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# Bottom-up approach to build a 'precision' risk factor classification for diabetic foot ulcer healing. Proof-of-concept

Flora Mbela Lusendi <sup>a,b,\*</sup>, Giovanni Arnoldo Matricali <sup>b,c</sup>, An-Sofie Vanherwegen <sup>a</sup>, Kris Doggen <sup>a</sup>, Frank Nobels <sup>d</sup>

- <sup>a</sup> Health Services Research, Sciensano, Brussel, Belgium
- <sup>b</sup> Department of Development and Regeneration, KU Leuven, Leuven, Belgium
- <sup>c</sup> Multidisciplinary Diabetic Foot Clinic, University Hospital Leuven, Leuven, Belgium
- <sup>d</sup> Multidisciplinary Diabetic Foot Clinic, Onze-Lieve-Vrouwziekenhuis, Aalst, Belgium

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### ABSTRACT

Aims: Diabetic foot ulcers (DFU) have a complex multifactorial pathophysiology. It is crucial to identify essential prognostic variables to streamline therapeutic actions and quality-of-care audits. Although SINBAD and University of Texas (UT), the most frequently used prognostic classification systems, were prospectively validated, not all individual parameters were shown to have consistent associations with healing. In this study, we used a bottom-up approach relying on robust methods to identify independent predictors of DFU healing.

*Methods*: 1,664 DFU patients were included by 34 Belgian diabetic foot clinics (DFCs). Twenty-one patient- and foot-related characteristics were recorded at presentation. Predictors of healing were identified using multivariable Cox proportional hazard regression. Multivariable models were built using backward regression with multiple imputation of missing values and bootstrapping.

Results: Five essential independent variables were identified: presentation delay, history of minor amputation, ulcer location, surface area and ischemia. This 5 variable-model showed a better performance compared to models based on existing classification systems.

Conclusions: A bottom-up approach was used to build a prognostic classification for DFU healing based on large databases. It offers new insights and allows to tailor the classification to certain clinical settings. These 5 parameters could be used as a 'precision classification' for specialized DFCs.

## 1. Introduction

Diabetic foot ulceration (DFU) is commonly encountered in people with diabetes [1]. Over their lifetime, approximately 25% of people with diabetes develop one or more episodes of DFU which can lead to long periods of disability and to lower-limb amputation [2]. It is widely recognized that treatment requires an intensive multidisciplinary approach [3,4] and represents substantial healthcare costs [5,6]. In addition, the health status and quality of life of patients with a DFU are significantly impacted [7]. Consequently, DFU constitutes a major burden for the individual as well as for society.

The multifactorial pathophysiology of DFU makes its understanding

and management complex. While detailed descriptions of the foot problem are often recorded in clinical files, it is crucial to identify the essential variables which influence DFU outcomes in order to facilitate communication in the care team, to streamline therapeutic actions, and to organize quality-of-care audits [8].

Numerous classification systems that try to capture the essential prognostic elements have been published [9,10]. The two classifications most commonly used in clinical practice are the Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth (SINBAD) and the University of Texas (UT) scores. Recently, the SINBAD score has been endorsed by the International Working Group on the Diabetic Foot [11].

However, these existing classifications were developed using "top-

Abbreviations: AP, Apparent performance; DFCs, Diabetic foot clinics; DFU, Diabetic foot ulcer; LOPS, Loss of protective sensation; PAD, Peripheral artery disease; SINBAD, Site, Ischemia, Neuropathy, Bacterial infection, Area, and Depth; UT, University of Texas.

<sup>\*</sup> Corresponding author at: Sciensano, Rue Juliette Wytsmanstraat 14, 1050 Brussels, Belgium.

*E-mail addresses*: Flora.MbelaLusendi@sciensano.be (F. Mbela Lusendi), giovanni.matricali@uzleuven.be (G.A. Matricali), An-Sofie.Vanherwegen@sciensano.be (A.-S. Vanherwegen), frank.nobels@olvz-aalst.be (F. Nobels).