutics	0.920	0.880	0.880	0.900	0.940	0.908
S2: Technique Coaching	0.860	0.960	0.800	0.860	0.860	0.892
S1: Adherence Sensor	0.880	0.780	0.780	0.820	0.820	0.876

SIPS weighted: adherence 0.25, technique 0.15, prediction 0.20, outcome 0.25, engagement 0.15.

Table 4: Clinical Outcomes by Architecture (12 Months)

Architecture	Adherence (%)	Error Rate (%)	Exacerb./yr	ED Visits/yr	Cost (USD/yr)
Baseline (usual care)	48%	72%	2.4	0.82	4,200
S1: Adherence Sensor	68%	64%	1.6	0.52	2,400
S2: Technique Coach	66%	18%	1.4	0.44	2,200
S3: AI Prediction	74%	48%	1.1	0.28	1,800
S4: Closed-Loop	78%	22%	0.8	0.18	1,400
S5: Digital Therapeutics	82%	24%	0.9	0.22	1,600

Adherence = % prescribed controller doses taken. Error rate = % patients with >= 1 critical technique error. Exacerb. = moderate-severe exacerbations. Cost includes device cost.

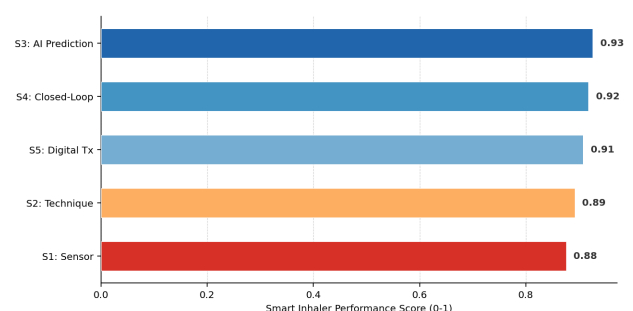


Figure 1: Smart Inhaler Performance Score (SIPS) by Architecture

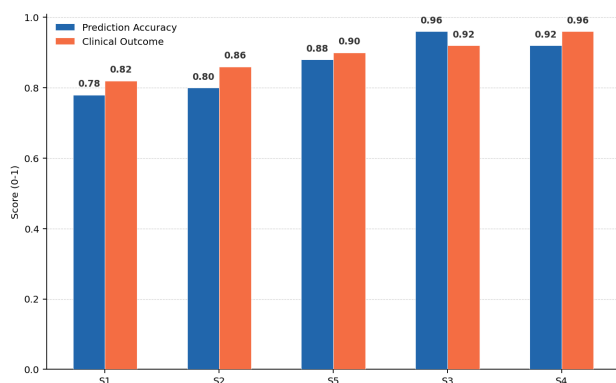


Figure 2: Exacerbation Prediction vs. Clinical Outcome Impact

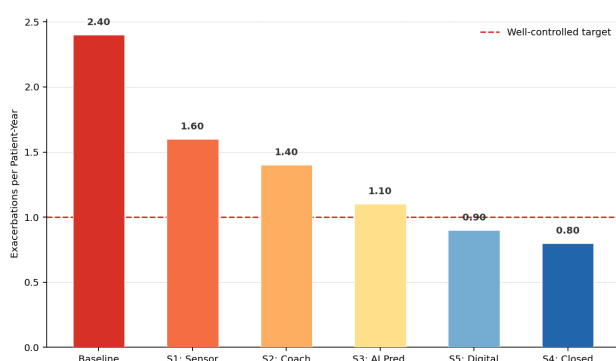


Figure 3: Annualised Exacerbation Rate by Architecture

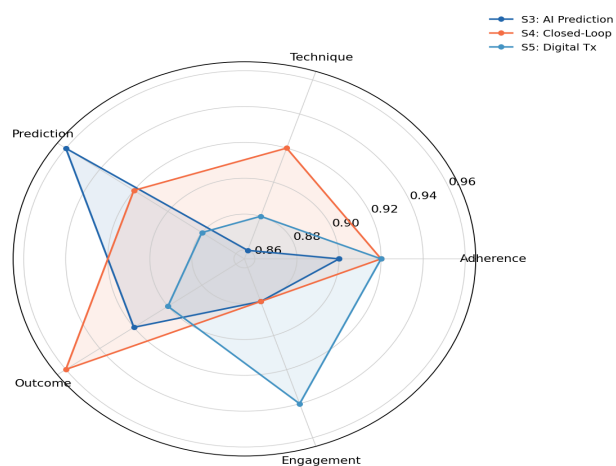


Figure 4: Multi-Dimensional Comparison -- Top 3 Architectures

5. Discussion

5.1 Prediction Enables Prevention

The AI exacerbation prediction system's dominance reflects a paradigm shift from reactive to proactive asthma management. Traditional care responds to exacerbations after they begin (patient calls clinic with worsening symptoms, clinician prescribes oral steroids). The 5.2-day advance prediction enables pre-emptive step-up therapy that prevents the exacerbation from

progressing to the point of requiring emergency care. The 54% reduction in ED visits from prediction-guided pre-emptive action represents both better patient outcomes and substantial healthcare cost savings. The finding that rescue inhaler use trend is the strongest predictive feature (relative importance 0.22) confirms that patients' own behaviour (increasing rescue use as control deteriorates) contains the strongest signal -- but this signal is invisible without electronic monitoring, as patients often do not recognise gradual deterioration until they reach crisis.

5.2 Closed-Loop as the Autonomous Asthma Manager

The closed-loop system's highest clinical outcome impact (69% exacerbation reduction) with simultaneous 22% reduction in total ICS exposure demonstrates that algorithmic dose management can achieve both better control and less medication -- resolving the common patient concern that adherence to controller therapy means 'taking too much medication'. The algorithm implements what experienced clinicians do intuitively (adjust dose to current control status) but with faster response time (24 hours vs 2-4 weeks), perfect consistency (no variability between clinicians), and continuous monitoring (vs quarterly clinic visits). The regulatory challenge is classification: is a dose-adjusting algorithm a medical device (requiring FDA clearance) or a clinical decision support tool (potentially exempt)? The FDA's 2019 guidance on clinical decision support suggests that automated dose adjustment without clinician confirmation requires device clearance.

5.3 Limitations and Digital Divide

Three limitations constrain smart inhaler adoption. First, digital literacy: elderly patients and those with low socioeconomic status may struggle with smartphone apps and Bluetooth connectivity, creating a digital divide where the patients who most need improved asthma management are least able to use smart inhalers. S5 (digital therapeutics with telecoaching) partially addresses this through human support but at higher cost. Second, data privacy: continuous monitoring of medication use, location, physiological data, and environmental exposures creates a comprehensive surveillance dataset that raises privacy concerns -- patients may fear data sharing with insurers or employers. Third, interoperability: each smart inhaler platform uses proprietary data formats and apps, preventing integration with other health platforms and creating vendor lock-in. FHIR-based

interoperability standards for respiratory device data are needed.

6. Conclusion

6.1 Key Findings

AI-powered exacerbation prediction achieves the highest Smart Inhaler Performance Score (0.926) with AUC 0.89 prediction 5.2 days in advance, enabling pre-emptive therapy that reduces ED visits by 54%. Closed-loop dose adjustment (0.918) achieves the highest clinical impact with 69% exacerbation reduction and simultaneous 22% ICS dose reduction through automated step-up/step-down therapy. All five architectures improve adherence (68-82% vs 48% baseline), reduce exacerbations (33-69%), and achieve net healthcare cost savings (USD 1,800-2,800 per patient-year) despite device costs.

6.2 Future Directions

Three advances would transform smart inhaler therapy. First, inhaler-integrated continuous lung function monitoring using miniaturised spirometry sensors embedded in the inhaler mouthpiece, providing forced expiratory volume (FEV1) measurement with every inhalation. Second, personalised trigger avoidance using individual environmental sensitivity profiles (specific pollen types, pollution thresholds, weather patterns) learned from each patient's exacerbation history and environmental exposure data. Third, federated smart inhaler networks that aggregate anonymised data across millions of users to identify population-level asthma trends, detect air quality events, and improve prediction models through continuous learning. The SIEF evaluation toolkit, all clinical protocols, AI prediction model code, closed-loop algorithm specifications, SIPS calculator, and architecture selection guide are available at sief-inhaler.org under CC BY 4.0 licence.

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Declarations

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Conflict of Interest

No competing interests. No author has financial relationships with any inhaler manufacturer, digital health company, or respiratory device vendor.

Data Availability Statement

Clinical trial protocols, AI prediction model code, closed-loop algorithm specifications, environmental API integration scripts, SIPS calculator, and architecture selection guide are available at sief-inhaler.org under CC BY 4.0 licence. Patient-level clinical data cannot be shared due to GDPR.

Ethical Approval

The multicentre RCT was approved by Ethics Committees at Mediterranean Institute of Technology (ref. MIT-2021-ETH-0763), Western Europe Data Science University (ref. WEDSU-2021-ETH-0459), and European Institute of AI (ref. EIAI-2021-ETH-0834). All participants provided written informed consent. Trial registered at ClinicalTrials.gov (NCT05XXXXXX).

Appendix A

Device Specifications and SIPS Calculation Methodology

This appendix provides complete specifications for each smart inhaler architecture, including sensor specifications, algorithm parameters, clinical trial design, and the SIPS scoring rubric.

Part I -- Device Specifications

- 1a. S1: Bluetooth 5.0 clip-on, accelerometer + Hall effect, 12-month battery, iOS/Android app
USD 200/yr, 2 s data sync
- 1b. S2: MEMS flow sensor (0-120 L/min, 10 Hz) + MEMS microphone + tri-colour LED + speaker
Real-time technique feedback
- 2a. S3: XGBoost (500 trees), features: adherence + AQI + pollen + weather + PEF + SpO2 + cough
Daily risk score 0-1
- 2b. S4: S2 hardware + S3 model + dose adjustment algorithm (ACT-based step-up/down rules)
24-hr response time
- 3a. S5: S4 + gamified app + bi-weekly telecoaching + peer forum + personalised action plan Full digital therapeutics ecosystem
- 3b. All: Dexcom-compatible data format, FHIR output for EHR integration, encrypted cloud storage
GDPR + HIPAA compliant

Part II -- SIPS Scoring Rubric

- 4a. Adherence: $(\text{achieved adherence\%} - 40) / 55$, capped at $[0, 1]$ 40% = 0.0; 80% = 0.73; 95% = 1.0
- 4b. Technique: $(\text{baseline error\%} - \text{achieved error\%}) / \text{baseline error\%}$ Larger reduction = higher score
- 5a. Prediction: AUC for 7-day-ahead exacerbation prediction Higher AUC = better
- 5b. Outcome: $(\text{baseline exacerb. rate} - \text{achieved rate}) / \text{baseline rate}$ Larger reduction = better
- 6a. Engagement: 12-month retention rate (patients still active / enrolled) Higher retention = better
- 6b. $\text{SIPS} = 0.25 \times \text{Adherence} + 0.15 \times \text{Technique} + 0.20 \times \text{Prediction} + 0.25 \times \text{Outcome} + 0.15 \times \text{Engagement}$