AMPUTATIONS IN DIABETICS: STATISTICAL MODELLING AND TRENDS IN PORTUGAL (2000–2023)

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Outline

1. Summary and Objectives
2. Data
3. Models
4. Results
5. Conclusions
6. Limitations
7. Acknowledgments
8. Bibliography

1. Summary and Objectives

- Amputation is the loss (surgical or traumatic) of a segment of the body, applied in the event of an injury (traumatic, vascular or other) that has irreparably affected the human being, causing functional limitation. Amputation also represents a considerable negative socio-economic impact for families and governments.

- Knowing the numbers, establishing the prevalence and future trends in limb loss is important for health care planning and for the rational allocation of resources, as a response to the growing indicators of demand for prostheses and related services.

- Diabetes is known as one of the leading causes of morbidity and mortality worldwide. Portugal is the fourth country in the European Union with the highest incidence rate of diabetes, according to the IDF Atlas (International Diabetes Federation, 2021). In the Annual Report of the National Diabetes Observatory (2019 Edition), it is estimated that in 2018 there will be between 605 and 618 new cases of diabetes per 100 000 inhabitants.

1. Summary and Objectives

- Although diabetes prevalence data are updated annually in Portugal through the INSA (*Medicos Sentinela*), with the COVID-19 pandemic, it is estimated that at least 20,000 diabetics have not had access to the necessary conditions for an early diagnosis. Therefore, data from this period underestimate the prevalence rate of Diabetes. The prevalence of complications related to diabetes, namely diabetic foot, tends to increase with the increasing number of people with the pathology.

- Studies show that 1 in 7 diabetics will develop foot ulcers in their lifetime, which is a risk factor for amputation. Amputation is probably the most feared and recognized complication of diabetes. It is estimated that about 50 % of amputations and ulcerations can be prevented by evaluating the foot, degree of risk of ulceration, thus allowing the implementation of preventive strategies.

1. Summary and Objectives

The main objectives of this work are:

Model, estimate and predict the number of amputations in diabetics, for the future.

- **This is an ecological time series study**, designed using the "Hospital Morbidity Database (BDGDH), for episodes with amputations", provided by the Central Administration of the Health System, IP. (ACSS), supervised by the Ministry of Health.

2. Data

- The data refer to hospitalizations related to amputations in public hospitals of the National Health Service (SNS) in Portugal, which occurred between 2000 and 2023.

- It includes the independent variables, calendar year, age, gender, etiology and amputation level.

- The disease and procedure criteria were defined according to the International Statistical Classification of Diseases, Injuries and Causes of Death, in the 11th revision of 1975 (ICD-11), with the respective code limits.

- Annual trends were estimated through Poisson and Negative Binomial regression models as well as the future prevalence rates, sex and age group stratified. Prevalence rate projections were adjusted to the distribution of the resident diabetic population in Portugal, considering the Annual Reports of the National Diabetes Observatory and the Portuguese statistical projections (National Institute of Statistics - INE).

3. Models: The Poisson Regression Model

The **Poisson distribution** models the probability of y events (i.e., failure, death, or existence) with the expression $P(Y = y|\mu, t) = \frac{e^{-\mu t}(\mu t)^y}{y!}$ $(y = 0, 1, 2, \dots)$, where μ represents the risk of a new occurrence of the event during a specified exposure period, t.
In the Poisson distribution we have $E[Y] = V[Y] = \mu$.

In **Poisson regression**, we suppose that the Poisson incidence rate μ is determined by a set of k regressor variables (the X's). The expression relating these quantities is $\mu = t\,\exp(\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_k X_k)$. The regression coefficients β_i $(i = 0, 1, \dots, k)$ are unknown parameters that are estimated from a set of data.

For an observation i, we have $P(Y_i = y_i|\mu_i, t_i) = \frac{e^{-\mu_i t_i}(\mu_i t_i)^{y_i}}{y_i!}$ $(y_i = 0, 1, 2, \dots)$, where

$$\mu_i = t_i \mu(\boldsymbol{X}'_i \boldsymbol{\beta}) \Leftrightarrow \mu_i = t_i \exp(\beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \cdots + \beta_k X_{ki})$$

To estimate the parameters β_i $(i = 0, 1, \dots, k)$ we used the hybrid method in which Fisher scoring iterations are performed before switching to the Newton-Raphson method. To test the significance of the parameters of the model, Wald test was used.

3. Models: The Poisson Regression Model

For the estimate of the Scale parameter, the Pearson chi-square method was used.

Concerning Covariance matrix, the robust (also called the Huber/White/sandwich) estimator was chosen. This is a "corrected" model-based estimator that provides a consistent estimate of the covariance, even when the specification of the variance and link functions is incorrect.

For the **Goodness of fit statistics,** the deviance and scaled deviance, Pearson chi-square and scaled Pearson chi-square, log-likelihood, Akaike's information criterion (AIC), finite sample corrected AIC (AICC), Bayesian information criterion (BIC), and consistent AIC (CAIC), were calculated. We also analysed the **Standardized Pearson residual.**

3. Models: The Negative Binomial Regression Model

The Poisson distribution may be generalized by including a gamma noise variable which has a mean of 1 and a scale parameter of υ. The Poisson-gamma mixture (**negative binomial**) distribution that results is

$$P(Y = y_i|\mu_i, \alpha) = \frac{\Gamma(y_i+\alpha^{-1})}{\Gamma(y_i+1)\Gamma(\alpha^{-1})}\left(\frac{\alpha^{-1}}{\alpha^{-1}+\mu_i}\right)^{\alpha^{-1}}\left(\frac{\mu_i}{\alpha^{-1}+\mu_i}\right)^{y_i} \quad (y = 0, 1, 2, \dots),$$

where $\mu_i = t_i\mu$ and $\alpha = \frac{1}{\upsilon}$. μ represents the risk of a new occurrence of the event during a specified exposure period, t.

The results below make use of the following relationship derived from the definition of the gamma function:

$$ln\left(\frac{\Gamma(y_i + \alpha^{-1})}{\Gamma(\alpha^{-1})}\right) = \sum_{j=0}^{y_i-1} ln(j + \alpha^{-1})$$

3. Models: The Negative Binomial Regression Model

In **negative Binomial regression**, the mean of y is determined by the exposure time t and a set of k regressor variables (the X's). The expression relating these quantities is $\mu_i = \exp(\ln(t_i) + \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \cdots + \beta_k X_{ki})$. The regression coefficients β_i $(i = 0, 1, \dots, k)$ are unknown parameters that are estimated from a set of data.

For an observation i, we have $P(Y = y_i|\mu_i, \alpha) = \frac{\Gamma(y_i+\alpha^{-1})}{\Gamma(y_i+1)\Gamma(\alpha^{-1})}\left(\frac{1}{1+\alpha\mu_i}\right)^{\alpha^{-1}}\left(\frac{\alpha\mu_i}{1+\alpha\mu_i}\right)^{y_i}$ $(y = 0, 1, 2, \dots)$.

To estimate the parameters β_i $(i = 0, 1, \dots, k)$ we used the hybrid method in which Fisher scoring iterations are performed before switching to the Newton-Raphson method. To test the significance of the parameters of the model, Wald test was used.

3. Models: The Negative Binomial Regression Model

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4. Results

Poisson and Negative Binomial Regression models were adjusted to the number of amputations.

Goodness of Fit[a]	Poisson Model			Negative Binomial Model		
	Value	df	Value/df	Value	df	Value/df
Deviance	3297,764	329	10,024	61,485	329	0,187
Scaled Deviance	3297,764	329		61,485	329	
Pearson Chi-Square	3356,501	329	10,202	53,631	329	0,163
Scaled Pearson Chi-Square	3356,501	329		53,631	329	
Log Likelihood[b]	-2679,132			-1797,635		
Akaike's Information Criterion (AIC)	5422,264			3659,270		
Finite Sample Corrected AIC (AICC)	5428,703			3665,709		
Bayesian Information Criterion (BIC)	5546,708			3783,714		
Consistent AIC (CAIC)	5578,708			3815,714		

Dependent Variable: Number of amputations
Model: (Intercept), Year, Sex, Age[a]

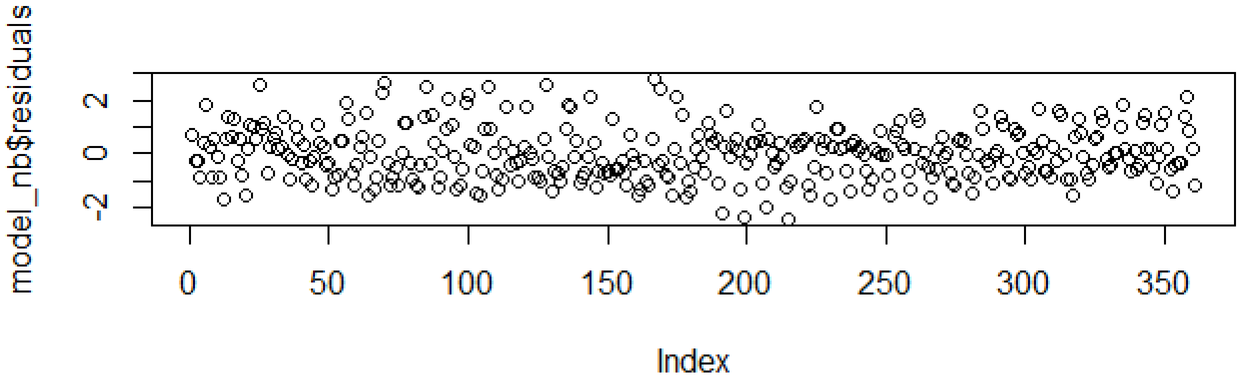
a. Information criteria are in smaller-is-better form.

b. The full log likelihood function is displayed and used in computing information criteria.

In both models, the year was not significant in the Wald test in the period under analysis, that is, there is no global effect and/or pattern of growth/decrease although we can observe a slight positive evolution in the prevalence of amputations

4. Results

Analysing the standardized Pearson residual plot, it can be seen that that all the points are within the interval [-2; 2].



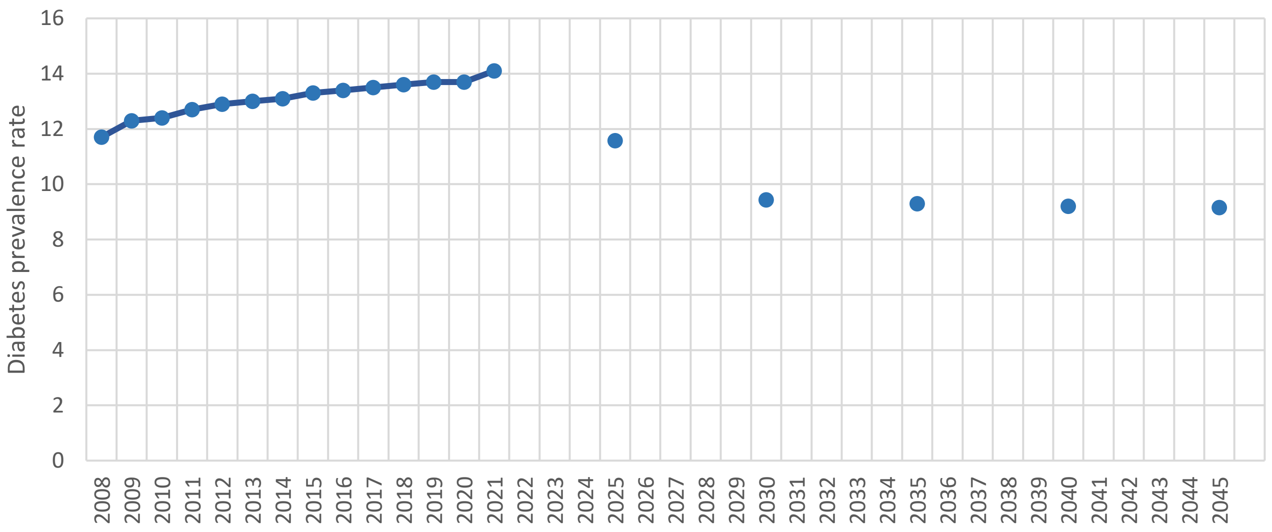
Standardized Pearson Residual – Negative Binomial Model

4. Results

Prevalence of Diabetes

Estimates and projections from 2025 to 2045

Sources: Annual Report of the National Observatory of Diabetes – "Diabetes: Factos e Números", 9ª Ed. (2019) Portugal, and IDF Diabetes Atlas 10th Ed.(2021) of the International Federation of Diabetes

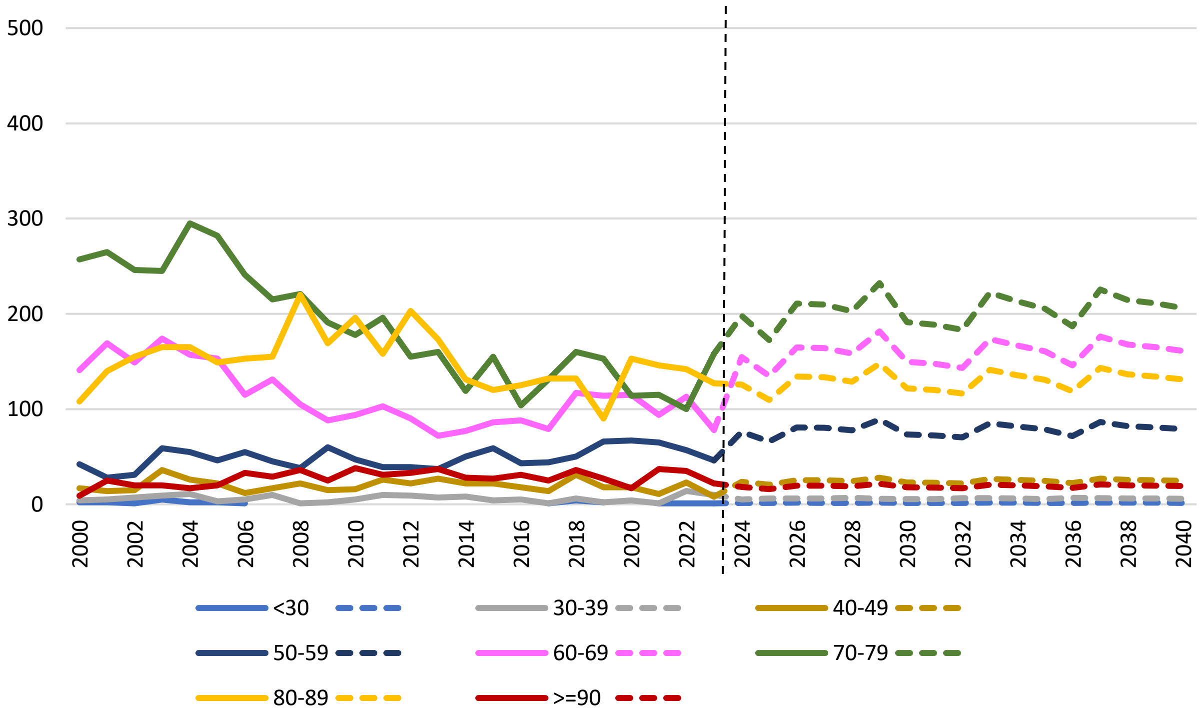


4. Results

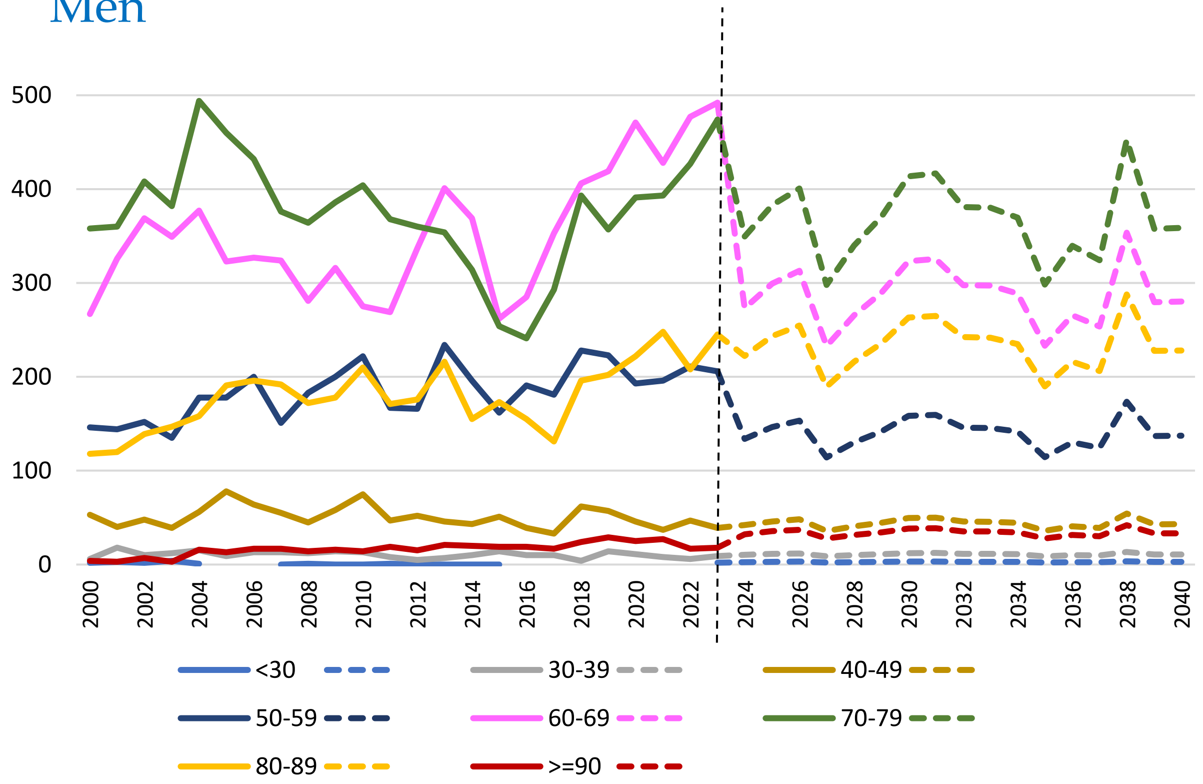
Total of amputations in diabetics – Negative Binomial model

Estimates and projections for 2025 and 2030 stratified by sex and age

Women



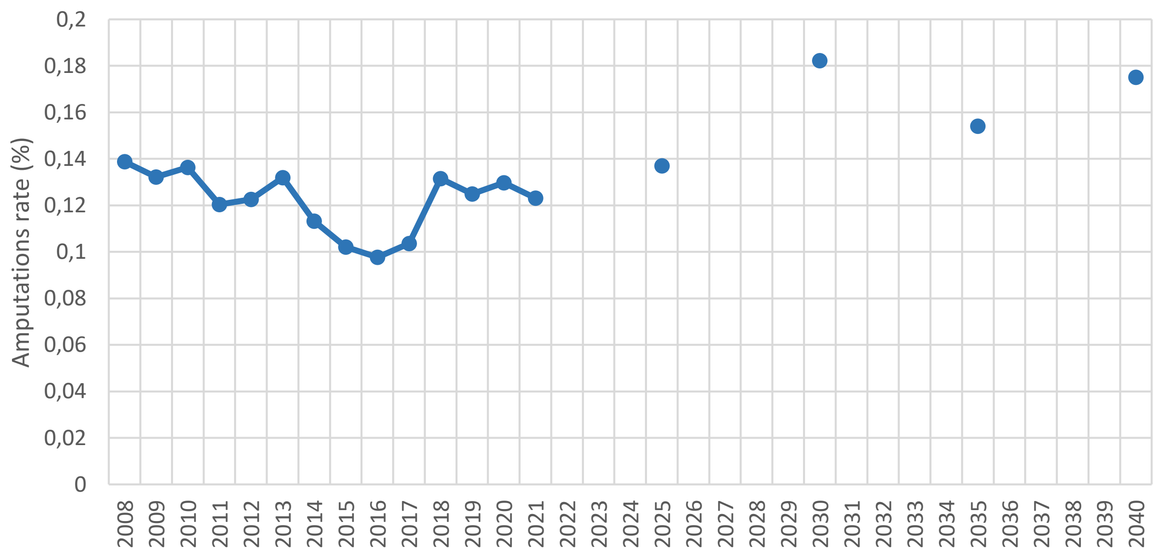
Men



4. Results

Amputations rate in diabetics –Negative Binomial Models

Estimates and projections from 2025 to 2040



Projections of the rate of amputations in diabetics point to an increase.

The empirical prediction intervals with 95% confidence were derived as in Hakulinen and Dyba (1991) for 2025, 2030, 2035 and 2040 such as:

Year	95% C.I. for n (%)	
	Lower	Upper
2025	1480 (0.12%)	1910 (0.15%)
2030	1631 (0.16%)	2061 (0.20%)
2035	1321 (0.13%)	1751 (0.18%)
2040	1507 (0.15%)	1938 (0.20%)

5. Conclusions

- The projections of the prevalence of diabetes point to a decrease over the next two decades
  - ❖ These results can be partially explained by the strong information campaigns on diabetes and the great focus on prevention.
- The projections of the prevalence of amputations in diabetics point to an increase. These results can be explained by the aging of the population, mainly in the age group 60 to 89 years, and the late diagnosis of diabetes.
  - ❖ Despite all the information campaigns on the diabetic foot, for example, there is still a little investment in prevention. Little investment in information, as one of the consequences of diabetes are amputations of both the lower and upper limbs (minor - for example fingers, major - for example leg, arm, etc).
  - ❖ Considering the increase in the prevalence of amputations in the diabetic population, the National Health System of Portugal has to invest both in prevention and in hospital services so that its users can have a timely and adequate response.

5. Conclusions

As previously mentioned, there are different levels of amputation, minor and major. It is our intention to make projections by amputation level, as it is something that should concern the Portuguese National Health System, as well as the National Social Security System.

An amputee with one or multiple amputations can pose a “burden” to both the Portuguese National Health System and the National Social Security System.

6. Limitations

The historical data is a relatively short ecological time series to produce the best model. Although the measures of fit do not reject the models, it is appropriate to continue the investigation with more data;

Apparently there was a not so high over-dispersion, but the Negative Binomial model presents better values in information criteria indicators that point to a better fit.

We hypothesize that the reduction of diabetic population might be associated with the population under the effective observation by the GP Sentinel Network;

The performance of prediction intervals depended on the number of cases on which the predictions are based, and so they should be interpreted with caution. Bootstrap based C.I. are an alternative to take into account in the next steps.

7. Acknowledgments

This work is partially financed by national funds through FCT Fundaçãao para a Ciência e a Tecnologia FCT/MCTES under the projects:
UIDP/05608/2020. DOI 10.54499/UIDP/05608/2020 (https://doi.org/10.54499/UIDP/05608/2020), UIDB/05608/2020. DOI 10.54499/UIDB/05608/2020 (https://doi.org/10.54499/UIDB/05608/2020) – Elisabete Carolino and UIDB/00006/2020. DOI: 10.54499/UIDB/00006/2020 (https://doi.org/10.54499/UIDB/00006/2020) – Rosário Ramos.

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THANK YOU FOR YOUR ATTENTION

Any suggestion is very welcome