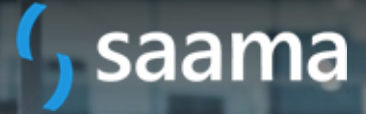


A Hybrid Machine Learning Framework for Predicting Amputation Risk in Diabetic Foot Ulcers

SAAMA



In Collaboration with
**Medical University of South Carolina
(MUSC)**



The Diabetes-Amputation Link



NON-DIABETIC PATIENTS

14.8%

Amputation Rate



n = 764 patients

3.8x

HIGHER RISK

Relative Risk

DIABETIC PATIENTS

56.0%

Amputation Rate



n = 2,043 patients

GLYCEMIC CONTROL: THE CRITICAL DIFFERENCE

7.8%

Avg HbA1c

Without Amputation



8.2%

Avg HbA1c

With Amputation

Based on

19,500+

HbA1c measurements

STUDY POPULATION

2,807

Total
Patients

1,258

Amputations

73%

Diabetic

Introduction



BACKGROUND

The rising global prevalence of diabetes mellitus has led to a proportional increase in severe complications. DFUs are the leading cause of non-traumatic lower-extremity amputations.

THE CLINICAL NEED

Early and accurate risk stratification is paramount for implementing preventive strategies. Traditional clinical scoring systems often lack the necessary granularity.

THE OPPORTUNITY

Machine Learning (ML) offers a promising solution by analyzing complex, high-dimensional EHR data to uncover subtle predictive patterns.

STUDY OBJECTIVES

- Develop hybrid ML framework for DFU risk assessment
- Predict amputation risk, type, and survival timeline
- Validate on real-world EHR data from MUSC
- Create LLM-enhanced clinical decision support tool

DIABETIC FOOT ULCER (DFU)



Open wounds on the foot due to neuropathic and vascular complications in diabetic patients

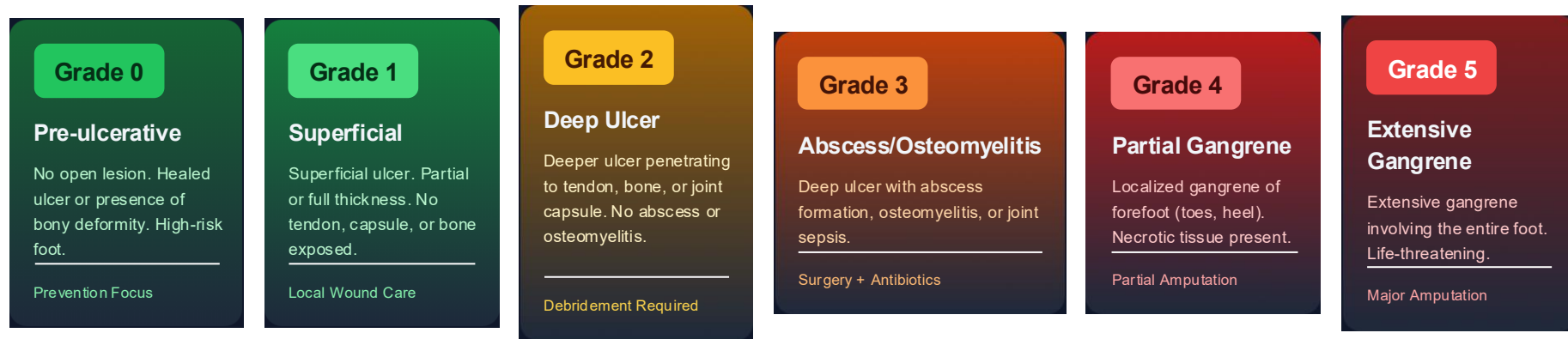
KEY CONTRIBUTION

A multi-dimensional risk assessment: **What is the risk?** **What type?** **When?**

Stages of Diabetic Foot Ulcer



Wagner Classification System — Most widely used grading scale for DFU severity



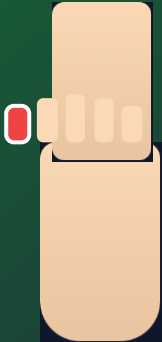
 Increasing Severity →

Key Insight: Early detection (Grade 0-2) significantly improves limb salvage rates

Types of Lower Limb Amputations



To Minor Amputation



Removal of one or more toes. Preserves foot function and mobility. Often performed for localized gangrene or osteomyelitis.

BKA Below-Knee



Amputation below the knee joint, preserving the knee. Better prosthetic outcomes. Requires adequate blood flow to heal.

AKA Above-Knee



Amputation above the knee joint. Most severe option. Higher energy cost for mobility. Often last resort when BKA not viable.

CLINICAL IMPACT

5-Year Mortality

~50%

Quality of Life

Significantly reduced, especially for major amputations

Prosthetic Success

BKA > AKA (preserved knee improves mobility)

WHY TYPE MATTERS

Management pathways differ vastly. Predicting type enables personalized intervention strategies.

Clinical Presentation: Amputation Types



Toe Amputation

Minor



Post-operative toe amputation. Preserves majority of foot function and weight-bearing ability.

BKA

Below-Knee



Post-operative BKA with surgical dressing. Knee joint preserved for prosthetic rehabilitation.

AKA

Above-Knee



Above-knee amputation stump. Requires specialized prosthetics and extensive rehabilitation.

Clinical Note: Early prediction of amputation type enables tailored pre-operative planning, rehabilitation strategies, and patient counseling

Data Sources & Collection Pipeline



MUSC EHR SYSTEM

8 Integrated Clinical Data Sources

Demographics

100%

Surgeries

100%

CPT Codes

100%

Medications

99.9%

Labs

97.4%

Comorbidities

96.3%

Hospitalizations

85.0%

Imaging

82.0%

PVD/PAD data merged into Comorbidities

DATA QUALITY

100% **70.8%**

Linkage Rate Complete Records

PATIENT IDENTIFICATION (6 Methods)

Diabetic Patients

Comorbidity flags, ICD codes, HbA1c $\geq 6.5\%$, Diabetes medications

Amputation Outcome

CPT codes, Surgical records, Imaging report keywords

STUDY TIMELINE

Data Collection Period

Jan 2015 - Dec 2023

Train

2015-22

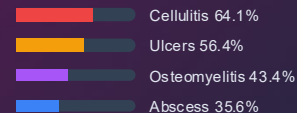
n=1,786

Test

2023

n=596

PRECURSOR EVENTS TRACKED



2,382 DFU Patients

Final Study Cohort

39.8%

Amputation Rate

28

Features

Study Population & Characteristics



2,382

DFU Patients

STUDY PERIOD

Jan 2015 – Dec 2023

DATA SOURCE

MUSC EHR System

9 integrated clinical data sources

TEMPORAL SPLIT

Train: 2015–2022 (n=1,786)

Test: 2023 (n=596)

DEMOGRAPHICS

Mean Age

58.2 $\pm$ 14.5 yrs

Male

56.8%

Amputation Rate

39.8%

KEY COMORBIDITIES



Hypertension 87.4%



CKD 68.2%



Anemia 68.0%



PVD/PAD 49.5%

FOOT COMPLICATIONS & GLYCEMIC CONTROL

Has Ulcers

51.9%

Osteomyelitis

40.6%

Mean HbA1c

7.4% $\pm$ 1.8

Charlson Score

7.9 $\pm$ 3.1

Feature Engineering: 28 Predictors Across 5 Domains



DEMOGRAPHICS

Age, Gender, Race

COMORBIDITIES

12 conditions including CKD, Hypertension, Heart Failure, PVD/PAD, Ischemic Heart Disease

Summarized by

Charlson Comorbidity Index

DIABETIC FOOT COMPLICATIONS

Binary indicators for history of Ulcers, Cellulitis, Osteomyelitis

GLYCEMIC CONTROL

Mean and Maximum longitudinal HbA1c values

TEMPORAL & MEDICATION

8 NEW features capturing trajectory & treatment

Albumin Slope

Insulin Use

Hospitalization Count

Statin Use

Antiplatelet Use

Antibiotic Use

CLASS IMBALANCE HANDLING

GATEKEEPER MODEL

No SMOTE applied

Reflects real-world prevalence

SPECIALIST MODEL

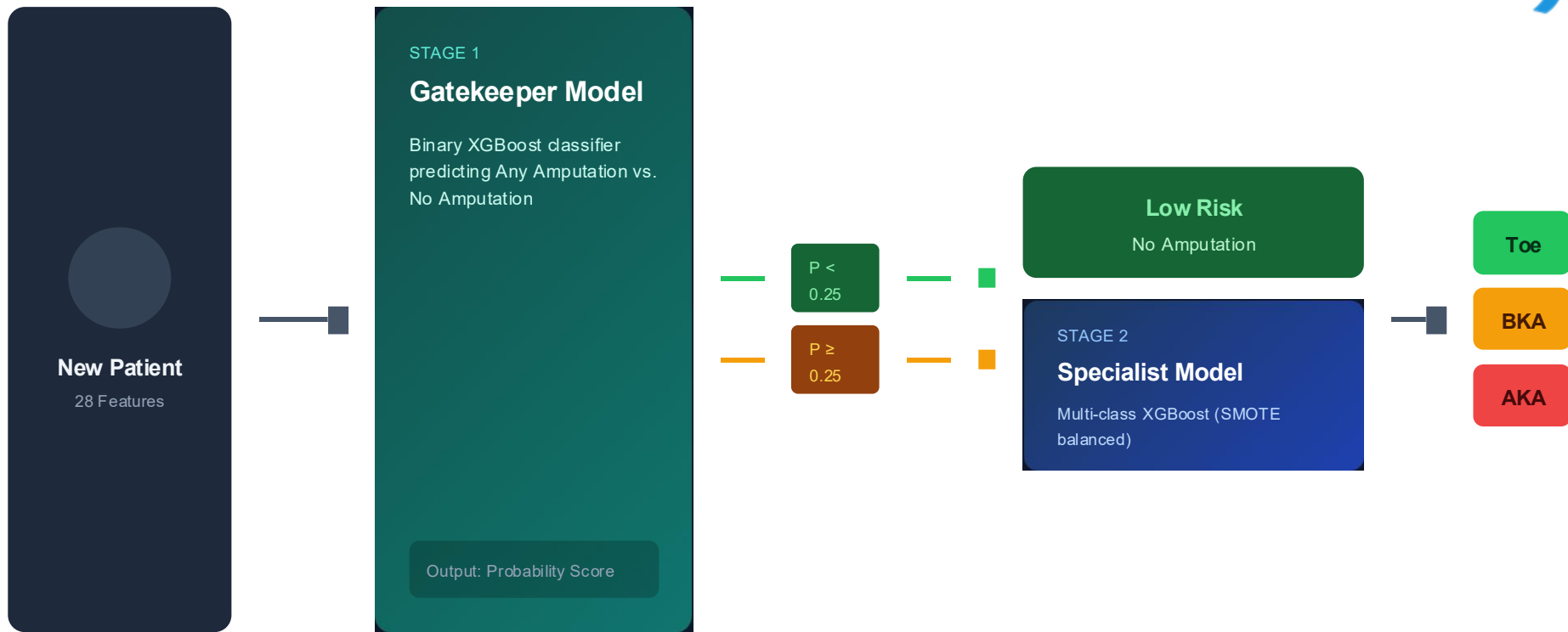
SMOTE on training data

Balances AKA, BKA, Toe classes

28

Total Features

Two-Stage XGBoost Architecture



● **Cox PH Model** runs in parallel for survival analysis

● **LLM Integration** generates narrative clinical insights

The Clinical Challenge

PREVALENCE

15–25%

of diabetic patients develop DFU in their lifetime

MORTALITY RISK

~50%

5-year mortality rate post-amputation

LEADING CAUSE

DFUs are the #1 cause of non-traumatic lower-extremity amputations

THE GAP IN CURRENT MODELS

Traditional models focus on a single binary outcome: any amputation vs. no amputation

This is clinically insufficient because management differs vastly between:

Toe

Minor

BKA

Below-Knee

AKA

Above-Knee

Clinicians need: degree of risk + probable type + timeline

Our Solution: A Hybrid ML Framework



Our framework answers **three critical clinical questions**:



Risk Assessment

What is the patient's overall risk of requiring any amputation?

MODEL

Gatekeeper XGBoost



Type Classification

If amputation is likely, what is the most probable type?

MODEL

Specialist XGBoost



Survival Forecast

What is the predicted amputation-free survival over time?

MODEL

Cox Proportional Hazards

+ LLM Integration: Claude 4.5 Sonnet translates predictions into narrative clinical insights and analyzes radiographic images

Results: Gatekeeper Model Performance



TEST AUC

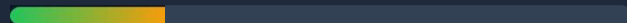
0.824

Strong discrimination ability

MODEL PURPOSE

Binary classification to identify patients at risk for any amputation. Acts as the initial risk stratifier.

DECISION THRESHOLD



P = 0.25

Below: Low Risk

Above: Specialist

KEY INTERPRETATION

AUC of 0.824 indicates the model correctly ranks a randomly chosen amputation patient higher than a non-amputation patient 82.4% of the time.

Clinical Significance

- Early identification of high-risk patients for intensive monitoring
- Probability scores reflect real-world prevalence (no SMOTE)
- Routes high risk patients to Specialist for type prediction

Evaluated on temporal test set (2023 data, n=596)

Results: Specialist Model & Classification Performance



WEIGHTED OVR AUC

0.864

4-class discrimination

RECALL ON SEVERE CASES

95.7%

AKA Recall

82.3%

BKA Recall

KEY FINDING

The model very rarely misclassifies severe amputations as less severe types.

0 BKAs were classified as Toe

CONFUSION MATRIX (Test Set)

	Pred: AKA	Pred: BKA	Pred: Toe	Pred: None
Actual: AKA	22	0	0	1
Actual: BKA	0	65	0	14
Actual: Toe	0	0	11	25
Actual: None	4	25	83	247

Correct Misclassified

Results: Cox Proportional Hazards Survival Model

C-INDEX

0.746

Excellent discrimination

MODEL PURPOSE

Forecasts amputation-free survival probability over time. Generates patient-specific survival curves for timeline visualization.

TRAINING DATA

1,904 observations

784 events observed

SIGNIFICANT HAZARD RATIOS

PVD/PAD



HR 2.25

Chronic Kidney Disease



HR 1.48

Hypertension



HR 1.43

Ischemic Heart Disease



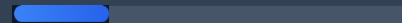
HR 1.34

Male Gender



HR 1.27

Smoker



HR 1.22

Age (per year)



HR 1.01

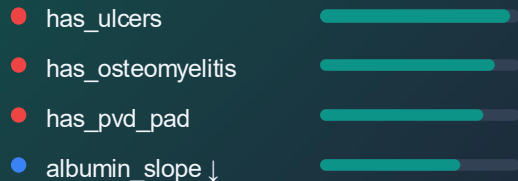
HR > 1 indicates increased hazard of amputation | Partial Log-Likelihood: -5442.32

Model Interpretability: SHAP Analysis



GATEKEEPER MODEL DRIVERS

Top features for predicting any amputation



INTERPRETATION

Gatekeeper focuses on **acute, local DFU complications** (ulcers, osteomyelitis) to determine if an amputation is needed.

SPECIALIST MODEL DRIVERS BY TYPE

AKA (Severe)

has_pvd_pad ↑↑
albumin_slope ↓↓
Severe vascular disease + declining nutrition

BKA (Major)

age ↑
hba1c_mean/max ↑
albumin_slope ↓
Systemic factors + poor glycemic control

Toe (Minor)

albumin_slope ↑
Stable/improving nutrition indicates local issue only

CLINICAL NARRATIVE

The Specialist uses a deeper **systemic health profile** (vascular status, glycemic control, age, nutritional trajectory) to determine amputation severity.

Poor systemic health → Major amputation likely

Stable systemic health → Minor (Toe) amputation likely

KEY INSIGHT

Gatekeeper
Local Factors

Specialist
Systemic Factors

Aligns with clinical reasoning

Clinical Decision Support Tool

LIVE APP

PATIENT INPUT INTERFACE

Patient Information

Patient Name
John Wick

Demographics & Vitals

Current Age
60

Age at Diagnosis
55

Gender
Female

Race
White

Charlson Score
3

Glycemic Control & Hospitalizations

HbA1c Values (comma-separated)
8.5, 9.1, 7.8, 10.0

Hospitalization Count (Last Year)
4

Key Clinical Conditions

- ☐ History of Foot Ulcers
- ☒ History of Osteomyelitis
- ☒ History of Peripheral vascular and artery disease
- ☐ History of Cellulitis

Albumin Lab Entries

Albumin Lab #1
Date of Lab #1: 2026/01/23
Albumin Value #1 (g/dL): 8.50

Albumin Lab #2
Date of Lab #2: 2025/12/24
Albumin Value #2 (g/dL): 8.30

Show Other Comorbidities & Medications

- ☒ Chronic Kidney Disease (CKD)
- ☒ Hypertension
- ☐ Anemia
- ☒ Is a Smoker
- ☒ Hyperlipidemia
- ☐ Heart Failure
- ☒ Depression
- ☒ Has Insurance
- ☐ Ischemic Heart Disease
- ☒ Atrial Fibrillation
- ☐ COPD

Medications

- ☒ On Insulin
- ☒ On Statins
- ☐ On Powerful Antibiotics
- ☐ On Antiplatelets
- ☒ On Anticoagulants
- ☐ On Metformin

INPUT CATEGORIES

- Demographics & Vitals
- Glycemic Control (HbA1c)
- Hospitalization History
- Key Clinical Conditions
- Albumin Lab Entries
- Comorbidities & Medications

KEY CLINICAL CONDITIONS

- History of Foot Ulcers
- History of Osteomyelitis
- Peripheral Vascular Disease
- History of Cellulitis

MEDICATIONS TRACKED

- Insulin
- Statins
- Antibiotics
- Antiplatelets
- Anticoagulants
- Metformin

Built with: Streamlit + XGBoost + Cox PH + LLM

Risk Assessment Output

SAMPLE PATIENT

MULTI-DIMENSIONAL RISK OUTPUT

Risk Assessment Result

Patient: John Wick

Overall Amputation Risk

Predicted Probability of Any Amputation

48.68%

Risk Category: Moderate Risk

Predicted Amputation Type

Most Likely Type: Toe Amputation

Amputation Type	Probability
0 AKA	9.80%
1 BKA	35.02%
2 Toe Amputation	55.18%

Amputation-Free Survival Forecast



OVERALL AMPUTATION RISK

48.68%

Risk Category: Moderate Risk

PREDICTED AMPUTATION TYPE

AKA 9.80%

BKA 35.02%

Toe Amputation 55.18%

Most Likely: Toe Amputation

SURVIVAL FORECAST

Kaplan-Meier style curve showing amputation-free survival probability over time (days)

Cox PH Model C-index: 0.746

3 Questions Answered: Risk? Type? When?

LLM-Powered Recommendations

CLAUDE 4.5



AI CLINICAL GUIDANCE

Clinical Recommendations

Immediate Actions (Within 2 Weeks)

1. Comprehensive Foot Examination
 - Monofilament testing for neuropathy assessment
 - Vascular assessment including ABI (Ankle-Brachial Index)
 - Detailed skin and nail examination
 - Footwear assessment
2. Glycemic Control Optimization
 - Endocrinology referral for intensive diabetes management
 - Consider continuous glucose monitoring
 - Review and optimize current diabetes medications
3. Smoking Cessation Program
 - Immediate referral to smoking cessation specialist
 - Consider pharmacological aids (varenicline, bupropion, or NRT)
 - Behavioral counseling support

Preventive Measures (Ongoing)

1. Daily Foot Care Protocol
 - Daily foot inspection with mirror for plantar surface
 - Proper foot hygiene and moisturization
 - Appropriate nail care techniques
2. Protective Footwear
 - Professional fitting for therapeutic shoes
 - Custom orthotics if indicated
 - Avoid walking barefoot
3. Regular Monitoring Schedule
 - Podiatry visits every 6-8 weeks
 - Quarterly HbA1c monitoring
 - Annual comprehensive foot screening

HOW IT WORKS

Claude analyzes patient data combined with ML model predictions to generate personalized, evidence-based clinical recommendations in natural language.

IMMEDIATE ACTIONS

Comprehensive Foot Examination
Glycemic Control Optimization
Smoking Cessation Program

Timeline: Within 2 weeks

PREVENTIVE MEASURES

Daily Foot Care Protocol
Protective Footwear
Regular Monitoring Schedule

Timeline: Ongoing

CLINICAL VALUE

Bridges the gap between complex ML predictions and actionable clinical interventions with patient-specific, prioritized guidance.

Key Findings Summary



Strong Risk Stratification

Gatekeeper model achieves AUC of 0.824 for identifying at-risk patients

AUC 0.824



Accurate Type Classification

Specialist model distinguishes amputation types with 95.7% AKA recall

OvR AUC 0.864



Excellent Survival Prediction

Cox PH model forecasts amputation-free survival over time

C-index 0.746

NOVEL FEATURE CONTRIBUTIONS

8 new temporal and medication features including **albumin_slope** (key predictor of severity) and hospitalization count

CLINICALLY INTERPRETABLE

SHAP analysis confirms model decisions align with established clinical reasoning: local factors for risk, systemic factors for severity

LLM-ENHANCED DECISION SUPPORT

Claude integration transforms quantitative outputs into actionable narrative insights with multimodal image analysis