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Incidence and Modifiable Risk Factors of Dementia: Evidence from Healthcare Utilization Databases of the PREV-ITA-DEM Study

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INTRODUCTION

In Italy, it was estimated that approximately 1,200,000 people were living with dementia in 2018 (1). International reports from the Lancet Commission indicate that intensive interventions targeting modifiable risk factors, such as diabetes mellitus, hypertension, obesity, physical inactivity, depression, smoking, and low educational attainment, could prevent or delay up to 35% of dementia cases worldwide. In Italy, a 20% reduction in these seven risk factors could lead to a 6.4% decrease in Alzheimer's dementia cases (2,3,4,5).

OBJECTIVES

The PREV-ITA-DEM project, a large-scale study funded in 2022 by the Italian Ministry of Health under the National Recovery and Resilience Plan (PNRR-MAD-2022-12375822), aimed to estimate the incidence of dementia in relation to risk factors such as diabetes, hypertension, and depression. The study adopted a population-based approach using data from Healthcare Utilization Databases (including Pharmaceuticals, Exemptions, Hospitalizations, Population Registry, and Mortality) with the goal of supporting prevention efforts.

MATERIALS E METHODS

This retrospective cohort study involved three distinct cohorts, each exposed to one of the three risk factors of interest: hypertension, diabetes, and depression. The reference population included the adult population (aged ≥ 50 years) living in and receiving healthcare in the metropolitan area of Turin, in Bologna Local Health Authority (AUSL), and in Lazio region. Exposure cohorts were defined between January 1, 2011, and December 31, 2020, using a 4-years look-back period (2007–2010) to identify only incident cases. Follow-up, with a maximum duration of 12 years, started on January 1, 2011, and ended at the earliest occurrence of one of the following events: dementia diagnosis, migration, death, or the end of the study period (December 31, 2022). A methodological approach based on a Common Data Model (CDM) was adopted, with a shared operational protocol, harmonized database structures, and a common script applied locally by each participating center, in compliance with data privacy regulations established by the Italian Data Protection Authority. A record linkage procedure of regional administrative health data flows was executed to generate the three studied cohorts.

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Quantitative variables were synthesized through means and standard deviations, while categorical variables were reported as absolute and relative frequencies. Incidence rates for dementia and the exposures (hypertension, diabetes, depression) were calculated based on the number of incident cases per person-time, also accounting for censored individuals (due to death or migration). The risk of dementia associated with each exposure was estimated using Cox proportional hazards models, both univariate and multivariate (adjusted for key confounders), with time-dependent exposures. Results were expressed as Hazard ratios (HRs) and 95% confidence intervals (95% CIs). Data were analysed using Stata and SAS software, with a p-value <0.05 for statistical significance.

RESULTS

During the follow-up period, dementia incident cases after a diagnosis of depression added up to 4,161 (12.3%) in Bologna, 15,412 (9.4%) in Lazio, and 6,775 (8.5%) in Turin. Regarding diabetes, the number of individuals who developed dementia was 1,163 (4.1%) in Bologna, 6,854 (3.6%) in Lazio, and 1,917 (2.1%) in Turin. Finally, for hypertension, dementia incident cases during follow-up amounted to 6,729 (3.8%) in Bologna, 13,018 (1.0%) in Lazio, and 3,321 (1.5%) in Turin.

Univariate analysis showed a positive association between depression and the risk of dementia in Bologna (HR: 6.0; 95% CI: 5.6–6.4), Lazio (HR: 5.06; 95% CI: 4.88–5.25), and Turin (HR: 7.56; 95% CI: 7.21–7.94). Diabetes was also significantly associated with dementia across all three studied areas: Bologna (HR: 2.2; 95% CI: 1.9–2.4), Lazio (HR: 1.8; 95% CI: 1.7–1.9), and Turin (HR: 2.4; 95% CI: 2.2–2.7). Hypertension showed a positive association in Bologna (HR: 1.5; 95% CI: 1.4–1.6) and Lazio (HR: 1.06; 95% CI: 1.0–1.1), while an inverse association was observed in Turin (HR: 0.94; 95% CI: 0.89–0.98).

After adjusting for sex, age, and Charlson Comorbidity Index, depression was strongly associated with an increased risk of dementia across all areas: Turin (HR: 6.0; 95% CI: 5.7–6.2), Bologna (HR: 2.8; 95% CI: 2.6–2.9), and Lazio (HR: 2.58; 95% CI: 2.49–2.68). Diabetes showed a significant association only in Turin (HR: 1.7; 95% CI: 1.5–1.8) and Bologna (HR: 1.1; 95% CI: 1.02–1.3), whereas the association was not confirmed in Lazio (HR: 0.98; 95% CI: 0.93–1.03). Hypertension was inversely associated with dementia in all areas: Turin (HR: 0.9; 95% CI: 0.9–1.0), Bologna (HR: 0.63; 95% CI: 0.60–0.66), and Lazio (HR: 0.80; 95% CI: 0.78–0.82).

CONCLUSIONS

These preliminary findings underscore the importance of prevention strategies focused on the early management of psychiatric and metabolic risk factors in the adult population, suggesting potential benefits in reducing the incidence of dementia.

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