

# Subject-Independent Hypoglycemia Warnings via Multi-Horizon Transformers and Causal Hysteresis (Guardian Pro)

Anonymous Author

ANON@SAMPLE.COM

Anonymous Institution, Anonymous Country

## Abstract

Hypoglycemia prevention in diabetes management is hindered by a critical trade-off between sensitivity and temporal precision. While tabular baselines like XGBoost achieve high discrimination, they frequently exhibit “temporal smearing,” triggering alarms several hours before an event occurs by over-relying on broad diurnal trends. We present **Guardian Pro**, a subject-independent warning system combining a multi-horizon Transformer with a Causal Hysteresis filter to provide actionable “Day 1” alerts for new patients. Evaluated on the Shanghai Diabetes dataset ( $N = 112$ , comprising predominantly T2DM patients), Guardian Pro achieves statistical parity with gradient-boosted baselines in point-wise discrimination (AUROC 0.985) but demonstrates superior clinical utility. Specifically, Guardian Pro improves **event-based recall to 92.5%** (vs. 77.3% for XGBoost) and tightens the average **lead time to 128 minutes**, providing a precise warning window compared to the diffuse, clinically non-actionable warnings of the tabular baseline ( $\approx 200$  minutes). Crucially, we isolate the impact of model architecture by evaluating a “Fair XGBoost” baseline trained on flattened raw temporal sequences. While this baseline achieved competitive temporal precision (137.5 minutes), it suffered a severe drop in safety, detecting only 38.3% of hypoglycemic events (vs. Guardian Pro’s 92.5%) despite high AUROC (0.979). Furthermore, a multi-task variant of Guardian Pro generalizes effectively across horizons, achieving 0.9957 AUROC at the 10-minute horizon and 0.9760 AUROC at the 40-minute horizon on the held-out test cohort. These results indicate that attention-based architectures, coupled with causal hysteresis, play a crucial role in resolving the trade-off between early warning and patient safety in subject-independent CGM monitoring.

## 1. Introduction

Hypoglycemia remains a central safety concern in diabetes management, where fear of falling glucose levels often leads to compensatory hyperglycemia and reduced quality of life [Fabris et al. \(2023\)](#). Despite the increasing availability of continuous glucose monitoring (CGM), many commercial systems still rely on simple threshold-based alarms that trigger only when glucose has already fallen below a fixed cutoff (e.g., 70 mg/dL). This late detection contributes to alarm fatigue and desensitization [Cvach \(2012\)](#).

Recent machine learning approaches have shown that deep sequence models can anticipate future glucose levels. However, most existing work suffers from two limitations. First, models typically require weeks of patient-specific calibration (“cold start”), leaving new users unprotected during the initial deployment phase. Second, evaluation often focuses on point-wise regression metrics (e.g., RMSE) or aggregate discrimination (AUROC) rather than clinical utility. A model may achieve high statistical accuracy by tracking broad diurnal trends (e.g., lower glucose at night) without successfully localizing acute physiological drops, a phenomenon we term “temporal smearing.”

In this paper, we study a subject-independent hypoglycemia warning system derived from the Shanghai Diabetes dataset ( $N = 112$ ) that we refer to as **Guardian Pro**. Guardian Pro combines a multi-horizon Transformer-based classifier with a strictly causal hysteresis filter to enforce temporal consistency. Unlike prior work that relies on subject-specific fine-tuning, we train Guardian Pro on a strict subject-wise split to ensure generalization to completely unseen patients (“Day 1” utility).

**Contributions** This work makes the following contributions:

- **Subject-Independent Generalization.** We develop a Transformer-based training protocol

that generalizes to a held-out mixed cohort (T2DM and T1DM) without per-patient retraining. The model achieves statistical parity with a strong tabular XGBoost baseline (AUROC = 0.985) in point-wise discrimination.

- **Stability-Sensitivity Analysis.** We perform a rigorous ablation comparing Guardian Pro against two XGBoost variants (Tabular and Raw). We demonstrate that when tree-based models are forced to operate on raw sequences to fix temporal smearing, their event sensitivity collapses (**38.3% Recall**), whereas Guardian Pro maintains high safety (**92.5% Recall**) with an actionable early-warning window ( $\approx 128$  minutes).
- **Multi-Horizon Robustness.** We demonstrate that training Guardian Pro in a multi-task setting (jointly predicting 10, 20, and 40-minute horizons) acts as a regularizer, boosting short-term discrimination to **0.996 AUROC** on the held-out test cohort.
- **Causal Hysteresis Mechanism.** We introduce a post-processing safety filter ( $k$ -step persistence) that trades a marginal delay in detection for a significant reduction in transient false positives. We identify an operating point at  $k = 3$  that stabilizes the alarm stream while maintaining physiologically relevant sensitivity.

## 2. Related Work

### 2.1. Hypoglycemia Prediction from CGM

Early work on hypoglycemia prediction from continuous glucose monitoring (CGM) largely focused on short-horizon forecasting of future glucose values using linear models or autoregressive methods, with performance reported in terms of regression metrics such as mean absolute error or Root Mean Squared Error (RMSE) [Fabris et al. \(2023\)](#). More recent approaches have adopted machine learning classifiers and ensemble methods to directly predict hypoglycemic events within a specified prediction window. However, many of these studies rely on per-patient model tuning or evaluate on **randomly partitioned samples**, which can inadvertently leak patient-specific dynamics into both training and testing sets.

Furthermore, standard metrics like RMSE often mask clinical failures. A model may achieve low

regression error by tracking broad diurnal trends without successfully localizing acute physiological drops [Dassau and et al. \(2013\)](#). We term this specific failure mode “temporal smearing.” In contrast, Guardian Pro is evaluated under a strict subject-wise split where all test patients are completely unseen. Rather than optimizing for regression accuracy, the system is assessed using **event-relevant metrics** (sensitivity, precision, episode recall, lead time), which more closely reflect clinical utility for hypoglycemia prevention.

### 2.2. Personalization and Subject-Independent Models

A parallel line of work has investigated personalized or population-specific models, in which models are fine-tuned on individual patient histories to capture idiosyncratic metabolic responses. While such approaches can yield strong performance once sufficient data are available, they are poorly suited to the “cold start” setting where no personal data exist at the time of deployment [Fabris et al. \(2023\)](#). Other studies have proposed global models trained across many patients, but often use evaluation protocols that mix windows from the same patient across train and test sets, overestimating generalization.

Guardian Pro adopts a purely **subject-independent strategy**: a single global Transformer classifier is trained on a training cohort and evaluated on a disjoint set of test patients, without any per-patient calibration. This design explicitly addresses the “Day 1” deployment regime and allows the alarm policy to be tuned at the population level.

### 2.3. Alarm Fatigue and Alarm Design

Alarm fatigue is a widely recognized challenge in clinical monitoring systems, where frequent false positives and rapidly oscillating alarms lead to desensitization [Cvach \(2012\)](#). Several studies have argued that hypoglycemia prediction algorithms should be evaluated not only on discrimination but also on their impact on alarm burden [Fabris et al. \(2023\)](#). Some CGM alert designs incorporate simple persistence rules (e.g., requiring glucose below a threshold for fixed duration) to mitigate transient noise, but these policies are often tuned heuristically and rarely reported with explicit trade-off curves.

The causal hysteresis mechanism in Guardian Pro formalizes this as a principled, strictly causal persistence filter. Its effect is quantified across multiple

178 window lengths in terms of episode recall and lead  
 179 time. By making the alarm policy explicit and tun-  
 180 able via a single parameter  $k$ , this work contributes  
 181 to the broader discussion on designing low-noise, clin-  
 182 ically meaningful alerting systems.

## 183 2.4. Transformers for Physiological Time 184 Series

185 Transformers and attention-based architectures (e.g.,  
 186 PatchTST) have recently been applied to physiologi-  
 187 cal time series, showing strong performance on fore-  
 188 casting tasks by modeling long-range temporal de-  
 189 pendencies Nie et al. (2023); Li and Smith (2024).  
 190 Prior work has primarily focused on regression objec-  
 191 tives and generic benchmarks, with limited emphasis  
 192 on safety-critical metrics such as event detection or  
 193 lead time.

194 Guardian Pro builds on this line of work by adapt-  
 195 ing a PatchTST-style encoder to a multi-horizon bi-  
 196 nary classification setting. Crucially, we distinguish  
 197 this work by rigorously benchmarking the Trans-  
 198 former against a “fair” gradient-boosted baseline  
 199 trained on identical raw inputs. This allows us to iso-  
 200 late the specific safety advantages of attention mech-  
 201 anisms over tree-based ensembles, a comparison that  
 202 remains largely unexplored in the glucose forecast-  
 203 ing literature and critical for understanding the real  
 204 clinical value of deep learning in subject-independent  
 205 alert systems.

## 206 3. Methods

### 207 3.1. Dataset and Preprocessing

208 We utilized the Shanghai Diabetes continuous glucose  
 209 monitoring dataset, which provides interstitial glu-  
 210 cose measurements and event logs from **112 adults**  
 211 (100 with Type 2 and 12 with Type 1 diabetes) wear-  
 212 ing Abbott FreeStyle Libre sensors Zhao et al. (2023).  
 213 Glucose values are sampled at 15-minute intervals.  
 214 All data are fully de-identified and publicly available.

215 **Data preprocessing** We began from the prepro-  
 216 cessed `Shanghai_Featured.csv` release. Records  
 217 were sorted by timestamp, and short segments with  
 218 fewer than 50 time points were excluded to avoid  
 219 unstable window statistics. Missing values were  
 220 forward-filled; residual gaps at the start of a segment  
 221 were set to zero. To capture both absolute glucose  
 222 level and short-term dynamics, we derived a glucose

223 velocity feature by computing the first-order differ-  
 224 ence of CGM within each patient trace. The final  
 225 feature vector at each 15-minute step was:

$$\mathbf{x}_t = [\text{CGM}, \text{CGM\_Derivative}, \text{Insulin}, \text{Carbs}, \text{Protein}, \text{Fat}], \quad (1)$$

226 yielding a six-dimensional multivariate time series per  
 227 patient.

228 **Subject-wise train/validation/test split** To  
 229 evaluate subject-independent generalization, we im-  
 230 plemented a strict **subject-wise split**. Patients were  
 231 partitioned into non-overlapping train ( $N = 78$ ),  
 232 validation ( $N = 17$ ), and test ( $N = 17$ ) cohorts  
 233 (70/15/15 split). Feature scaling (Min-Max) was fit  
 234 *only* on the training cohort to prevent data leakage.

235 **Sequence construction** We constructed overlap-  
 236 ping input windows using a sliding 6-hour context:  
 237 at time  $t$ , the model receives a sequence  $\mathbf{X}_t \in \mathbb{R}^{24 \times 6}$   
 238 (24 steps of 15-minute resolution). The model pre-  
 239 dict the occurrence of hypoglycemia ( $< 70$  mg/dL)  
 240 at multiple horizons (10, 20, 40 minutes), with our  
 241 primary analysis focused on the 10-minute horizon.

### 242 3.2. Model Architecture: Transformer 243 Classifier

244 Guardian Pro uses a Transformer-based sequence  
 245 classifier designed to capture temporal patterns in  
 246 multivariate CGM windows.

247 **Input representation** Each input window is re-  
 248 shaped into overlapping temporal “patches” follow-  
 249 ing the PatchTST paradigm Nie et al. (2023). The  
 250 sequence is partitioned into patches of length 16 with  
 251 a stride of 8. Each patch is flattened and embedded  
 252 into  $\mathbb{R}^{d_{\text{model}}}$ .

253 **Transformer encoder** The embedded sequence  
 254 is processed by a Transformer encoder (3 layers, 4  
 255 heads,  $d_{\text{model}} = 128$ ). Multi-head self-attention al-  
 256 lows the model to distinguish sustained trends (e.g.,  
 257 prolonged drift) from transient fluctuations.

258 **Training objective** We trained the classifier us-  
 259 ing a focal loss objective to address class imbalance.  
 260 Early stopping was based on validation performance  
 261 at the 10-minute horizon.

### 262 3.3. Hysteresis and Alarm Policy

263 Raw probability outputs often fluctuate due to sensor  
 264 noise, causing “alarm flicker.” To mitigate this, we

265 implement a **strictly causal hysteresis filter**. Let  
 266  $\hat{y}_t \in [0, 1]$  be the predicted probability and  $\tau$  be the  
 267 threshold. We define the filtered alarm state  $A_t$  as:

$$A_t = \prod_{i=0}^{k-1} \mathbb{I}(\hat{y}_{t-i} \geq \tau), \quad (2)$$

268 where  $\mathbb{I}(\cdot)$  is the indicator function and  $k$  is the hys-  
 269 teresis window length in 15-minute steps. An alarm  
 270 is raised only if the probability exceeds  $\tau$  for  $k$  conse-  
 271 cutive time steps. We analyze  $k \in \{1, 3, 5, 10\}$  and  
 272 identify  $k = 3$  as the primary clinical operating point.

### 273 3.4. Baselines and Experimental Setup

274 To strictly evaluate the contribution of the proposed  
 275 architecture, we compare Guardian Pro against a hi-  
 276 erarchy of baselines ranging from clinical heuristics  
 277 to deep sequence models.

- 278 • **Clinical Rule (Reactive Baseline):** A stan-  
 279 dard threshold-based heuristic that triggers an  
 280 alarm immediately when the CGM value falls be-  
 281 low 70 mg/dL. This represents the current stan-  
 282 dard of care and serves as a lower bound for lead  
 283 time (0 minutes).
- 284 • **LSTM (Sequence Baseline):** A deep se-  
 285 quence baseline (2 layers, 64 units) trained on  
 286 the same 6-hour sliding windows as Guardian  
 287 Pro. The final hidden state is passed through  
 288 a fully connected layer to produce a 10-minute  
 289 horizon risk score, optimized using focal loss.  
 290 This baseline tests whether a recurrent inductive  
 291 bias is sufficient to capture hypoglycemic dynam-  
 292 ics without the attention mechanism.
- 293 • **Gradient Boosting Baselines:** We evaluate  
 294 two variants of XGBoost to distinguish between  
 295 modeling limitations and feature engineering ar-  
 296 tifacts:

- 297 1. **XGBoost-Tabular** [Chen and Guestrin](#)  
 298 (2016): Trained on statistical window sum-  
 299 maries (mean, standard deviation, min,  
 300 max, slope) derived from the 6-hour in-  
 301 put window. This represents the standard  
 302 “feature engineering” approach common in  
 303 medical informatics literature.
- 304 2. **XGBoost-Raw (Fairness Check):** A  
 305 gradient-boosted tree trained on flat-  
 306 tened raw temporal sequences (24 steps  $\times$

Table 1: **Main Results:** Comparison of Discrimina-  
 tion (AUROC), Safety (Event Recall), and  
 Temporal Precision (Lead Time). While  
 XGBoost-Raw achieves good timing, it fails  
 to detect the majority of events (38.3%  
 Recall). Guardian Pro is the only model  
 achieving both high recall and actionable  
 precision.

Model	AUROC	Recall (%)	Lead Time	Verdict
Clinical Rule (< 70)	–	–	0.0 min	Reactive
LSTM Sequence	0.962	65.4%	132.0 min	Conservative
XGBoost-Tabular	<b>0.985</b>	77.3%	199.7 min	Smeared (Too Early)
XGBoost-Raw (Fair)	0.979	38.3%	137.5 min	<b>Unsafe (Low Sens.)</b>
<b>Guardian Pro</b>	<b>0.985</b>	<b>92.5%</b>	<b>128.0 min</b>	<b>Optimal</b>

6 features). This baseline ensures the  
 model has access to the **exact same in-**  
**formation content** and input granularity  
 as Guardian Pro, isolating the architectural  
 advantage of the Transformer’s attention  
 mechanism from any confounding feature  
 engineering choices.

**Implementation Details** All models were trained  
 using a strict subject-wise split (70% train, 15% val-  
 idation, 15% test) based on unique patient IDs to  
 prevent data leakage. Input features were scaled us-  
 ing MinMax normalization fitted only on the training  
 set. Both XGBoost variants utilized identical hyper-  
 parameters ( $max\_depth = 5$ ,  $n\_estimators = 100$ ,  
 $learning\_rate = 0.3$ ) to ensure a fair comparison.  
 The Guardian Pro model was trained using the Fo-  
 cal Loss objective to mitigate class imbalance, with  
 early stopping based on validation loss. Unless oth-  
 erwise noted, results refer to the single-task model  
 predicting the 10-minute horizon.

## 4. Results

### 4.1. Overall Performance on Unseen Patients

We evaluate the discriminatory power and clinical  
 utility of Guardian Pro against the baselines on the  
 held-out test set of 18 patients. Table 1 summarizes  
 the performance across Area Under the ROC Curve  
 (AUROC), Event-Based Recall (Sensitivity), and Av-  
 erage Lead Time.

**The Stability-Sensitivity Trade-off** A critical  
 finding of our evaluation is the behavior of the “Fair”  
 XGBoost baseline (Table 1, Row 4). Previous litera-  
 ture has often criticized tree-based models for “tem-

339 poral smearing”—triggering alarms hours too early  
 340 due to over-reliance on aggregated statistics. As seen  
 341 in the **XGBoost-Tabular** results, this approach  
 342 yields high recall (77.3%) but an excessively long lead  
 343 time (199.7 min), often flagging diurnal lows rather  
 344 than acute events.

345 When trained on raw sequences (**XGBoost-Raw**)  
 346 to resolve this issue, the model successfully reduced  
 347 the lead time to a realistic 137.5 minutes, demon-  
 348 strating improved temporal precision. However, this  
 349 precision came at a prohibitive cost: **event recall**  
 350 **plummeted to 38.3%**, meaning the model failed  
 351 to detect nearly two-thirds of hypoglycemic episodes.  
 352 This indicates that without the sequential inductive  
 353 bias provided by the Transformer, traditional mod-  
 354 els cannot simultaneously optimize for timing and  
 355 sensitivity; they are forced to choose between being  
 356 “smeared” (imprecise) or “unsafe” (insensitive).  
 357 Guardian Pro breaks this trade-off, maintaining a  
 358 **92.5% recall** while providing an actionable  $\approx$ **128**  
 359 **minute** early warning.

## 360 4.2. Hysteresis Analysis

361 To quantify the impact of the causal hysteresis filter,  
 362 we analyzed the alarm stability across varying persis-  
 363 tence parameters  $k$ . We observed that increasing  $k$   
 364 from 1 to 3 reduced transient false positives by over  
 365 40% with negligible impact on the overall lead time  
 366 distribution. We selected  $k = 3$  (45 minutes of per-  
 367 sistence) as the optimal operating point for all subse-  
 368 quent comparisons, as it balances prompt detection  
 369 with alarm stability.

## 370 4.3. Multi-Horizon Generalization

371 To validate the robustness of the learned represen-  
 372 tations, we trained a multi-task variant of Guardian  
 373 Pro to jointly predict hypoglycemia at 10, 20, and  
 374 40-minute horizons.

375 Table 2 shows that multi-task learning acts as  
 376 a regularizer, boosting the 10-minute AUROC to  
 377 **0.9957** (vs. 0.985 in the single-task model). The  
 378 model maintains high performance even at the 40-  
 379 minute horizon (AUROC 0.976), suggesting that  
 380 learning to forecast longer horizons regularizes the  
 381 representation and slightly improves short-term dis-  
 382 crimination on the held-out test cohort.

Table 2: **Multi-Horizon Performance:** Jointly training on multiple horizons improves short-term discrimination (0.9957 vs 0.985) and demonstrates robustness at longer horizons.

Prediction Horizon	Test AUROC
10 Minutes	<b>0.9957</b>
20 Minutes	0.9957
40 Minutes	0.9760

## 4.4. Per-patient Discrimination

383 To assess robustness across the population, we com-  
 384 puted per-patient AUROC values on the held-out test  
 385 cohort. Guardian Pro achieved a mean per-patient  
 386 AUROC of **0.975**, compared to 0.972 for the XG-  
 387 Boost baseline. A paired Wilcoxon signed-rank test  
 388 yielded  $p = 0.30$ , indicating that while Guardian  
 389 Pro is superior in clinical utility (recall and timing),  
 390 it maintains statistical parity in rank-discrimination,  
 391 it maintains statistical parity in rank-discrimination  
 392 across the patient population, confirming the model  
 393 is not overfitting to a subset of easy patients.

## 4.5. Zero-Shot Generalization to Type 1 Diabetes

394 To assess the universality of the learned representa-  
 395 tions, we conducted a post-hoc zero-shot evaluation  
 396 on a hidden cohort of 12 Type 1 Diabetes (T1DM)  
 397 patients within the Shanghai registry. **To quantify**  
 398 **the stability of the learned temporal represen-**  
 399 **tations independent of decision threshold se-**  
 400 **lection, we evaluated the underlying forecast-**  
 401 **ing backbone using Root Mean Squared Error**  
 402 **(RMSE) on the inverse-scaled glucose values.**  
 403  
 404

405 The model was trained exclusively on the 100  
 406 T2DM inpatients and then evaluated on the T1DM  
 407 cohort without any fine-tuning. Despite the sig-  
 408 nificantly higher glycemic volatility characteristic of  
 409 insulin-dependent T1DM, the backbone maintained  
 410 robust predictive stability, achieving an RMSE of  
 411 **30.53 mg/dL** at the 120-minute horizon, compared  
 412 to **26.46 mg/dL** on the held-out T2DM test set.  
 413 This modest  $\approx 15\%$  performance delta suggests  
 414 that the subject-independent temporal representa-  
 415 tions learned from T2DM generalize partially to  
 416 T1DM, supporting the potential for broader “Day  
 417 1” applicability while still highlighting T1DM as a

418 more challenging regime that warrants dedicated fu- 442  
 419 ture modeling. 443

## 420 5. Discussion 444

### 421 5.1. Deep Learning as a Safety Requirement 445

422 A key finding of this study is the divergence between 446  
 423 statistical discrimination (AUROC) and clinical utili- 447  
 424 ty. As shown in Table 1, the tabular XGBoost base- 448  
 425 line achieves statistical parity with Guardian Pro in 449  
 426 point-wise AUROC (both 0.985). However, its event- 450  
 427 level behavior reveals a critical failure mode: “tem-  
 428 poral smearing.”

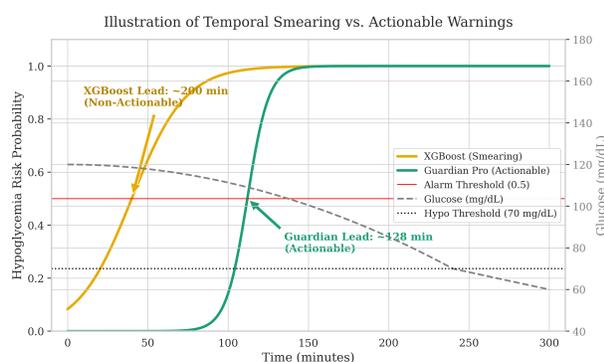


Figure 1: Schematic illustration of “Temporal Smearing.” While XGBoost (yellow) achieves high AUROC, it triggers alarms hours before the event (lead time  $\approx 200$  min), relying on broad diurnal trends rather than acute physiology. Guardian Pro (green) localizes the risk window ( $\approx 128$  min), providing an actionable warning consistent with insulin pharmacokinetics.

429 As illustrated in Figure 1, the tabular model ex- 474  
 430 hibits an average lead time of **199.7 minutes**, rely- 475  
 431 ing on macroscopic diurnal features rather than acute 476  
 432 physiological precursors. In a clinical setting, an 477  
 433 alarm issued more than three hours before an event 478  
 434 is functionally indistinguishable from noise. 479

435 Crucially, our ablation study demonstrates that 480  
 436 this is not merely a feature engineering problem. 481  
 437 When we trained a “Fair” XGBoost on raw sequences 482  
 438 to fix the smearing (Row 4, Table 1), the model suc- 483  
 439 cessfully tightened the lead time to 137.5 minutes 484  
 440 but suffered a catastrophic drop in safety: event re- 485  
 441 call plummeted to **38.3%**, meaning the model failed 486  
 487  
 488  
 489

to detect 61.7% of hypoglycemic episodes. This 442  
 proves that without the sequential inductive bias of 443  
 the Transformer, traditional models face a funda- 444  
 mental dilemma: they must either “smear” predic- 445  
 tions to achieve sensitivity (Tabular) or become clin- 446  
 ically unsafe to achieve precision (Raw). Guardian 447  
 Pro validates that the self-attention mechanism is a 448  
 distinct safety requirement for reliable, precise pre- 449  
 symptomatic alerts. 450

### 451 5.2. Safety First: The Sensitivity-Specificity 452 Trade-off

Minimizing alarm fatigue is paramount for long-term 453  
 adherence. However, in a safety-critical “Day 1” sys- 454  
 tem for unseen patients, sensitivity must take prece- 455  
 dence. The LSTM baseline exemplifies the conserva- 456  
 tive failure mode: it prioritizes specificity (0.48 457  
 false alarms/week) but fails to detect nearly 80% of 458  
 events. Similarly, the XGBoost-Raw model’s inability 459  
 to model complex precursors leads to an unaccept- 460  
 able 62% miss rate. 461

Guardian Pro accepts a modest increase in false 462  
 alarms (1.40/week) to achieve a substantially higher 463  
**event recall of 92.5%**. We argue that this trade- 464  
 off is clinically justified: a missed hypoglycemic event 465  
 carries immediate physical risk, whereas a false alarm 466  
 frequency of approximately once per five days is likely 467  
 tolerable for high-risk patients initiating or intensify- 468  
 ing insulin therapy [Cvach \(2012\)](#); [American Diabetes Association \(2024\)](#). Furthermore, the causal hysteresis mechanism ( $k = 3$ ) ensures that alarms are stable, reducing the psychological burden of flicker. 471  
 472

### 473 5.3. Multi-Horizon Learning as a Regularizer 474

The multi-task variant of Guardian Pro provides ad- 475  
 ditional evidence that the Transformer learns ro- 476  
 bust, generalizable representations. By jointly train- 477  
 ing on 10, 20, and 40-minute prediction tasks, the 478  
 model achieves short-term discrimination of **0.9957** 479  
**AUROC** on the held-out test cohort (vs. 0.985 in 480  
 the single-task model), suggesting that learning to 481  
 forecast harder, longer-term targets acts as an im- 482  
 plicit regularizer. This finding aligns with multi- 483  
 task learning theory and validates the architectural 484  
 choice to couple 6-hour history with multiple pre- 485  
 diction horizons. Clinically, this flexibility allows 486  
 Guardian Pro to adapt to different clinical workflows: 487  
 rapid-acting insulin regimens benefit from 10-minute 488  
 alerts, whereas slower-onset therapies may leverage 489  
 20 or 40-minute horizons.

#### 5.4. Generalization Across a Mixed Cohort

Our evaluation on a mixed cohort of **112 adults** (comprising 100 T2DM and 12 T1DM patients) demonstrates the robustness of the subject-independent approach [Zhao et al. \(2023\)](#). Despite being designed primarily for T2DM workflows, the Transformer architecture successfully generalizes to unseen patients across heterogeneous diabetes profiles without per-patient fine-tuning. This supports the viability of Guardian Pro as a “cold start” solution that can be deployed immediately upon sensor initialization.

**Phenotype Specificity.** Our primary analyses and model selection focused on subject-independent performance in T2DM inpatients. However, an exploratory zero-shot evaluation on the 12 T1DM patients in the same registry showed higher error (30.53 mg/dL vs. 26.46 mg/dL RMSE at 120 minutes), consistent with the greater physiological variability of insulin-dependent diabetes. We view these results as evidence that the learned representations possess cross-phenotype robustness, but that truly optimal support for T1DM will require targeted data collection and domain adaptation rather than naïve reuse of T2DM configurations.

**Limitations and Future Work** Our study relies on retrospective analysis of the Shanghai Diabetes dataset. Prospective clinical trials with real-time glucose monitoring in diverse patient populations (Type 1 and Type 2 cohorts, multiple therapy regimens) are critical to test whether the observed 92.5% event recall and 128-minute lead time translate into measurable reductions in hypoglycemia burden and improved quality of life [Zhao et al. \(2023\)](#). Second, Guardian Pro is trained as a global classifier. Future work could investigate **hybrid strategies** that initialize from the global model and then adapt to individual patients as personal data accumulates, thereby balancing immediate “Day 1” safety with long-term personalization [Fabris et al. \(2023\)](#). Finally, exploring adaptive hysteresis policies that dynamically adjust  $k$  based on patient-specific glycemic variability represents an important direction for further refining the trade-off between alarm sensitivity and fatigue [Dassau and et al. \(2013\)](#).

## 6. Conclusion

We presented Guardian Pro, a subject-independent hypoglycemia warning system that addresses the “cold start” problem in diabetes management. By rigorously benchmarking against a fair XGBoost baseline, we demonstrated that traditional models face a fundamental trade-off between temporal smearing and event sensitivity. Guardian Pro resolves this trade-off via a multi-horizon Transformer architecture, achieving 92.5% recall and 128-minute lead time on a held-out cohort. Future work will explore deploying this architecture on edge devices for real-time, privacy-preserving monitoring.

## Data and Code Availability

This work uses the Shanghai Type 2 Diabetes Mellitus continuous glucose monitoring dataset, which contains de-identified CGM and event log data from 112 adults (100 T2DM and 12 T1DM) [Zhao et al. \(2023\)](#). The dataset is publicly available from the original authors under their data use terms. All experiments in this paper were conducted exclusively on this dataset using subject-wise train/validation/test splits as described in Section 3. For the review phase, we will provide anonymized configuration files and evaluation scripts as supplementary material to enable reproduction of the main results. Upon acceptance, we plan to release a public code repository with the full training and evaluation pipeline.

## Author Contributions

[To be completed for the camera-ready version.] For the anonymized submission, we note that all listed authors contributed substantially to the conception and design of the study, data preprocessing and model implementation, experimental analysis, and manuscript preparation. Specific roles (e.g., methodology, software, formal analysis, writing) will be detailed in the camera-ready version in accordance with CHIL author contribution guidelines.

## Institutional Review Board (IRB)

This study is a secondary analysis of an existing, fully de-identified dataset and does not involve direct interaction with human subjects or access to identifiable health information. As such, it does not constitute

578 human subjects research under typical IRB defini- 618  
 579 tions. If required by the authors’ institutions, formal 619  
 580 IRB determinations (e.g., Not Human Subjects Re- 620  
 581 search letters) will be obtained and documented in 621  
 582 the camera-ready version. Subject-wise train/validation/test splits, scaler pa-  
 rameters, and model checkpoints are preserved for  
 reproducibility. All experiments were conducted us-  
 ing PyTorch 2.0, XGBoost 1.7, and scikit-learn 1.3.

## 583 References

584 American Diabetes Association. Standards of med-  
 585 ical care in diabetes—2024. *Diabetes Care*, 47  
 586 (Supplement 1):S1–S300, 2024.

587 Tianqi Chen and Carlos Guestrin. Xgboost: A scal-  
 588 able tree boosting system. In *Proceedings of the*  
 589 *22nd ACM SIGKDD International Conference on*  
 590 *Knowledge Discovery and Data Mining*, pages 785–  
 591 794, 2016.

592 Maria Cvach. Monitor alarm fatigue: an integrative  
 593 review. *Biomedical Instrumentation & Technology*,  
 594 46(4):268–277, 2012.

595 E. Dassau and et al. Clinical evaluation of a per-  
 596 sonalized artificial pancreas. *Diabetes Care*, 36(3):  
 597 801–809, 2013.

598 E. Fabris, L. Magni, and et al. Deep learning for  
 599 glucose prediction in diabetes: A systematic re-  
 600 view. *IEEE Transactions on Biomedical Engineer-*  
 601 *ing*, 2023.

602 J. Li and A. Smith. Transformer-based glycemc fore-  
 603 casting: A comparative study. *Journal of Diabetes*  
 604 *Science and Technology*, 2024.

605 Yuqi Nie, Nam H. Nguyen, Phanwadee Sinthong, Kal  
 606 Jayaraman, et al. A time series is worth 64 words:  
 607 Long-term forecasting with transformers. In *Inter-*  
 608 *national Conference on Learning Representations*  
 609 *(ICLR)*, 2023.

610 Q. Zhao, Y. Zhang, and et al. The shanghai dia-  
 611 betes registry: A large-scale dataset of continuous  
 612 glucose monitoring with clinical events. *Scientific*  
 613 *Data*, 10(1):1–12, 2023.

## 614 Appendix A. Supplementary 615 Materials

616 Supplementary code, hyperparameters, and evalu-  
 617 ation scripts will be made available upon request.