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Effects of social deprivation and healthcare access on major amputation following a diabetic foot ulcer in a French administrative area: Analysis using the French claim data

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Abstract

Aim: The link between social deprivation and the development of diabetic foot ulcer (DFU) is still widely debated. The study objective was to evaluate the relationship between lower limb amputation, social deprivation level, and inequalities in access to care service among people with DFU. This regional pilot study was conducted at the living area level and based on the French National Health Data System (SNDS).

Methods: We conducted a retrospective cohort study using hospital and primary care claim data in the Languedoc-Roussillon region. DFUs were determined using an original algorithm of care consumption or hospital diagnosis. The primary end point was amputation at 1 year. Secondary end points were mortality at 1 year and impact of potential access to care on amputation.

Results: We included 15,507 people from 2015 to 2017. Amputation and mortality rates were 17.5 and 117 per 1000 person-years. The least precarious living areas showed better prognoses (relative risk = 0.46; 95% CI 0.27–0.66). Territorial accessibility to a private-practice nurse, unlike physician accessibility, was associated with better results on major outcomes ($p = 0.004$).

Conclusion: This is the first study using SNDS to study the care pathway of DFU management within and outside the hospital. High social deprivation in a living areas seems to be associated with more major amputations after a DFU.

KEYWORDS

amputation, diabetes, diabetic foot ulcer, epidemiology, French National Health Data System, social deprivation

1 | INTRODUCTION

Diabetic foot ulcer (DFU) is a major complication of diabetes mellitus, with an estimated lifetime incidence of 19%–34%¹ and estimated direct cost more than 17 billion dollars in the United States.² Amputation and death are the main complications of diabetes-related foot disease,

amputation resulting in many disabilities with major social impact.²

Even in countries with universal health care systems, social deprivation continues to have an impact on diabetes prognosis.³ The pathways leading to DFU are complex and, unlike most diabetes complications and diabetes control itself,⁴ the association between social deprivation and

DFU incidence has been inconsistent.⁵ Thus, several studies have explored the impact of where people live on DFU prognosis, coming to different conclusions.^{6,7} As the results may depend on the definition of social deprivation,⁸ Hurst et al. carefully and accurately mapped DFU incidence and complications (amputation and death) using the Scottish government's official social deprivation index and reported that the poorest DFU prognoses and highest DFU incidences were found in the most socially deprived quintile neighbourhoods.⁹ The same results were noted in Los Angeles.¹⁰ These studies pointed to the importance of taking geographic location into account in elaborating new health policies for care provision in response to the deleterious effect of deprived neighbourhoods on diabetes complications on the history of diabetes.

The French ENTRED study, which included 1/97th of the French population living with diabetes, randomly enrolled people according to their National Identification Number. Despite good health insurance coverage in France, the ENTRED study confirmed links among social deprivation, educational level, diabetes complications and podiatric complications.¹¹ It also showed a gradation between area of residency deprivation level and foot ulcer or amputation incidence.¹²

The French National Health Data System (*Système National des Données de Santé*—SNDS) includes all hospital diagnoses from the Medicalization of Information Systems Program (*Programme de Médicalisation des Systèmes d'Information*—PMSI) and the mandatory health insurance refund history for each individual from the National Inter-Insurance Health Insurance System (*Système national d'information inter-régime de l'assurance maladie*—SNIIR-AM) for more than 99% of the French population.¹³ Although this database closely reflects the reality of health consumption and health access, to our knowledge, it has never been used to explore DFU.

Thus, the main aim of this study was to analyse the link between social deprivation and major amputation at the living area and individual levels of people with DFU, whether or not the ulcer had led to hospitalization. Secondary aims were mortality at 1 year and impact of potential access to care measured at the living area level on major lower limb amputation.

2 | METHODS

This retrospective cohort study used hospital and primary care claim data from a French administrative area of 2.727 million people. All fully anonymized individual claim data in France are registered in the SNDS. Socioeconomic data at the living area level are registered in the database of the French National Institute of

What's new?

- The link between social deprivation and diabetic foot ulcer (DFU) is widely debated. This study tests the impact of social deprivation level and access to out-of-hospital primary care using French health claim databases (SNDS).
- Major DFU outcomes were associated with nurse but not general practitioner accessibility. Social deprivation in living areas was linked to major DFU outcomes.
- This is the first study of major amputation following DFU for in-hospital and out-of-hospital individuals. It shows the impact of paramedical care networks in amputation and mortality after DFU.

Statistics and Economic Studies (*Institut national de la statistique et des études économiques*—INSEE) as open-source data. INSEE defines living areas as the smallest territories within which residents have access to facilities and everyday services. All care was associated with an individual and his/her primary zip code of residence, not with the location where care was given. Individuals were included from January 2015 to December 2017. This study was part of the usual public health assessment of the Regional Medical Department of the *Caisse Nationale d'Assurance Maladie* (CNAM), the national health insurance institution in charge of the SNDS. Therefore, there was no need to obtain authorization from a Research Review Board.

2.1 | Population

The population was defined as people living with any type of diabetes with a complication of DFU. Diabetes is defined in the SNDS database according to Fuentes et al.¹⁴: At least three diabetes medication refills or an International Classification of Disease 10th (ICD-10) diagnostic code of diabetes registered with CNAM or in hospital charts. Each individual was included once at the onset of the first DFU occurring within the study period, and thus, they could not be included twice.

DFU was defined as:

- hospitalization with a primary diagnosis of DFU (Table S1) defined by Fosse-Edorh et al.¹²
- bandage refund for at least 28 days, as defined by the International Working Group for Diabetic Foot (IWGDF). All refunds made after hospitalization with

a principal diagnosis of decubitus ulcer or a burn of any kind and after surgery unrelated to the lower limb (Table S2) were excluded.

Wound onset was defined as the date of hospitalization admission or the first bandage refund. Exclusion criteria were:

- hospitalization as defined in Table S3.
- living in a residential institution for dependent elderly persons (*Etablissement d'Hébergement pour Personnes Agées Dependantes*—EHPAD) or a long-term unit.
- age under 20 years.

2.2 | Outcomes: Amputation, death and potential access to care

The primary outcome was major amputation (mid-foot amputations and above, Table S1) within the year following wound onset. Secondary outcomes were all-cause mortality within the year following wound onset and the impact of potential access to care measured at the living area level on major lower limb amputation.

2.3 | Deprivation and access to care assessment

Deprivation was assessed at the living area level using fDep, the French deprivation index.¹⁵ fDep is the first component in the principal component analysis of median household income, percentage of high school graduates in the population aged 15 years and older, percentage of blue-collar workers in the active population and unemployment rate. We calculated it using the 2012 data. The 2012 INSEE data showed 100 living areas in the former Languedoc-Roussillon (recently renamed Occitanie).

Access to care can be estimated through the number of general practitioners (GPs), private-practice nurses and GPs and private-practice nurses combined per 1000 inhabitants. We also considered the potential localized accessibility (*Accessibilité potentielle localisée*—APL) to GPs and private-practice nurses, a variable built by French regulatory authorities as the standardized number of consultations available in a territory.¹⁶ We used the last available index, calculated in 2016.

2.4 | Statistical analysis

Data are presented using mean \pm SD or incidence per 1000 person-years. To compare incidences of different

living areas, DFU incidences and outcomes were standardized according to age and sex using the direct method, with the whole study sample as the reference population ($n = 15,507$). Strictly, the 'DFU incidence' is the incidence of inclusion in this study in the general population. The incidence of outcomes is the incidence in our sample ($n = 15,507$). All incidences were calculated in each living area. Amputation and death rates are calculated on the population of people with DFU.

Living areas were classified in quartiles of fDep, and medians and quartiles of incidences of outcomes were described for each quartile of deprivation. We calculated the relative risk (RR) with the most deprived quartile as the reference. We conducted a log-rank analysis to compare the people with the best accessibility to a GP and, separately, a nurse. We compared the quartile of people with DFU with the worst access versus the others.

For each living area, the amputation rate was divided by the sum of the density of GPs and private-practice nurses. This ratio of amputation/primary care offer is graphically shown using maps at the living area level. The legends of these maps use quintiles of the ratio. Mortality rate and the composite of death and amputation were analysed using the same method.

3 | RESULTS

In 2012, our administrative area had 2,700,266 inhabitants, 2,323,679 if we only consider people living in commune attached to living areas belonging mainly to Languedoc-Roussillon. During the 3 years of the inclusion period, we identified 197,832 persons with diabetes and 32,923 cases of DFU, with 7204 requiring hospitalization. After assessment of the exclusion criteria, we included 15,507 people at the date of their first DFU (Figure 1). Mean age was 70 (SD 23) years. There were 55% men (Table 1).

Two hundred and fifty-three amputations occurred during the first year of follow-up (17.5 amputations per 1000 person-years) and 117 deaths per 1000 person-years (Table 1). The mean GP accessibility was 4.7 ± 1.2 and the mean nurse accessibility was 234 ± 63 .

3.1 | DFU, amputation and death maps

We observed individuals with DFUs in all living areas, except one low-density area in the north of the administrative area. Figure 2 shows the amputation and death incidence by living area. Living areas around the coast and major cities seemed to have better prognoses regarding amputation. This was also the case in living areas with higher healthcare access (Figures 3 and 4; Figures S1–S5).

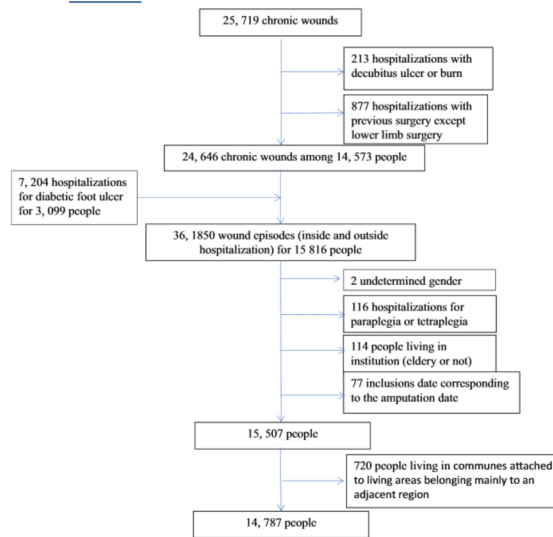


FIGURE 1 Flow chart

TABLE 1 Description of the population with diabetic foot ulcer (DFU) in the Languedoc-Roussillon region between 2015 and 2017, and rates of DFU with reference to the population of Languedoc-Roussillon ($n = 2,700,266$). Rates of major amputations and death are for the year following inclusion in the study for those who suffered a DFU

Numbers with DFU	15,507
DFU rate (per 1000 person-years)	1.9
Requiring hospitalization	3099 (20)
Age (years)	70 ± 23
Men	8498 (55)
Amputations, n (%)	
Amputation rate (per 1000 person-years)	17.5
Deaths, n (%)	
Death rate (per 1000 person-years)	117

Note: Data displayed are n (%), mean ± SD, rates (per 1000 person-years).

3.2 | Deprivation impact

We first highlighted a difference in amputation rate from one to two between the three most deprived quartiles of living areas and those less deprived. However, this was not observed for mortality rate (Table 2). Thus, less deprived areas seem to have better prognoses concerning

amputation (quartile 4 vs. quartile 1: RR = 0.46; 95% CI 0.27–0.66) but not mortality (Table 2).

3.3 | Care accessibility

Maps created according to healthcare access (measured by healthcare provider density) showed that rural living areas at the periphery of the administrative area were more likely to have higher amputation rates according to healthcare access.

Low accessibility to a private-practice nurse was linked to higher rates of amputation (log-rank, $p < 0.001$), unlike GP accessibility, which showed no link (log-rank, $p = 0.195$).

4 | DISCUSSION

For the first time, we used the SNDS database at a regional level and demonstrated that living areas with the worst amputation rates appeared to be the most deprived and the least populated, with the lowest access to nurses. Interestingly, good GP accessibility was not linked to less major amputation following DFU. Our results also highlight that amputation and death risks were not strictly geographically superimposable.

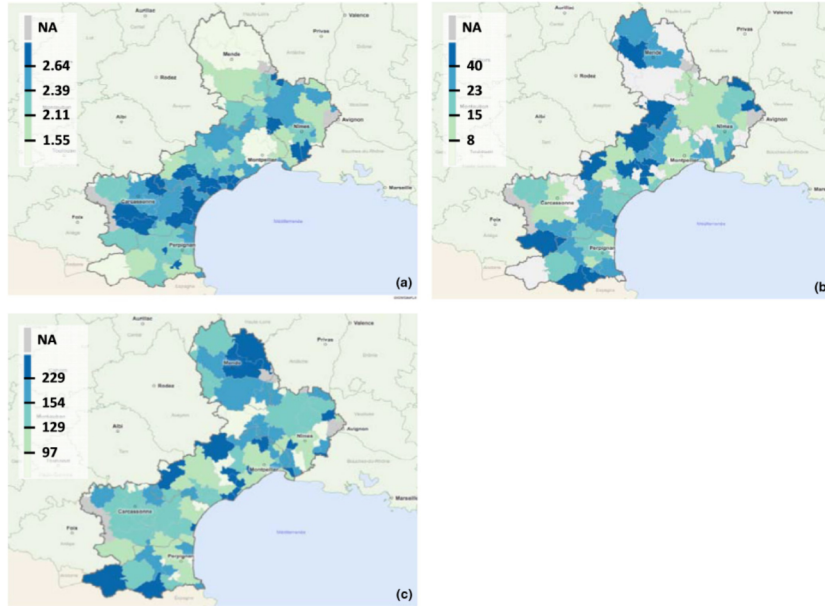


FIGURE 2 Incidence rate in living areas of Languedoc-Roussillon between 2015 and 2018. (a) Diabetic foot ulcer (DFU) rate; (b) amputation rate; (c) mortality rate. Incidence is standardized on age and sex and is given for 1000 person-years. DFU rate is calculated on the total population of Languedoc-Roussillon. Amputation and death rates are calculated on the population of people with DFU

4.1 | Impact of social deprivation on major amputation following DFU

According to the fDep score, the least precarious living areas had the lowest rates of amputation among people with DFU. fDep is a complex and progressive score.¹⁵ With fDep, we noted lower amputation rates only for the less deprived living areas. This is not fully consistent with the findings of Hurst et al.⁹ and Riley et al.,¹⁷ who highlighted the difference in burden between the most deprived quintile of areas and the other quintiles. Living in a deprived area with a low educational level¹⁸ and high unemployment rate was associated with poor DFU prognosis but, paradoxically, a low household income can ensure better medical care for the person. This might thus point towards a pull-down effect.¹⁰

After adjustment for the primary care offer, rural areas appeared to be correlated with major amputation following DFU. It is interesting to note that the most deprived living areas of Languedoc-Roussillon were the least populated.

Improving access to public services, reducing geographic isolation and strengthening connections between small living areas and the largest areas might be public policy options to decrease the gap in major amputation following DFU between the most and the least populated living areas.

4.2 | Access to healthcare

Regarding access to healthcare, the ratio between amputation and death rates and GP or nurse numbers was lower in the larger cities of Languedoc-Roussillon (Figures S5 and S6).

Nonetheless, in contrast to other studies, we did not find a link between GP accessibility and major amputation following DFU¹⁹ but did find a link with nurse accessibility. A consultation before the wound might be a marker of the severity of the person's medical background. Thus, accessibility to a GP or nurse according to an available communal

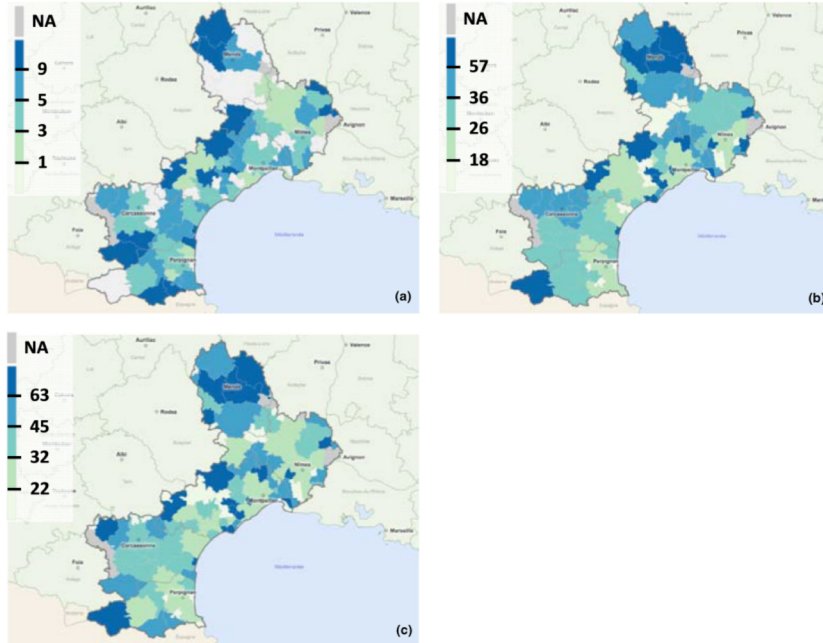


FIGURE 3 (a) Amputation rate per living area in relation to primary healthcare access (general practitioner [GP] and private-practice nurse density); (b) mortality rate per living area in relation to primary healthcare access (GP and private-practice nurse); (c) Amputation and death rate per living area in relation to primary healthcare access (GP and private-practice nurse). Amputation and death rates are calculated on the population of people with diabetic foot ulcer. Incidence is standardized on age and sex and is given for 1000 person-years. GP and nurse density are calculated according to the whole population of Languedoc-Roussillon

data set like the APL is more relevant. A previous study using SNDS found a link between the prognosis of heart failure, another chronic disease and nurse accessibility.²⁰ To our knowledge, this is the first time that a clear link between nurse accessibility and major amputation following DFU has been found using SNDS, which makes sense as local care is provided by nurses. This may argue for healthcare policies that promote nurse installation in rural areas.

4.3 | DFU and primary care consumption

Using the SNDS and our algorithm had the advantage of being more representative of ambulatory care. As already mentioned, previous epidemiological studies focused only on hospitalized individuals with DFU²¹ or self-reported DFU.¹¹ We conducted

an exhaustive analysis of people with diabetes and DFU across all living areas in the administrative area, Languedoc-Roussillon. We found five times more individuals with DFUs than by using PMSI only. Thus, healthcare organizations will have to manage these unseen DFUs in calibrating the medical response. It is indeed crucial that new healthcare pathways for managing DFU and other diabetes complications include GPs and nurses. These professionals need to be coordinated with the DFU reference centres.

4.4 | Geographic difference in mortality and amputation risks

Several hypotheses may explain the differences between the geographic maps of amputation and death rates. First,

FIGURE 4 Nurse density per 1000 people per living areas according to the total population (with or without diabetic foot ulcer)

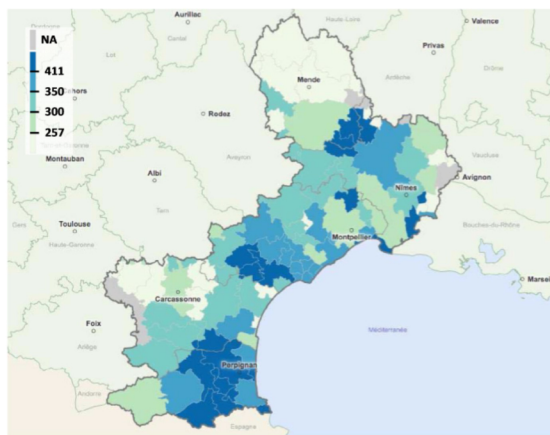


TABLE 2 Amputation rate, death rate and composite criteria of amputation or death rate of living areas, according to the quartile of the deprivation index (fDep). Total population corresponds to the numbers living in quartile groups. Amputation and death rates are standardized on age and sex. Diabetic foot ulcer (DFU) rate are calculated on the total population of Languedoc-Roussillon. Amputation and death rates are calculated on the population of people with DFU. DFU rates are not standardized on age and sex. The total number of people with DFUs included in this table is 14,787. People living in communes attached to living areas belonging mainly to an adjacent region were excluded from this analysis

	Quartile 1 (most deprived)	Quartile 2	Quartile 3	Quartile 4 (least deprived)
Total population	352,255	668,936	673,764	738,724
Number of DFUs	3498	3050	4550	3689
DFU rate (/1000 person-year)	2.35 (1.9–2.85)	2.45 (1.85–2.85)	2.14 (1.75–2.39)	1.8 (1.48–2.26)
Deprivation index	1.42 ± 0.22	0.90 ± 0.12	0.52 ± 0.11	−0.33 ± 0.60
Amputation rate (/1000 person-year)	17 (0–49)	18 (0–23)	15 (0–29)	8 (0–23)
Amputation—RR 95% CI	1	1.06 (0.96–1.15)	0.89 (0.77–1.01)	0.46 (0.27–0.66)
Death rate (/1000 person-year)	162 (118–300)	129 (77–173)	134 (101–158)	137 (101–242)
Death—RR 95% CI	1	0.80 (0.64–0.96)	0.83 (0.68–0.98)	0.85 (0.71–0.99)
Amputation or death rate (/1000 person-year)	169 (130–269)	140 (106–189)	158 (130–179)	153 (111–319)

Note: Data displayed are median (Q1–Q3) or mean ± SD, unless otherwise indicated. Abbreviation: RR, relative risk.

care may be delayed or suboptimal due to the lack of a multidisciplinary approach or material resources.²² Also, risk factors for mortality may not be the same as for amputation. Thus, variations in medical decisions have been identified.²³

Moreover, the populations that suffered the least from DFUs were not those with the best prognoses, as example in Lozère (around the city of Mende). Lozère has a high rate of isolated people a known factor of renunciation of care and a much discussed factor of DFU prognosis.²⁴

4.5 | Study strengths and algorithm validation

Our study's first strength is its power and exhaustiveness. To our knowledge, this is the first wide epidemiological study in France that included people with DFU whether or not the DFU had led to hospitalization. We assumed that including only those hospitalized with DFU might constitute a bias. Using the algorithm, five times more people with DFU were included. Therefore, the cohort does not present the same characteristics as in previous works based on the French healthcare insurance database.²⁵

In addition, the SNDS presents several advantages. First, it covers almost the entire French population. Second, all French residents have access to universal healthcare. Thus, there is no more exhaustive database in France¹³ and, even though we confined ourselves only to Languedoc-Roussillon, we created one of the biggest published cohorts of people with DFU. Third, using the SNDS provides real-life analysis without volunteer bias or recall bias. The largest population not covered by the SNDS are migrants in an irregular situation.

Several results validate our algorithm. The amputation rate 1 year after wound onset is congruent with that of other international studies,^{26,27} despite being lower than the amputation rates of several studies that recruited people with DFU during hospitalization or in specialized centres.^{18,28} This was the same case for our mortality rate, according to the mean age of the cohort.²⁸

In addition, our analysis of the link between geographic deprivation and major amputation following DFU is quite strong because it uses a living area's deprivation level for the analysis, which corresponds to the social organization of territorial populations and not to artificial partitions.²⁹ Furthermore, the fDep is a complex score of deprivation that was built specifically for France and is not based only on household incomes.²⁵ Specific variables include educational level and occupational trends. Both variables have shown their relevance in diabetes and DFU.¹¹ This is the first study of this type in France.

4.6 | Study limitations

The first study limitation was our reliance on an algorithm to define DFU, which depended on the SNDS database for the first time regarding this issue. We therefore cannot state with certainty, despite all the safeguards put into place, that all the people in the study had DFUs.

Some limitations were necessarily associated with SNDS. We did not know all the social characteristics of

the study individuals, except for what was available from the health insurance regime. In addition, all other information concerning deprivation was geographic data. This deserves further research.

It should be recalled that Languedoc-Roussillon is a specific administrative area of France and caution is needed in generalizing these results. Previous studies have seen opposite results regarding deprivation and diabetes as a result of differences in the social structure of the studied areas.³⁰

We performed only descriptive and univariate analyses. As it is known that social, geographical and clinical characteristics may be associated, the complete assessment of risk factors of amputations would need multivariable analyses. However, this was out of the scope of this study.

5 | CONCLUSION

Our work highlights the relationship between deprived areas and higher risk of amputation, whereas no relationship has been demonstrated with mortality. We also show that nurse accessibility might be a key strategic point for DFU medical care. Also, if improving healthcare accessibility for the most deprived people has a global effect on other factors of social deprivation, such as a low educational level or unemployment, it should become a key factor to decrease amputation rates. Social deprivation continues to have a complex relation with major amputation following DFU, but this study suggests ways to improve healthcare access that may be of interest to healthcare policymakers. Confirmation of the model and results at the national level and in other countries, especially where social security is not universal, seems necessary.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

JBB, AS and CD involved in study concept and design, and wrote the manuscript; GN, CD, JBB and LP involved in statistical analysis and acquisition of data; AA, AS, CD involved in study supervision. All authors read and approved the final version of the manuscript.

ETHICS STATEMENT

All procedures performed in studies involving human participants are in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was part of the usual public health assessment of the Regional Medical Department of the *Caisse Nationale d'Assurance Maladie* (CNAM), the national health insurance institution in charge of the SNDS.

DATA AVAILABILITY STATEMENT

According to SNDS rules, data are not available on request from the authors.

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DFU incidence has been inconsistent.⁵ Thus, several studies have explored the impact of where people live on DFU prognosis, coming to different conclusions.^{6,7} As the results may depend on the definition of social deprivation,⁸ Hurst et al. carefully and accurately mapped DFU incidence and complications (amputation and death) using the Scottish government's official social deprivation index and reported that the poorest DFU prognoses and highest DFU incidences were found in the most socially deprived quintile neighbourhoods.⁹ The same results were noted in Los Angeles.¹⁰ These studies pointed to the importance of taking geographic location into account in elaborating new health policies for care provision in response to the deleterious effect of deprived neighbourhoods on diabetes complications on the history of diabetes.

The French ENTRED study, which included 1/97th of the French population living with diabetes, randomly enrolled people according to their National Identification Number. Despite good health insurance coverage in France, the ENTRED study confirmed links among social deprivation, educational level, diabetes complications and podiatric complications.¹¹ It also showed a gradation between area of residency deprivation level and foot ulcer or amputation incidence.¹²

The French National Health Data System (*Système National des Données de Santé*—SNDS) includes all hospital diagnoses from the Medicalization of Information Systems Program (*Programme de Médicalisation des Systèmes d'Information*—PMSI) and the mandatory health insurance refund history for each individual from the National Inter-Insurance Health Insurance System (*Système national d'information inter-régime de l'assurance maladie*—SNIIR-AM) for more than 99% of the French population.¹³ Although this database closely reflects the reality of health consumption and health access, to our knowledge, it has never been used to explore DFU.

Thus, the main aim of this study was to analyse the link between social deprivation and major amputation at the living area and individual levels of people with DFU, whether or not the ulcer had led to hospitalization. Secondary aims were mortality at 1 year and impact of potential access to care measured at the living area level on major lower limb amputation.

2 | METHODS

This retrospective cohort study used hospital and primary care claim data from a French administrative area of 2.727 million people. All fully anonymized individual claim data in France are registered in the SNDS. Socioeconomic data at the living area level are registered in the database of the French National Institute of

What's new?

- The link between social deprivation and diabetic foot ulcer (DFU) is widely debated. This study tests the impact of social deprivation level and access to out-of-hospital primary care using French health claim databases (SNDS).
- Major DFU outcomes were associated with nurse but not general practitioner accessibility. Social deprivation in living areas was linked to major DFU outcomes.
- This is the first study of major amputation following DFU for in-hospital and out-of-hospital individuals. It shows the impact of paramedical care networks in amputation and mortality after DFU.

Statistics and Economic Studies (*Institut national de la statistique et des études économiques*—INSEE) as open-source data. INSEE defines living areas as the smallest territories within which residents have access to facilities and everyday services. All care was associated with an individual and his/her primary zip code of residence, not with the location where care was given. Individuals were included from January 2015 to December 2017. This study was part of the usual public health assessment of the Regional Medical Department of the *Caisse Nationale d'Assurance Maladie* (CNAM), the national health insurance institution in charge of the SNDS. Therefore, there was no need to obtain authorization from a Research Review Board.

2.1 | Population

The population was defined as people living with any type of diabetes with a complication of DFU. Diabetes is defined in the SNDS database according to Fuentes et al.¹⁴: At least three diabetes medication refills or an International Classification of Disease 10th (ICD-10) diagnostic code of diabetes registered with CNAM or in hospital charts. Each individual was included once at the onset of the first DFU occurring within the study period, and thus, they could not be included twice.

DFU was defined as:

- hospitalization with a primary diagnosis of DFU (Table S1) defined by Fosse-Edorh et al.¹²
- bandage refund for at least 28 days, as defined by the International Working Group for Diabetic Foot (IWGDF). All refunds made after hospitalization with

a principal diagnosis of decubitus ulcer or a burn of any kind and after surgery unrelated to the lower limb (Table S2) were excluded.

Wound onset was defined as the date of hospitalization admission or the first bandage refund. Exclusion criteria were:

- hospitalization as defined in Table S3.
- living in a residential institution for dependent elderly persons (*Etablissement d'Hébergement pour Personnes Agées Dependantes*—EHPAD) or a long-term unit.
- age under 20 years.

2.2 | Outcomes: Amputation, death and potential access to care

The primary outcome was major amputation (mid-foot amputations and above, Table S1) within the year following wound onset. Secondary outcomes were all-cause mortality within the year following wound onset and the impact of potential access to care measured at the living area level on major lower limb amputation.

2.3 | Deprivation and access to care assessment

Deprivation was assessed at the living area level using fDep, the French deprivation index.¹⁵ fDep is the first component in the principal component analysis of median household income, percentage of high school graduates in the population aged 15 years and older, percentage of blue-collar workers in the active population and unemployment rate. We calculated it using the 2012 data. The 2012 INSEE data showed 100 living areas in the former Languedoc-Roussillon (recently renamed Occitanie).

Access to care can be estimated through the number of general practitioners (GPs), private-practice nurses and GPs and private-practice nurses combined per 1000 inhabitants. We also considered the potential localized accessibility (*Accessibilité potentielle localisée*—APL) to GPs and private-practice nurses, a variable built by French regulatory authorities as the standardized number of consultations available in a territory.¹⁶ We used the last available index, calculated in 2016.

2.4 | Statistical analysis

Data are presented using mean \pm SD or incidence per 1000 person-years. To compare incidences of different

living areas, DFU incidences and outcomes were standardized according to age and sex using the direct method, with the whole study sample as the reference population ($n = 15,507$). Strictly, the 'DFU incidence' is the incidence of inclusion in this study in the general population. The incidence of outcomes is the incidence in our sample ($n = 15,507$). All incidences were calculated in each living area. Amputation and death rates are calculated on the population of people with DFU.

Living areas were classified in quartiles of fDep, and medians and quartiles of incidences of outcomes were described for each quartile of deprivation. We calculated the relative risk (RR) with the most deprived quartile as the reference. We conducted a log-rank analysis to compare the people with the best accessibility to a GP and, separately, a nurse. We compared the quartile of people with DFU with the worst access versus the others.

For each living area, the amputation rate was divided by the sum of the density of GPs and private-practice nurses. This ratio of amputation/primary care offer is graphically shown using maps at the living area level. The legends of these maps use quintiles of the ratio. Mortality rate and the composite of death and amputation were analysed using the same method.

3 | RESULTS

In 2012, our administrative area had 2,700,266 inhabitants, 2,323,679 if we only consider people living in commune attached to living areas belonging mainly to Languedoc-Roussillon. During the 3 years of the inclusion period, we identified 197,832 persons with diabetes and 32,923 cases of DFU, with 7204 requiring hospitalization. After assessment of the exclusion criteria, we included 15,507 people at the date of their first DFU (Figure 1). Mean age was 70 (SD 23) years. There were 55% men (Table 1).

Two hundred and fifty-three amputations occurred during the first year of follow-up (17.5 amputations per 1000 person-years) and 117 deaths per 1000 person-years (Table 1). The mean GP accessibility was 4.7 ± 1.2 and the mean nurse accessibility was 234 ± 63 .

3.1 | DFU, amputation and death maps

We observed individuals with DFUs in all living areas, except one low-density area in the north of the administrative area. Figure 2 shows the amputation and death incidence by living area. Living areas around the coast and major cities seemed to have better prognoses regarding amputation. This was also the case in living areas with higher healthcare access (Figures 3 and 4; Figures S1–S5).

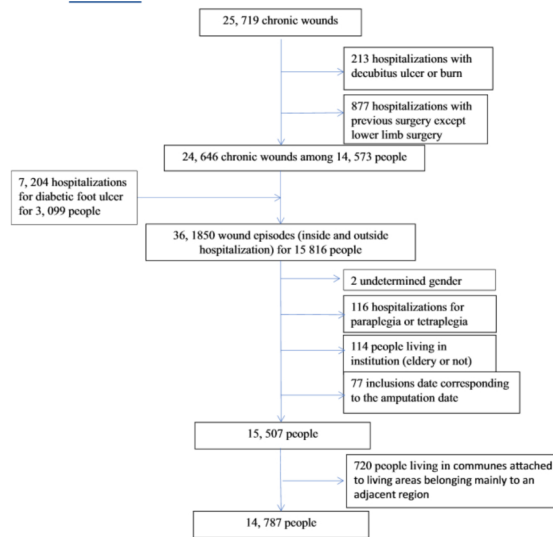


FIGURE 1 Flow chart

TABLE 1 Description of the population with diabetic foot ulcer (DFU) in the Languedoc-Roussillon region between 2015 and 2017, and rates of DFU with reference to the population of Languedoc-Roussillon ($n = 2,700,266$). Rates of major amputations and death are for the year following inclusion in the study for those who suffered a DFU

Numbers with DFU	15,507
DFU rate (per 1000 person-years)	1.9
Requiring hospitalization	3099 (20)
Age (years)	70 ± 23
Men	8498 (55)
Amputations, n (%)	
Amputation rate (per 1000 person-years)	17.5
Deaths, n (%)	
Death rate (per 1000 person-years)	117

Note: Data displayed are n (%), mean ± SD, rates (per 1000 person-years).

3.2 | Deprivation impact

We first highlighted a difference in amputation rate from one to two between the three most deprived quartiles of living areas and those less deprived. However, this was not observed for mortality rate (Table 2). Thus, less deprived areas seem to have better prognoses concerning

amputation (quartile 4 vs. quartile 1: RR = 0.46; 95% CI 0.27–0.66) but not mortality (Table 2).

3.3 | Care accessibility

Maps created according to healthcare access (measured by healthcare provider density) showed that rural living areas at the periphery of the administrative area were more likely to have higher amputation rates according to healthcare access.

Low accessibility to a private-practice nurse was linked to higher rates of amputation (log-rank, $p < 0.001$), unlike GP accessibility, which showed no link (log-rank, $p = 0.195$).

4 | DISCUSSION

For the first time, we used the SNDS database at a regional level and demonstrated that living areas with the worst amputation rates appeared to be the most deprived and the least populated, with the lowest access to nurses. Interestingly, good GP accessibility was not linked to less major amputation following DFU. Our results also highlight that amputation and death risks were not strictly geographically superimposable.

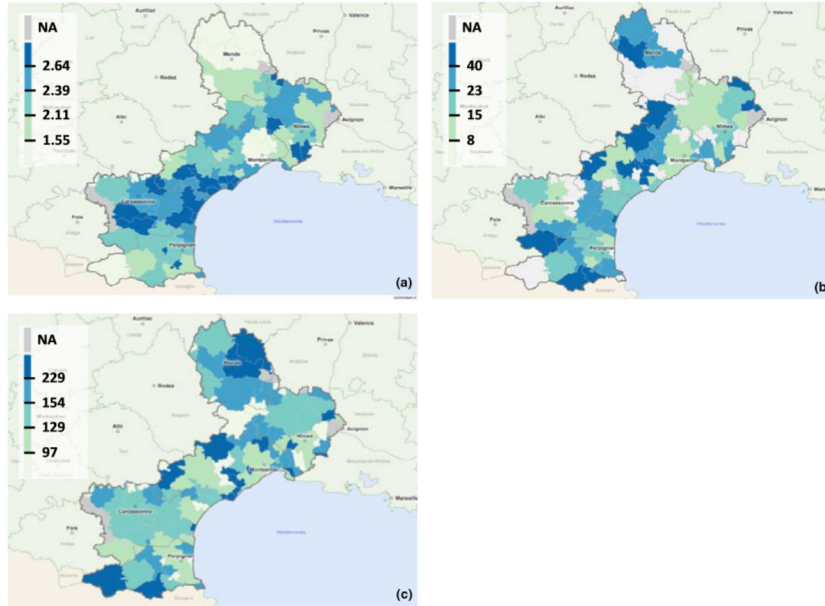


FIGURE 2 Incidence rate in living areas of Languedoc-Roussillon between 2015 and 2018. (a) Diabetic foot ulcer (DFU) rate; (b) amputation rate; (c) mortality rate. Incidence is standardized on age and sex and is given for 1000 person-years. DFU rate is calculated on the total population of Languedoc-Roussillon. Amputation and death rates are calculated on the population of people with DFU

4.1 | Impact of social deprivation on major amputation following DFU

According to the fDep score, the least precarious living areas had the lowest rates of amputation among people with DFU. fDep is a complex and progressive score.¹⁵ With fDep, we noted lower amputation rates only for the less deprived living areas. This is not fully consistent with the findings of Hurst et al.⁹ and Riley et al.,¹⁷ who highlighted the difference in burden between the most deprived quintile of areas and the other quintiles. Living in a deprived area with a low educational level¹⁸ and high unemployment rate was associated with poor DFU prognosis but, paradoxically, a low household income can ensure better medical care for the person. This might thus point towards a pull-down effect.¹⁰

After adjustment for the primary care offer, rural areas appeared to be correlated with major amputation following DFU. It is interesting to note that the most deprived living areas of Languedoc-Roussillon were the least populated.

Improving access to public services, reducing geographic isolation and strengthening connections between small living areas and the largest areas might be public policy options to decrease the gap in major amputation following DFU between the most and the least populated living areas.

4.2 | Access to healthcare

Regarding access to healthcare, the ratio between amputation and death rates and GP or nurse numbers was lower in the larger cities of Languedoc-Roussillon (Figures S5 and S6).

Nonetheless, in contrast to other studies, we did not find a link between GP accessibility and major amputation following DFU¹⁹ but did find a link with nurse accessibility. A consultation before the wound might be a marker of the severity of the person's medical background. Thus, accessibility to a GP or nurse according to an available communal

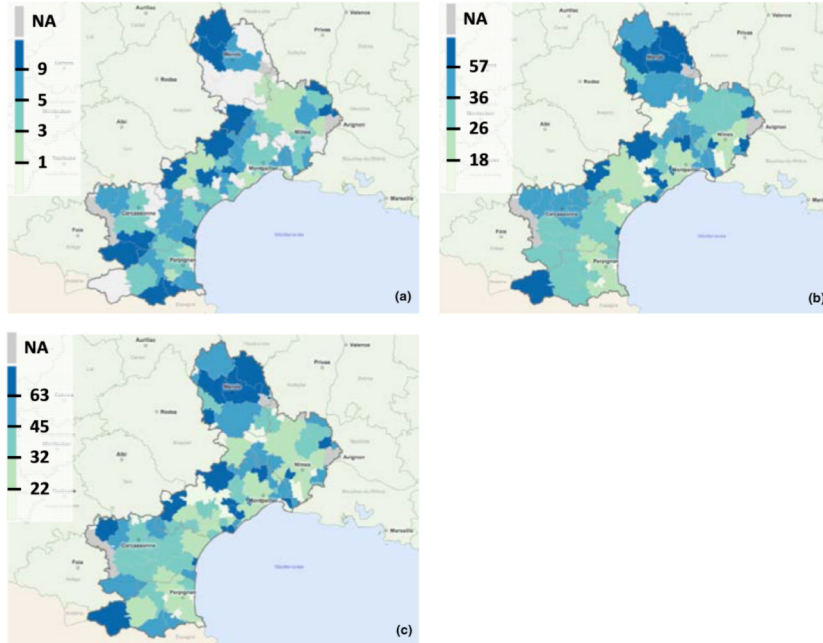


FIGURE 3 (a) Amputation rate per living area in relation to primary healthcare access (general practitioner [GP] and private-practice nurse density); (b) mortality rate per living area in relation to primary healthcare access (GP and private-practice nurse); (c) Amputation and death rate per living area in relation to primary healthcare access (GP and private-practice nurse). Amputation and death rates are calculated on the population of people with diabetic foot ulcer. Incidence is standardized on age and sex and is given for 1000 person-years. GP and nurse density are calculated according to the whole population of Languedoc-Roussillon

data set like the APL is more relevant. A previous study using SNDS found a link between the prognosis of heart failure, another chronic disease and nurse accessibility.²⁰ To our knowledge, this is the first time that a clear link between nurse accessibility and major amputation following DFU has been found using SNDS, which makes sense as local care is provided by nurses. This may argue for healthcare policies that promote nurse installation in rural areas.

4.3 | DFU and primary care consumption

Using the SNDS and our algorithm had the advantage of being more representative of ambulatory care. As already mentioned, previous epidemiological studies focused only on hospitalized individuals with DFU²¹ or self-reported DFU.¹¹ We conducted

an exhaustive analysis of people with diabetes and DFU across all living areas in the administrative area, Languedoc-Roussillon. We found five times more individuals with DFUs than by using PMSI only. Thus, healthcare organizations will have to manage these unseen DFUs in calibrating the medical response. It is indeed crucial that new healthcare pathways for managing DFU and other diabetes complications include GPs and nurses. These professionals need to be coordinated with the DFU reference centres.

4.4 | Geographic difference in mortality and amputation risks

Several hypotheses may explain the differences between the geographic maps of amputation and death rates. First,

FIGURE 4 Nurse density per 1000 people per living areas according to the total population (with or without diabetic foot ulcer)

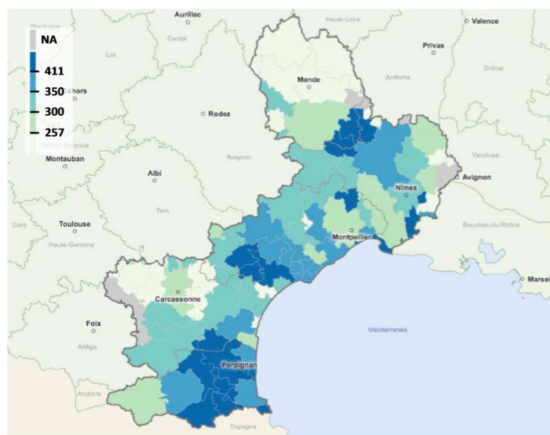


TABLE 2 Amputation rate, death rate and composite criteria of amputation or death rate of living areas, according to the quartile of the deprivation index (fDep). Total population corresponds to the numbers living in quartile groups. Amputation and death rates are standardized on age and sex. Diabetic foot ulcer (DFU) rate are calculated on the total population of Languedoc-Roussillon. Amputation and death rates are calculated on the population of people with DFU. DFU rates are not standardized on age and sex. The total number of people with DFUs included in this table is 14,787. People living in communes attached to living areas belonging mainly to an adjacent region were excluded from this analysis

	Quartile 1 (most deprived)	Quartile 2	Quartile 3	Quartile 4 (least deprived)
Total population	352,255	668,936	673,764	738,724
Number of DFUs	3498	3050	4550	3689
DFU rate (/1000 person-year)	2.35 (1.9–2.85)	2.45 (1.85–2.85)	2.14 (1.75–2.39)	1.8 (1.48–2.26)
Deprivation index	1.42 ± 0.22	0.90 ± 0.12	0.52 ± 0.11	−0.33 ± 0.60
Amputation rate (/1000 person-year)	17 (0–49)	18 (0–23)	15 (0–29)	8 (0–23)
Amputation—RR 95% CI	1	1.06 (0.96–1.15)	0.89 (0.77–1.01)	0.46 (0.27–0.66)
Death rate (/1000 person-year)	162 (118–300)	129 (77–173)	134 (101–158)	137 (101–242)
Death—RR 95% CI	1	0.80 (0.64–0.96)	0.83 (0.68–0.98)	0.85 (0.71–0.99)
Amputation or death rate (/1000 person-year)	169 (130–269)	140 (106–189)	158 (130–179)	153 (111–319)

Note: Data displayed are median (Q1–Q3) or mean ± SD, unless otherwise indicated. Abbreviation: RR, relative risk.

care may be delayed or suboptimal due to the lack of a multidisciplinary approach or material resources.²² Also, risk factors for mortality may not be the same as for amputation. Thus, variations in medical decisions have been identified.²³

Moreover, the populations that suffered the least from DFUs were not those with the best prognoses, as example in Lozère (around the city of Mende). Lozère has a high rate of isolated people a known factor of renunciation of care and a much discussed factor of DFU prognosis.²⁴

4.5 | Study strengths and algorithm validation

Our study's first strength is its power and exhaustiveness. To our knowledge, this is the first wide epidemiological study in France that included people with DFU whether or not the DFU had led to hospitalization. We assumed that including only those hospitalized with DFU might constitute a bias. Using the algorithm, five times more people with DFU were included. Therefore, the cohort does not present the same characteristics as in previous works based on the French healthcare insurance database.²⁵

In addition, the SNDS presents several advantages. First, it covers almost the entire French population. Second, all French residents have access to universal healthcare. Thus, there is no more exhaustive database in France¹³ and, even though we confined ourselves only to Languedoc-Roussillon, we created one of the biggest published cohorts of people with DFU. Third, using the SNDS provides real-life analysis without volunteer bias or recall bias. The largest population not covered by the SNDS are migrants in an irregular situation.

Several results validate our algorithm. The amputation rate 1 year after wound onset is congruent with that of other international studies,^{26,27} despite being lower than the amputation rates of several studies that recruited people with DFU during hospitalization or in specialized centres.^{18,28} This was the same case for our mortality rate, according to the mean age of the cohort.²⁸

In addition, our analysis of the link between geographic deprivation and major amputation following DFU is quite strong because it uses a living area's deprivation level for the analysis, which corresponds to the social organization of territorial populations and not to artificial partitions.²⁹ Furthermore, the fDep is a complex score of deprivation that was built specifically for France and is not based only on household incomes.²⁵ Specific variables include educational level and occupational trends. Both variables have shown their relevance in diabetes and DFU.¹¹ This is the first study of this type in France.

4.6 | Study limitations

The first study limitation was our reliance on an algorithm to define DFU, which depended on the SNDS database for the first time regarding this issue. We therefore cannot state with certainty, despite all the safeguards put into place, that all the people in the study had DFUs.

Some limitations were necessarily associated with SNDS. We did not know all the social characteristics of

the study individuals, except for what was available from the health insurance regime. In addition, all other information concerning deprivation was geographic data. This deserves further research.

It should be recalled that Languedoc-Roussillon is a specific administrative area of France and caution is needed in generalizing these results. Previous studies have seen opposite results regarding deprivation and diabetes as a result of differences in the social structure of the studied areas.³⁰

We performed only descriptive and univariate analyses. As it is known that social, geographical and clinical characteristics may be associated, the complete assessment of risk factors of amputations would need multivariable analyses. However, this was out of the scope of this study.

5 | CONCLUSION

Our work highlights the relationship between deprived areas and higher risk of amputation, whereas no relationship has been demonstrated with mortality. We also show that nurse accessibility might be a key strategic point for DFU medical care. Also, if improving healthcare accessibility for the most deprived people has a global effect on other factors of social deprivation, such as a low educational level or unemployment, it should become a key factor to decrease amputation rates. Social deprivation continues to have a complex relation with major amputation following DFU, but this study suggests ways to improve healthcare access that may be of interest to healthcare policymakers. Confirmation of the model and results at the national level and in other countries, especially where social security is not universal, seems necessary.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

JBB, AS and CD involved in study concept and design, and wrote the manuscript; GN, CD, JBB and LP involved in statistical analysis and acquisition of data; AA, AS, CD involved in study supervision. All authors read and approved the final version of the manuscript.

ETHICS STATEMENT

All procedures performed in studies involving human participants are in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was part of the usual public health assessment of the Regional Medical Department of the *Caisse Nationale d'Assurance Maladie* (CNAM), the national health insurance institution in charge of the SNDS.

DATA AVAILABILITY STATEMENT

According to SNDS rules, data are not available on request from the authors.

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