Unravelling The Longitudinal Dynamics of Neurodegenerative Disease Mortality: Insights from 50 years of Belgian Demographic Data

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Background

The global decline in fertility and mortality rates has led to the emergence of aging societies, marking a significant demographic transition. The Gompertzian hypothesis posits that as life expectancy increases, individuals develop degenerative diseases that are less prevalent in earlier stages of life. This phenomenon has fuelled growing concerns about the burden of neurodegenerative diseases (NDDs) worldwide (1, 2). NDDs encompass a spectrum of conditions, each characterized by a gradual and progressive loss of neural cells (3). Dementia, the most common NDD, encompasses Alzheimer's disease (AD), vascular dementia, frontotemporal lobar degeneration (FTLD) and Lewy body dementia (4). Another prominent manifestation is parkinsonism, including Parkinson's disease (PD) and secondary parkinsonism due to diverse causes (5).

The primary aim of this study is to investigate spatial variations in NDD mortality in Belgium, focusing specifically on dementias and PD, spanning the period from 1970 to 2020. Despite Belgium's longstanding tradition of examining spatial disparities in mortality (6), and the prominence of dementias as a leading cause of death in the country (7), a comprehensive analysis of spatial variations in NDD mortality is lacking. Noteworthy spatial variations in NDD mortality have been observed in several European countries. In France, dementia mortality rates were higher in five regions in the North East of the country (8). The highest dementia mortality rates in England were observed in the North East, South Central and South West (9). In Spain, higher mortality rates were noted for PD in the northern half compared to the rest of the country (10, 11). Italian mortality rates for PD were the highest in North-West and Central Italy (12).

Potential explanatory factors for spatial variations include environmental pollutants. Convincing evidence suggests a link between pesticide exposure and the risk of PD (13). Similarly, a growing body of research has implicated air pollution in the risk of dementia (14). Other potential explanatory variables include socioeconomic indicators such as educational level and income, which have been associated with NDD morality at the individual level in Belgium (15). At an aggregated level, mortality among individuals with dementia was found higher in the most deprived areas of England (9). Lastly, studies from the United States (16, 17), and Australia (18) have shown geographical variation in reporting NDDs as contributing causes of death. While these existing studies have contributed valuable insights into NDD mortality, none have undertaken an examination spanning a period longer than a decade. Consequently, this study aims to be a first effort, comprehensively exploring spatiotemporal variations in NDD mortality over an extensive five-decade timeframe in Belgium.

Data

Our analysis is grounded in cause-specific mortality data spanning the years 1970 to 2020, sourced from Statistics Belgium. These individual-level records cover all Belgians and foreigners on Belgian territory and are aggregated to the municipal level. The population size and structure were derived from the Belgian censuses conducted in 1970, 1991, 2001, 2011, and register data from 2018. The creation of this comprehensive dataset is the result of a collaboration between the Quetelet Center at Ghent University and Interface Demography at the Vrije Universiteit Brussel. For the explanatory analyses we employed additional data to include social- and environmental indicators from 2001. We used the Belgian Index of Multiple Deprivation (excluding the health dimension) to account for deprivation at the municipal level (19). Environmental indicators include air pollution (PM10, NO2, and O3) and pesticide exposure, obtained from the Belgian Interregional Environmental Agency (IRCEL-CELINE). We further controlled for the amount of care homes in the municipality and the population density, calculated based on the 2001 Belgian census.

Methods

Age-standardized mortality rates were calculated for dementias (ICD8-290; ICD9-290,331; ICD10-F00-F03, G30) and Parkinson's Disease (ICD8-342; ICD9-332; ICD10-G20) at the municipal level for the population aged 45 or older. To ensure accurate comparisons, the mortality rates for the entire population of Belgium in 1970 were used as the reference standard for age-standardization. In the light of the small size of certain municipalities, we opted for the indirect standardization method. Recognizing the fluctuations and the small number of deaths in some municipalities, we used the average deaths over 3-year periods. We stratified all analyses by gender because differences were observed between mortality in men and women. Subsequently, these mortality rates were transformed into spatial representations through mapping techniques for the periods 1969-1971, 1989-1991, 2000-2002, 2009-2011, and 2017-2019, offering insights into both temporal and geographical variations in NDD mortality.

Moreover, to delve deeper into the relationships and patterns within our data, we employed Exploratory Spatial Data Analysis (ESDA) techniques, including spatial autocorrelation analysis (Moran's I Index) and spatial regression (Spatial Auto-Regressive models). Because we found significant differences in (registration practices of) NDD mortality between regions, we performed the spatial regression for the three Belgian regions - Flanders, the Walloon region, and Brussels - separately.

Results

Descriptive results

In our analysis, we initially examined total dementia mortality by considering two broad ICD categories: dementia (ICD8-290, ICD9-290, ICD10-F001-F03) and AD (ICD9-331, ICD10-G30). We observed a significant increase in dementia-related mortality since the 1980s. Spatial analysis revealed significant clustering of dementia cases in Flanders in 1970 and 1991, with a more uniform distribution observed by 2000. However, a resurgence of dementia mortality in Flanders was noted in 2019. Subsequently, we analysed dementia and AD separately, uncovering a significant shift in classification between 1980 and 1993, with AD becoming the primary classification for dementia-related deaths. Spatially, differences in classification patterns were noticeable, with Flanders showing a preference for dementia classification and the Walloon region for AD. Possible explanations include variations in medical training between regions. We also observed a gender disparity in dementia-related deaths, with a higher proportion of deaths occurring among women.

Regarding PD, we found a doubling of PD-related deaths in Belgium between 1997 and 2020. Spatial analysis revealed notable regional discrepancies, with the Walloon region experiencing a significant increase in PD mortality rates by 2000, surpassing those of Flanders. However, by 2019, this pattern had reversed, with higher mortality rates in Flanders. When studying sex differences in PD-related deaths, we observed a shift over time, with PD accounting for a higher proportion of deaths among women before 2004 but becoming more predominant among men from 2004 to 2020. This aligns with historical trends and underscores the evolving understanding of PD epidemiology. No significant differences in spatial clustering between sexes were noted for PD mortality.

Explanatory results

In investigating spatial patterns, we utilized Spatial Auto-Regressive (SAR) models to analyse mortality in 2019, incorporating indicators for 2001 to address time-lags. For dementia mortality, we observed significant positive associations with population density in all three regions. Additionally, we found a significant positive association with PM10 and NO2 levels in the Walloon region only. Neither deprivation, nor the amount of care homes in the municipality showed a significant association with dementia mortality. Regarding PD-mortality, we observed a significant positive association with the amount of care homes in Walloon municipalities. Furthermore, we found significant negative associations with PM10 and NO2 levels in Brussels. Although significant associations between indicators at the municipality in 2001 and NDD mortality at the municipality level in 2019 were identified, the effect sizes of these indicators were small, and the models displayed limited predictive power.

Conclusion

In summary, this study unveils significant insights into dementias and PD mortality trends. Dementia-related mortality has surged notably since the 1980s, with spatial analysis revealing higher rates in Flanders. Examination of dementias and AD separately exposes a shift in classification, reflecting evolving scientific understanding. Spatial disparities in classification between Flemish and Walloon regions suggest variations in registration practices, with dementia registrations clustered in Flanders and AD registrations in the Walloon regions. Gender differences in dementia-related deaths exhibit a widening gap over time.

Regarding PD, the study identifies a marked increase in PD-related deaths between 1997 and 2020. Spatial analysis highlights a significant rise in PD mortality rates in the Walloon region by 2000, with a contrasting pattern emerging by 2019. Sex differences in PD-related deaths shift from higher mortality among women before 2004 to a more predominant impact on men from 2004 to 2020. Similar to dementia, PD mortality displays no significant spatial differences between men and women.

This research underscores the complex dynamics of NDD mortality, emphasizing the importance of nuanced interpretation considering evolving disease classifications, gender disparities, and regional variations. It calls for future research to address underreporting issues and adopt a comprehensive approach to refine our understanding of NDD mortality patterns.

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