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# Temporal trends of selected diabetic foot deformities and risk factors: an exploratory analysis from a tertiary diabetes clinic

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ABSTRACT

*Aims:* While classical diabetic foot risk factors are well established, their temporal progression remains insufficiently understood, particularly for deformities. Therefore, we aimed to analyze trends in selected diabetic foot risk factors and to design a practical monitoring model for long-term clinical use.
*Methods:* From 51,001 routine foot examinations at tertiary diabetes clinic (1998–2024), we included 14,436 screenings from 3,049 patients with complete data. Using generalized estimating equations, we modelled the temporal trends in the prevalence of six diabetes-related complications.
*Results:* Loss of Protective Sensation (LOPS) significantly increased the odds (adjusted for age at diagnosis, sex, diabetes type, and duration) of five complications: fat pad atrophy (OR = 2.12), toenail deformity (OR = 2.44), toe deformities (OR = 2.57), callus (OR = 3.66), and xerosis (OR = 2.27). Toenail deformity was the most prevalent complication, while fat pad atrophy showed the steepest relative increase over time. Female sex was a risk factor for specific deformities and fat pad atrophy but protective against xerosis (OR = 0.76).
*Conclusion:* The developed models provide clinically actionable risk trajectories, revealing distinct patterns by complication type, LOPS status, and demographic factors. These findings can directly support targeted screening protocols and inform resource allocation.

## 1. Introduction

Diabetic foot syndrome, characterized by neuropathy, ischemia, and infection leading to tissue breakdown, represents a major healthcare challenge, underscoring the critical need for effective strategies through early identification and management of risk factors [1]. Foot deformities serve as a salient example of foot complication complexity, functioning both as independent risk factors and consequences of diabetic foot disease progression – a dual role that remains undercharacterized in real-world and experimental settings [2,3]. The pathogenesis of diabetic foot deformities involves a complex interplay of neuropathy, biomechanical stress, and chronic hyperglycemia [4]. Global epidemiological studies reveal substantial variation in prevalence, ranging from 33.4% in the Ethiopian population [5] to 56.5% among elderly Chinese patients [6]. The most common deformities include hammer/claw toes, hallux valgus, and pes cavus, with key risk factors consistently emerging across studies: prolonged diabetes duration [5], peripheral neuropathy [5,7], and improper footwear [5]. These deformities frequently coexist with dermatological manifestations (hyperkeratosis in 50–75% of cases) [7,8] and vascular complications, substantially elevating ulceration risks (diabetic foot ulcer (DFU) prevalence: 1.7–27%) [7,8].

The Canadian PEDAL study from 2023 [7], the most comprehensive Western investigation to date (n = 4,373), provides additional insights into deformity patterns in developed healthcare systems. It identified foot deformities in 42.3% of type 1 diabetes mellitus and 44.8% of type 2 diabetes mellitus patients, with pes planus (40.1%), pes cavus (24.4%), and hallux valgus (13.5%) being most prevalent. Notably, the study established neuropathy as the primary driver of deformity progression, with loss of protective sensation (LOPS; 29.3% in type 2 diabetes mellitus) increasing DFU risk eightfold. Biomechanical factors, particularly

*Abbreviations:* CI, confidence interval; DFU, Diabetic Foot Ulcer; FAIR, Findable, Accessible, Interoperable, Reusable; GEE, Generalized Estimating Equations; LOPS, Loss of Protective Sensation; MRI, Magnetic Resonance Imaging; OR, Odds Ratio; QIC, Quasi-likelihood under the Independence model Criterion.

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hyperkeratosis (50.9%) and abnormal pressure distribution, further increased these risks. Emerging evidence suggests a temporal progression pattern: early-stage (≤5 years) deformities like hallux valgus [7,9] appear modifiable through glycemic control and proper footwear, while late-stage (≥10 years) complications (Charcot foot, amputations) become strongly associated with irreversible neuropathy [9] and chronic hyperglycemia.

Given the rising global prevalence of diabetes and the severe consequences of foot complications, structured organizational management of diabetic foot care is essential for improving patient outcomes [10]. To optimize clinical practice and provide integrated foot care, healthcare teams need comprehensive insights into the local dynamics of patient pathologies. Current evidence demonstrates significant limitations in generalizing research findings about diabetes mellitus prevalence across diverse geographical populations and healthcare settings (primary, secondary, or tertiary care levels) [11]. Therefore, tailored analytical tools are needed to generate actionable data for personalized, locally-adapted care strategies. This study addressed two primary objectives: (1) to analyze temporal trends in selected diabetic foot risk factors for DFU (fat pad atrophy, toenail deformities, toe deformity, callus formation, hallux valgus, and xerosis) based on systematically collected local registry data, and (2) to develop a clinically implementable long-term monitoring proposal for routine practice and further research.

## 2. Materials and methods

The study was conducted at the Clinical Department for Diabetes at the University Medical Center Ljubljana, where a standardized entry form [12] has been used for diabetic foot screening since 1998, with data stored digitally. To investigate the development of diabetic foot complications over time, the core foot examination data was augmented, where available, with demographic variables (sex, age at diagnosis) and clinical data (diabetes mellitus type and duration) from electronic health records. The study sample was refined by excluding individuals not under the care of our centre, those with inconsistent data entries, and those with a history of amputations.

### 2.1. Primary Aim: Epidemiological model development

We conducted a comprehensive longitudinal analysis with the primary outcomes defined as six binary foot complications: fat pad atrophy, any toenail deformity, toe deformity (mallet toe, hammer toe, and claw toe), callus, xerosis (dry skin), and hallux valgus. A complication was considered present if identified in either foot or both feet. Hallux valgus was characterized as a deformity of the great toe involving abduction, valgus angulation, and pronation, accompanied by a bony prominence on the medial aspect of the first metatarsal head (bunion). Hammer toe was defined by plantar flexion at the distal and proximal interphalangeal joints. Claw toe was identified as a combination of dorsal flexion at the metatarsophalangeal joint with a concurrent hammer toe deformity. Mallet toe was specified as a flexion contracture solely at the distal interphalangeal joint. A callus was defined as a broad, diffuse area of hyperkeratosis with a relatively even thickness [12]. Key independent variables included LOPS, time since diagnosis, age at diagnosis, sex, and diabetes type (type 1, type 2, or other types of diabetes mellitus). LOPS was a binary variable, defined as the inability to sense $> 2$ points on either foot using a standardized 10–g Semmes–Weinstein monofilament test (10–point protocol) [13]. Submetatarsal fat pad atrophy was assessed through physical examination via palpation for thinning of the plantar soft tissue and prominence of the metatarsal heads [14].

After standardizing continuous predictors (age at diagnosis and time since diagnosis) to z-scores, we employed generalized estimating equations (GEE) to model complication probabilities, accounting for within-subject correlations. All models used a binomial distribution with a logit link and an independent working correlation structure for robust population-averaged estimates. A model comparison approach was used to determine the optimal functional form for the continuous predictors. This approach was biologically justified by the potential for non-linear risk patterns and interaction effects. For each complication, four candidate models were compared, defined by the parameterization of these variables (linear or natural cubic splines with 3 knots) and the inclusion of an interaction term between them. Model selection was based on the Quasi-likelihood under the Independence model Criterion (QIC)[15], calculated using the MuMIn R package [16]. As different optimal models were identified for each complication, all subsequent analyses used the specific best-fitting model for the respective outcome.

The study was approved by the National Medical Ethics Committee of Slovenia (reference no. 0120–568/2024–2711-5). All analyses were implemented in R (version 4.5.2) [17] using the geepack [18], splines [19], tidyverse [20] and ggplot2 [21] packages.

### 2.2. Evaluation of risk factor contributions

The contribution of risk factors was assessed using adjusted odds ratios (ORs) with 95% confidence intervals derived from generalized estimating equation (GEE) models, with significance determined via Wald tests. For categorical predictors, we report ORs from multivariate models adjusted for other covariates. For continuous predictors (age at diagnosis and diabetes duration), results are presented as ORs per one-unit increase in linear models without interaction. For models with interactions or non-linear splines, relationships are visualized using predictive probability plots and summarized in probability tables.

To estimate complication prevalence across clinically relevant time periods, we applied a non-overlapping fixed-window approach. Specifically, we used 5-year intervals for age at diagnosis (30–35, 35–40, 40–45, 45–50, 50–55, 55–60, 60–65, 65–70, 70–75, 75–80, 80–85 and 85–90 years) and for diabetes duration (0–5, 5–10, 10–15, 15–20, and 20–25 years). For each combination of age-at-diagnosis and duration windows, we identified all unique individuals meeting these criteria. Only window combinations containing at least five individuals were included in the analysis.

Within each window, prevalence was estimated by averaging predictions from a GEE model fitted to the full dataset. Specifically, prevalence estimates were obtained by first calculating each patient's average predicted probability across their visits within a window, then averaging these patient-level probabilities across all patients in that window. The 95% confidence intervals (CIs) were obtained by performing a cluster bootstrap. Here, the analysis was repeated on 1000 bootstrap resamples obtained using patient-level resampling with replacement, and the CIs were calculated using the percentile method. Furthermore, probabilities were recalculated with the same steps using age at observation windows. Results were visualized from two complementary perspectives: fixed age at diagnosis with varying follow-up duration, and fixed age at observation with varying diabetes history.

## 3. Results

Only screening records containing complete and valid data on observed diabetes-related risk factors, duration, and diabetes mellitus type were included in the final sample (Fig. 1) of 14,436 screenings from 3,049 unique patients. The mean age at diabetes mellitus diagnosis was 47.8 years (SD = 16.0), age at observation was 63.4 years (SD = 12.8), with a mean diabetes duration of 16.2 years (SD = 11.4), and 46.2% (n = 1,408) of the cohort were female. Analysis revealed consistent patterns across both encounter-level and patient-level assessments. Toenail deformity was the most prevalent complication (46.8% per encounter; 52.9% cumulative), followed by toe deformity (35.4% per encounter; 37.1% cumulative). Fat pad atrophy showed the lowest prevalence at both levels (9.4% per encounter; 10.5% cumulative). Patients developed a mean of 2.36 (SD = 1.73) different foot complications over time. Both age at observation and sex distribution showed statistically significant differences between included patients and those excluded due to

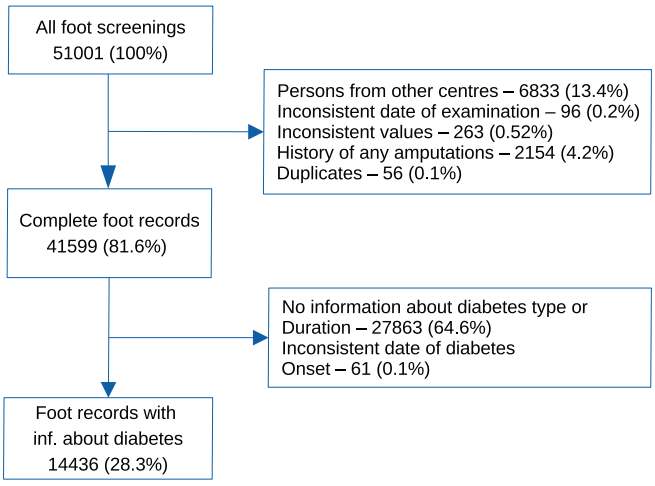


**Fig. 1.** Flowchart of study population derivation.

incomplete data ($p < 0.001$). However, effect sizes were negligible (Cohen's d = -0.06 for age; a 2.1 percentage point difference for sex), indicating that these differences lack clinical significance despite being statistically detectable due to the large sample sizes.

### 3.1. Functional Forms of the final models

A linear model without an interaction was best for fat pad atrophy, while a linear model with a significant interaction ($p = 0.019$) was optimal for toenail deformity. Spline models without interactions were best for toe deformity, callus, and hallux valgus. For dry skin, the spline interaction model was optimal (lowest QIC). All subsequent analyses used these complication-specific optimal models. Complete model rankings and QIC values are provided in Supplementary Table 1. Model parameters are presented in Supplementary Tables 2-7. The substantial to very substantial QIC differences (8.3–73.7 points) observed across all six complications indicate clear empirical preferences rather than marginal differences, thereby justifying the use of complication-specific model structures.

### 3.2. Complication-Specific associations

Sex and diabetes mellitus type exhibited distinct and complication-specific risk patterns (Table 1). Female sex was associated with significantly higher odds of hallux valgus, toe deformities, and fat pad atrophy, but significantly lower odds of xerosis. Type 2 diabetes mellitus was a significant risk factor only for xerosis, while the "other" diabetes category significantly increased the risk of toenail and toe deformities. When examining risk factors over the study period, LOPS demonstrated strong and consistent associations with most complications in models adjusted for sex, diabetes mellitus type, age at diagnosis, and diabetes duration (Fig. 2, Table 1). Therefore, LOPS is established as a significant independent risk factor for the diabetic complications analyzed.

### 3.3. Average patient-level risk predictions

Average patient-level probabilities for six diabetic foot complications, presented in Fig. 3, Fig. 4, and Supplementary Table 8, show distinct risk trajectories across complications and selected age groups. Supplementary Fig. 1 and 2 illustrate the number of patients available for analysis in each age at diagnosis or at observation range, and diabetes duration interval across all complications. For patients diagnosed with diabetes in the 40–45 years age range, fat pad atrophy demonstrated the most dramatic relative increase over 15 years, rising from 1.9% (95% CI: 1.3–2.7%) within 5 years of diagnosis to 6.2% (95% CI: 4.9–7.6%) after 15 years, representing an approximate 3.3-fold increase. Toenail deformity showed the highest overall prevalence, increasing from 22.3% (95% CI: 19.7–24.9%) to 43.3% (95% CI: 40.7–45.8%) over the same period. Mechanical complications including toe deformity and hallux valgus exhibited steady diabetes duration-dependent increases, with toe deformity rising from 13.6% (95% CI: 11.3–15.9%) to 33.7%

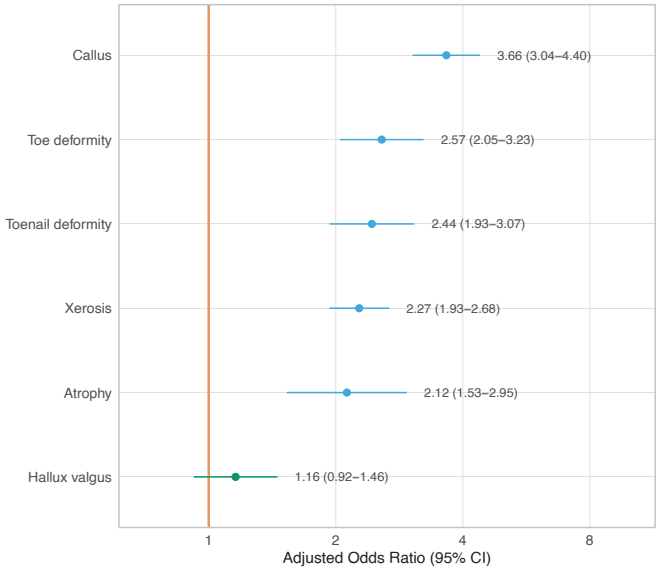


**Fig. 2.** Forest plot showing adjusted odds ratios (95% CIs) for LOPS association with diabetic foot complications. GEE models adjusted for sex, age at diagnosis, diabetes mellitus type and duration. Blue points = significant ($p < 0.05$). Orange line = no effect (OR = 1). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

**Table 1**
Adjusted odds ratios for selected complications with 95% CIs for LOPS, sex, and diabetes mellitus type, derived from multivariable GEE models adjusted for all variables shown in the table plus age at diagnosis and diabetes duration. Reference categories: Type 1 diabetes mellitus, no LOPS, male sex.

| Complication | LOPS OR | P-value | Female Sex | P-value | Type 2 DM OR | P-value | Other DM OR | P-value |
|---|---|---|---|---|---|---|---|---|
| **Fat pad atrophy** | 2.12 [1.53–2.95] | <0.001 | 2.01 [1.49–2.71] | <0.001 | 1.52 [0.78–2.96] | 0.219 | 1.54 [0.60–3.91] | 0.366 |
| **Toenail deformity** | 2.44 [1.93–3.07] | <0.001 | 0.93 [0.79–1.09] | 0.373 | 1.14 [0.85–1.54] | 0.378 | 1.79 [1.20–2.67] | 0.004 |
| **Toe deformity** | 2.57 [2.05–3.23] | <0.001 | 1.62 [1.35–1.94] | <0.001 | 1.20 [0.83–1.75] | 0.334 | 1.89 [1.17–3.06] | 0.009 |
| **Callus** | 3.66 [3.04–4.40] | <0.001 | 1.16 [0.99–1.37] | 0.073 | 1.26 [0.94–1.68] | 0.124 | 1.31 [0.84–2.06] | 0.236 |
| **Xerosis** | 2.27 [1.93–2.68] | <0.001 | 0.76 [0.66–0.87] | <0.001 | 1.88 [1.39–2.53] | <0.001 | 1.34 [0.88–2.04] | 0.170 |
| **Hallux valgus** | 1.16 [0.92–1.46] | 0.208 | 2.50 [2.08–3.01] | <0.001 | 0.72 [0.50–1.03] | 0.075 | 0.71 [0.43–1.17] | 0.181 |

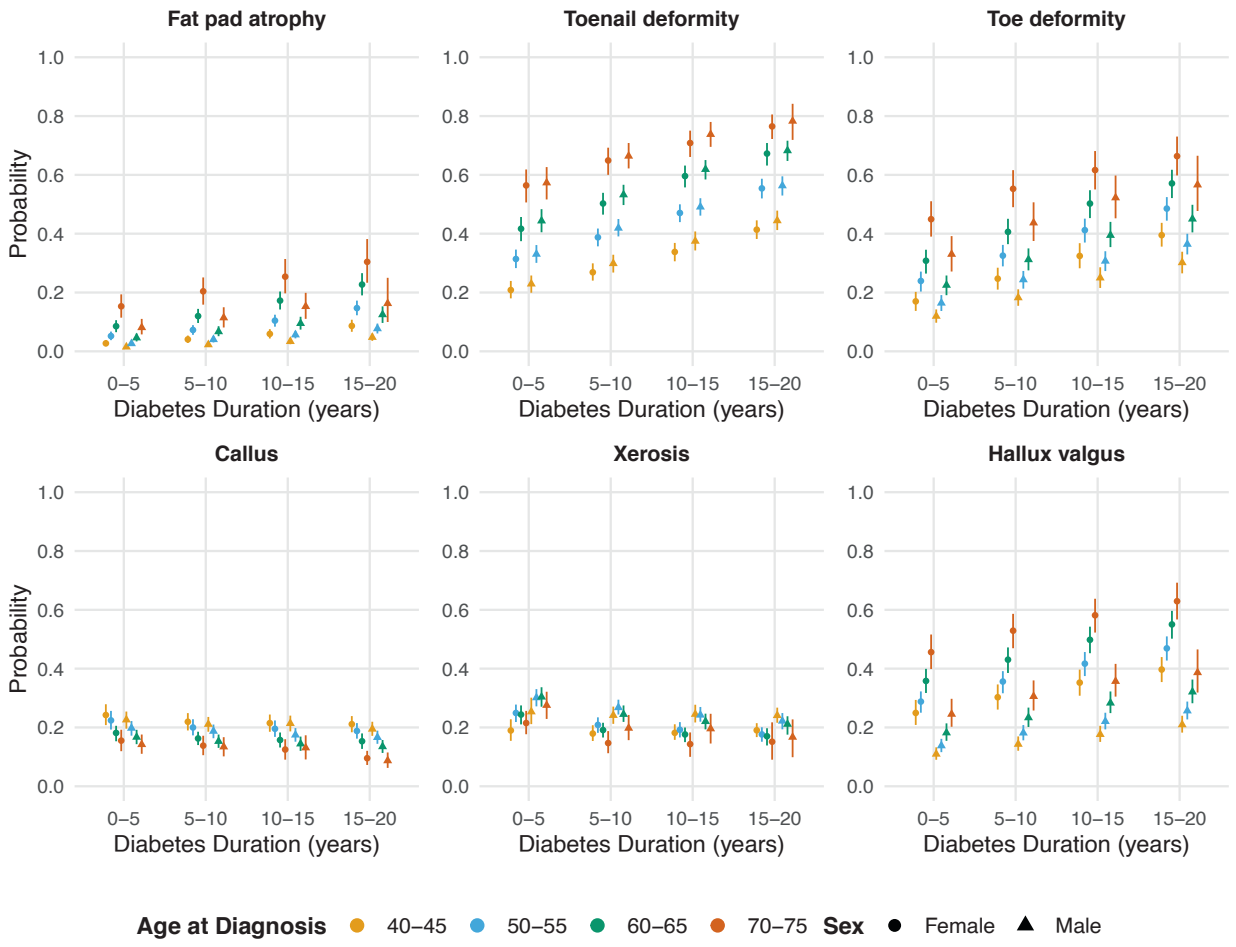


**Fig. 3.** Complication probabilities by age at diagnosis range and diabetes duration interval. Points show average patient-level probabilities of foot complications for specific age-at-diagnosis ranges and diabetes duration intervals. The 95% confidence intervals were obtained from 1000 cluster bootstrap resamples using patient-level resampling with replacement and the percentile method.

(95% CI: 30.4–36.9%) and hallux valgus from 15.5% (95% CI: 13.0–18.3%) to 27.9% (95% CI: 24.7–31.1%) over 15 years.

In contrast, cutaneous and some mechanical complications displayed divergent patterns. Callus prevalence decreased from 23.1% (95% CI: 20.2–25.8%) to 20.1% (95% CI: 18.0–22.2%), while xerosis remained relatively stable, changing from 23.3% (95% CI: 19.5–27.7%) to 22.2% (95% CI: 20.1–24.6%) over the same period.

Age at diagnosis substantially influenced both baseline risk and longitudinal trajectories. Patients diagnosed at age 70–75 years showed markedly higher baseline prevalence for most complications compared to those diagnosed at age 40–45 years. For instance, toenail deformity prevalence within 5 years of diagnosis was 56.8% (95% CI: 51.7–61.7%) for the 70–75 years age range versus 22.3% (95% CI: 19.7–24.9%) for the 40–45 years age range, though the relative increase over 15 years was more pronounced in the younger-onset group.

## 4. Discussion

We developed longitudinal prediction models to quantify diabetic foot complication progression over time, assessing variations by sex and diabetes mellitus type while adjusting for age at diagnosis. Several key patterns emerged from our analysis. First, the combination of multiple risk factors resulted in substantially higher complication probabilities, with patients exhibiting LOPS, longer diabetes duration, and older age at diagnosis demonstrating the highest risk profiles across most complications. Second, model selection using QIC criteria revealed distinct pathophysiological pathways. A linear model without interaction was optimal for fat pad atrophy, suggesting straightforward additive effects of age and duration. A linear model with significant interaction was preferred for toenail deformity, indicating synergistic effects between age and duration. Spline models without interactions were best for toe deformity, callus, and hallux valgus, capturing complex non-linear effects while maintaining additive relationships. For xerosis, the spline interaction model was optimal, reflecting the most complex relationship with both non-linear and interactive effects of age and diabetes duration. Collectively, these population-averaged estimates provide clinically actionable risk projections that account for the complex interplay between diabetes duration, age at diagnosis, and time-varying complication status.

### 4.1. Complication patterns

We included loss of protective sensation (LOPS) due to its established causal role in diabetic foot pathology [22]. As a key mechanistic link between diabetes duration and structural foot changes (e.g., fat pad atrophy, claw toes), it was evaluated for its independent association with complications. Exploratory analyses confirmed LOPS improved model fit ($\Delta$QIC = -87.7 to −508.7), supporting its relevance. Our model captured the dynamic development of neuropathy, with LOPS probabilities varying by age and diabetes duration. This ensured that estimates reflected the appropriate covariate distributions for each age-duration combination, enhancing clinical relevance.

Toenail deformities were the most frequent complications, with prevalence increasing with age and diabetes duration independently of

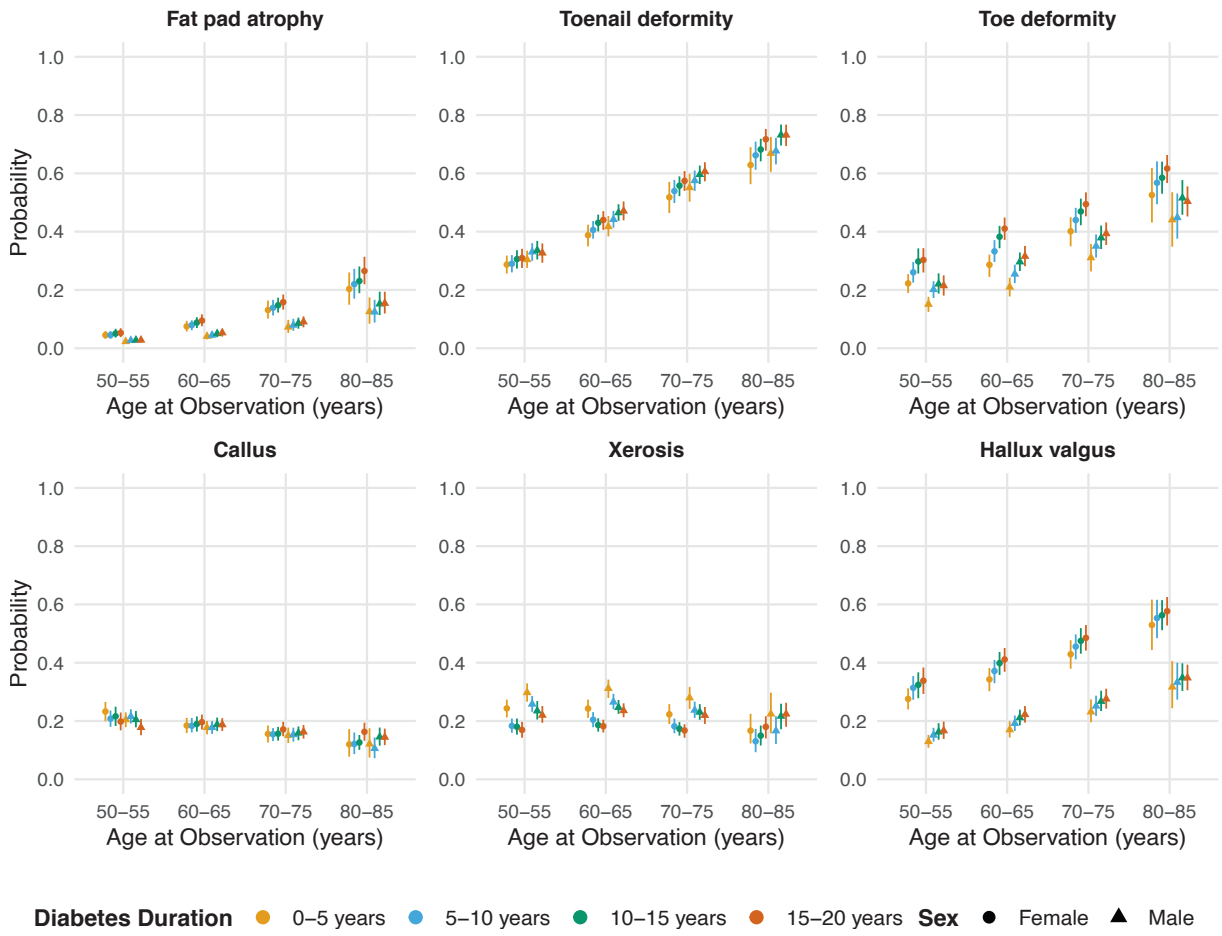


**Fig. 4.** Complication probabilities by age at observation and diabetes duration range. Points show average patient-level probabilities of foot complications in specific age at observation ranges (50–55, 60–65, 70–75, 80–85 years) and diabetes duration intervals (0–5, 5–10, 10–15, 15–20 years). The age at observation range represents the patient's age at the time of visit, derived from the combination of their age-at-diagnosis range and diabetes duration interval. The 95% confidence intervals were obtained from 1000 cluster bootstrap resamples using patient-level resampling with replacement and the percentile method.

sex or diabetes mellitus type. While prevalence rates vary across studies [23], our dynamic models provide more insight than static prevalence numbers, which are often limited in their local applicability due to variation across different populations. Nail health is intricately linked to diabetes pathophysiology [24]. Systematic analysis of nail changes holds translational potential for precision care, particularly through artificial intelligence enhanced diagnostic tools [25]. Integrating deformity data with epidemiological modeling could improve diagnostics and optimize foot care delivery [26].

Our study provides one of the few longitudinal insights into diabetic fat pad atrophy in persons with diabetes, demonstrating its clear temporal progression with age and disease duration. While the precise pathological mechanisms remain unclear, fat pad atrophy may be part of a progressive biomechanical process, evolving alongside—and likely driven by—neuropathy, muscular atrophy [27], and the subsequent deformities that lead to plantar fat pad displacement [14]. Likewise, biomechanically linked toe deformity [3] progresses with similar factors. Female sex was a significant independent risk factor, with markedly increased odds for hallux valgus, fat pad atrophy, and toe deformity. Genetic studies indicate these deformities are highly heritable in Caucasian adults [28]. Individuals probably inherit predisposing anatomical or functional traits rather than the condition itself. Extending the work of Menz et al. [29], we identified complex non-linear effects of age and diabetes duration in hallux valgus development, independent of neuropathy. This aligns with Sarı et al. [30], who also reported distinct etiological pathways. These additive patterns suggest that risk accelerates at older ages and longer durations, implying that clinical assessment should prioritize patients at the upper extremes of both factors.

Model-based analysis confirmed complications cluster into groups with straightforward (e.g., fat pad atrophy) versus complex, non-linear risk patterns (e.g., callus, xerosis). Paradoxically, cutaneous complications—callus and xerosis—decreased in prevalence with longer diabetes duration. Previous xerosis studies are scarce and report divergent estimates, likely due to non-standardized tools and demographic differences [31]. Our results confirm a strong connection between xerosis and neuropathy/anhidrosis [32], but add that longer duration decreases risk and female sex is protective. This negative association may reflect a survivorship effect or improved prophylactic care [33]. A similar pattern for callus, also noted by Liu et al. [34], suggests structured long-term management may mitigate these risks. However, this decrease may not just reflect successful care. Progressive comorbidities often reduce mobility, lessening mechanical stress and calluses despite worsening neuropathy [35] – a trend possibly signaling a shift to a more sedentary state. The female protective effect in xerosis could be mediated by sociobehavioral factors like consistent self-care. Further research is needed on its pathomorphological foundations [36]. Our spline models revealed a significant non-linear age-duration interaction for xerosis, indicating its decreasing prevalence is complex and context-dependent.

Foot deformity prevalence is higher in type 2 diabetes mellitus, with risk increased by disease duration and associated neuropathy [6]. Elevated risk with age and in women aligns with prior findings [6,37]. Yu et al. [6] observed that worse glucose regulation was protective against skeletal deformity, potentially due to activity changes. We

observed a time-related risk pattern for hallux valgus that could also be attenuated by such mechanisms. It still remains unclear whether abnormal nerve function and subsequent muscle weakness drive foot deformities [38].

### 4.2. From usual global prevalences to more meaningful local insights

This work was motivated by the need to better characterize our foot clinic's patient population, as existing published data provided limited insights into this question. As demonstrated in a recent global *meta*-analysis by Cai et al. [39], studies on hallux valgus prevalence report highly heterogeneous results, ranging from 1% to 82%. Although our data confirmed established risk factors like increased age and female sex [40,41], our derived model again provides more specific risk estimates and locally actionable insight than the generalized trends from pooled global prevalence or results from populations that differ substantially from ours. The substantial global variation in complication rates necessitates tailored, region-specific prevention strategies aligned with local epidemiological patterns [42]. The SCORE-2 Diabetes study exemplifies how population-specific calibration can refine prediction models [43], an approach made increasingly viable by expanding real-world data resources [44]. Future prevalence studies should adopt FAIR–based reporting with detailed provenance and derivation tracking [45]. As demonstrated, prevalence estimates are derived from windows and data with varying characteristics, which should be translated into comprehensive quality dimensions and also reported in a FAIR manner to capture variation in precision [46]. This would advance a field often hindered by prevalence data that are fragmented, non-comparable, and not reusable. The resulting, machine-readable estimates could be incorporated into actionable risk models, enabling data-driven diabetic foot management to optimize services, improve early detection, and allocate resources to high-risk groups [26,47].

## 5. Limitations and further research

This study has several important limitations. First, the observational design introduces potential selection bias, and foot deformity assessment involves inherent subjectivity [48] despite standardized protocols administered by certified nurses. While these limitations restrict etiopathological conclusions, the study provides relevant insights into local pathology dynamics, though screening selection bias and the exclusion of patients with prior amputations may affect the accuracy of prevalence estimates. Second, estimates at distributional extremes should be interpreted with caution, as sparse data can lead to inflated risk estimates. Third, although the models adjusted for major demographic and clinical predictors, residual confounding by unmeasured factors cannot be excluded.

This study provides a foundation for further exploration and validation of the methodological approach. Future research should incorporate additional risk factors, such as metabolic control and comorbidities, to improve the predictive accuracy and clinical utility of the models. Further studies are also needed to clarify the relationship between specific deformity types and broader clinical outcomes, including mortality [49] and cardiovascular complications, to better understand the clinical significance of individual deformities beyond foot-specific morbidity.

## 6. Conclusions

Our study provides dynamic prediction models that elucidate distinct epidemiological pathways for diabetic foot complications within a tertiary care population. By employing GEE, we captured temporal progression patterns and leveraged available longitudinal data. This analytical approach provides a reproducible framework for generating locally relevant risk profiles. The resulting models offer a practical tool for clinicians, enabling dynamic risk stratification and informing the timing of complication-specific screenings and interventions. Our findings underscore that diabetic foot complications represent a spectrum of distinct conditions, each with unique risk trajectories. This necessitates a move away from a one-size-fits-all management approach and toward the development of tailored, complication specific prevention strategies and reporting.

## CRediT authorship contribution statement

**Iztok Štotl:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Rok Blagus:** Writing – review & editing, Supervision, Methodology. **Vilma Urbančič-Rovan:** Writing – review & editing, Supervision, Resources, Methodology, Formal analysis.

## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2026.113299.

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