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Age of type 2 diabetes onset as a risk factor for dementia: A 13-year retrospective cohort study

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ABSTRACT

Aims: To examine whether age at type 2 diabetes onset is an independent predictor of dementia risk.
Methods: Retrospective cohort drawn from healthcare administrative records of all inhabitants within Romagna's catchment area, Italy, with an estimated onset of type 2 diabetes in 2008–2017 and aged ≥ 55, with follow-up until 2020. Time to dementia or censoring was estimated with the Kaplan–Meier method, using diabetes onset as the time origin. Age groups were compared with the log-rank test. Multivariable competing-risks analysis was used to assess predictors of dementia.
Results: In patients aged ≥ 75 years, dementia-free survival (DFS) declined to below 90 % within five years and linearly decreased to 68.8 % until the end of follow-up. In contrast, DFS for those aged 55–64 years showed a marginal decrease, reaching 97.4 % after 13 years. Competing-risks regression showed that individuals aged ≥ 75 and 65–74 had a significantly higher risk of dementia compared to those aged 55–64 years. Having more comorbidities at diabetes onset and initial treatment with ≥ 2 antidiabetics were clinical predictors.
Conclusions: Later age at onset of diabetes is strongly associated with dementia. A better understanding of the diabetes–dementia relationship is needed to inform strategies for promoting specific healthcare pathways.

1. Introduction

Type 2 diabetes is one of the most common health conditions, affecting 10.5 % of the adult European population; the prevalence of type 2 diabetes in Europe is projected to increase to 13 % by 2045 [1]. This increase is due, in part, to population aging; nearly one-third of people with diabetes in Italy are ≥ 75 years old [2]. Currently, Italy has the highest median age of any European country at 48.4 years; in addition, 21 % of the European population is aged ≥ 65, a figure expected to increase to 33 % by 2100 [3]. The net result is that health concerns that are more common among older adults, such as cognitive decline, are expected to become more pressing issues for social and health services that comprise diabetes care [4].

There is growing evidence that people with type 2 diabetes are at an increased risk for developing all-cause dementia. For example, a recent review indicated that diabetes is associated with a 1.5- to 2.5-fold greater risk of dementia among community-dwelling older adults compared to people without diabetes [5]. Diabetes has been associated with an increased risk for mild cognitive impairment and both vascular dementia and Alzheimer's disease [6]. The risk of dementia is evident in people with diabetes in both midlife and older age [7]. Prior studies suggest that the relationship is multifaceted, involving both biological pathways, such as hyperglycemia-induced vascular damage, chronic inflammation [8–10], and behavioral factors, including poor sleep, physical inactivity, and alcohol misuse [11,12].

Some researchers have suggested that earlier age of diabetes onset is a unique risk factor for dementia. For example, a population-based study in the UK with 34 years of follow-up [13] reported that, by age 70, every 5-year decrease in age of diabetes onset was associated with 1.24-times higher risk of subsequent dementia. Similarly, Hu et al. [14] showed that

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transitioning from pre-diabetes to type 2 diabetes before age 60 was associated with approximately three times higher dementia risk. Finally, Wang et al. [15] reported that type 2 diabetes onset before age 45 was associated with 2.9-times higher risk of dementia. For each of these studies, the comparison group was never developing diabetes. These findings were interpreted by the authors to indicate that earlier age of diabetes onset is independently associated with greater dementia risk.

However, it is not clear whether the modifying effect of age on the association between these two conditions translates into a significantly large absolute risk of dementia among younger patients with type 2 diabetes. Indeed, the Barbiellini et al. [13], Hu et al. [14], and Wang et al. [15] studies described above used *never* developing diabetes as the reference group for the age of diabetes onset comparisons. This approach to estimating the relative risk does not answer the question "*Does developing diabetes earlier in life—relative to later in life—uniquely confer additional risk for dementia?"*. Rather, this question can be answered by examining a cohort of individuals that all have type 2 diabetes, and then testing whether those who developed this condition earlier in life have a higher risk of dementia than those who developed it later.

The finding that diabetes increases the risk of dementia has led to calls for adopting screening for cognitive impairment as part of diabetes care. For example, the American Diabetes Association (ADA) [16] recommends screening for early detection of mild cognitive impairment or dementia for those aged $\geq$ 65. If, however, earlier age of type 2 diabetes onset was a unique risk factor for dementia, screening guidelines should incorporate this information into clinical practice.

Therefore, we examined the relationship of demographic and clinical characteristics with dementia risk in a large cohort of adults aged $\geq$ 55 with type 2 diabetes, identified using healthcare administrative records and followed over 13 years (2008–2020). This study aims to assess whether age at type 2 diabetes onset acts as an independent risk factor for dementia development adjusting for relevant demographic and clinical characteristics.

2. Subjects, materials and methods

2.1. Setting and data sources

This retrospective cohort study encompassed all inhabitants within the jurisdiction of the Local Healthcare Authority (LHA) of Romagna who were estimated to have developed type 2 diabetes between 2008 and 2017, spanning ten years. Follow-up extended up to 13 years until December 31, 2020. Romagna's LHA, located in Northeastern Italy, caters to approximately 1,123,000 individuals as of January 1, 2023. Data were drawn from various sources, each with a unique patient identifier, including: (I) Hospital Discharge Records (in Italian, *Schede di dimissione ospedaliera* [SDO]); (II) Integrated Home Care (*Assistenza domiciliare integrata* [ADI]); (III) Residential and Semi-Residential Healthcare for the Elderly (*Assistenza residenziale e semi-residenziale anziani* [FAR]); (IV) Outpatient Pharmaceutical Database (*Assistenza farmaceutica territoriale* [AFT] and *Farmaci a erogazione diretta* [FED]); and (V) Vital Registration System (*Registro mortalità* [REM]). Please see Lenzi et al., 2024 [17] for comprehensive details of these data systems.

The Ethics Committee of Romagna's LHA approved this research on December 14, 2020 (Registration #9502/2020), with reapproval for extension on September 27, 2023 (Registration #5869/2023).

All LHA's health administrative data are pseudonymized before analysis. Each individual is assigned a unique patient identifier, eliminating the possibility to trace the patient's identity or access other sensitive data. According to Article 9 of the General Data Protection Regulation (European Union [EU] Regulation 2016/679), pseudonymized administrative data can be used without specific written informed consent when patient information is collected for healthcare management, quality evaluation, and improvement. All procedures adhered to the 1964 Helsinki Declaration and its subsequent amendments.

2.2. Inclusion and exclusion criteria

New cases of type 2 diabetes were identified based on meeting either of the following inclusion criteria (sources: SDO, AFT, and FED) [18]: (I) admission to a hospital with a primary or secondary diagnosis of diabetes (coded as 250 according to the International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]) along with a filled prescription of glucose-lowering medication (coded as A10 according to the Anatomical Therapeutic Chemical [ATC] Classification System); or (II) at least three prescriptions of glucose-lowering medications (e.g., metformin, insulin).

The date of entry into the study was determined as either the admission to hospital, residential healthcare or integrated home care, or the date of the first filled prescription, whichever occurred first. Cases of gestational diabetes in women (ICD-9-CM code 648.8) and of probable type 1 diabetes (indicated by treatment with insulin as their initial and sole treatment within the first year of diagnosis) were not included in the cohort.

This analysis was limited to 40,159 people aged $\geq$ 55 who had complete data on covariates and diabetes status, and who had no history of dementia treatment within the five years preceding the estimated onset of diabetes. The algorithm used to detect prevalent cases of dementia was identical to that used for identifying dementia cases following diabetes onset (described below).

2.3. Dementia outcome

In line with the surveillance algorithm established by Emilia-Romagna [19], all-cause dementia was identified in any of the databases (SDO, ADI, FAR, AFT, and FED) by either (I) admission to a hospital or provision of home care with an ICD-9-CM diagnosis indicating dementia (0461 [Jakob–Creutzfeldt disease], 290 [senile and presenile organic psychotic conditions], 291 [alcoholic psychoses], 292 [drug psychoses], 294 [other organic psychotic conditions with a chronic course], 331 [other cerebral degenerations, including Alzheimer's disease]) (see Lenzi et al., 2024 [17] for further details); (II) residential care for dementia and significant behavioral/cognitive impairment; or (III) two or more filled prescriptions of anti-dementia medications (ATC codes N06DA02 [donepezil], N06DA03 [rivastigmine], N06DA04 [galantamine] and N06DX01 [memantine]).

The index date for the onset of dementia was determined as the date of the earliest event among the three criteria mentioned above. Data concerning all-cause mortality were obtained from the vital registration system (REM).

2.4. Covariates

The following demographic characteristics, informed by prior literature, were investigated for their potential association with the time to onset of dementia: sex (male or female); age group at the onset of diabetes (55–64, 65–74, or $\geq$ 75 years); citizenship (Italian or non-Italian); and level of urbanization of the municipality of residence, categorized using the Eurostat's Degree of Urbanization (DEGURBA) classification system, as revised in 2014 (city [densely populated area], town or suburb [intermediate density area], or rural area [sparsely populated area]). In addition, medical morbidity and initial diabetes treatment regimen were investigated as indicators of baseline health status. Morbidity was quantified using a list of clinical conditions identified up to three years before the onset of diabetes (sources: SDO, AFT, and FED) and summarized using the Multisource Comorbidity Score (MCS) by summing specific weights assigned to each condition, as outlined in studies by Corrao et al., 2017 [20] and Lenzi et al., 2024 [17]. The MCS includes 31 clinical conditions divided into 11 groups: infectious and parasitic diseases; neoplasms; endocrine, nutritional, metabolic, and immunity disorders; diseases of the blood and blood-forming organs; mental disorders; diseases of the nervous system; diseases of the

circulatory system; diseases of the respiratory system; diseases of the digestive system; diseases of the genitourinary system; diseases of the musculoskeletal system and connective tissue [20]. Diabetes and dementia were excluded from the MCS calculation as the study population, by definition, had neither of these conditions before entry into the study. Initial diabetes treatment regime was measured as medications filled within 30 days of diabetes onset (one oral antidiabetic only vs. ≥ 2 antidiabetic medications [including insulin]), as a proxy for timeliness of diagnosis and glycemic control at disease onset.

2.5. Statistical analysis

Initially, to confirm prior reports that the incidence of dementia among individuals with type 2 diabetes is higher than that observed in the general population [13–15], we used the 2017 estimates published in Emilia-Romagna's surveillance report as a reference [19]. To align with the data presented in this report, this initial descriptive analysis was restricted to residents aged ≥ 65 years within Romagna's LHA who had an onset of diabetes in 2016 and 2017. The age-standardized incidence of dementia within one year of diabetes onset was then calculated and accompanied by a 95 % confidence interval (CI) to account for statistically significant deviations from the regional estimate of dementia incidence in 2017. The 95 % CI was computed using a method developed by Fay [21] and modified by Tiwari et al., 2006 [22]. Like Fay's method, Tiwari's CI is based on the gamma distribution but introduces a modification to enhance the efficiency of the upper confidence limit estimation.

Next, the time to dementia or censoring in the type 2 diabetes cohort aged ≥ 55 years was estimated with the Kaplan–Meier method, using the date of diabetes onset as the time origin. Individuals lost to follow-up before December 31, 2020, and deaths were right-censored. Person-time was measured in years, beginning with the date of diabetes diagnosis until the date of first dementia diagnosis or right-censoring. Age group comparisons were conducted with the log-rank test. A multivariable competing-risks regression model was then used to assess the association of demographic and clinical baseline characteristics with the onset of dementia while accounting for mortality events [23]. Effect sizes were expressed as sub-distribution hazard ratios, or *sub-hazard ratios* (SHRs), whose interpretation is similar to hazard ratios in Cox regression. The proportional-hazards assumption was confirmed by examining the nonzero slope of scaled Schoenfeld residuals over time [24], while the overall model fit was verified by plotting the Nelson–Aalen cumulative hazard function of the Cox–Snell residuals versus the residuals themselves.

All data were managed with SPSS 25.0 (IBM Corp. 2017. *IBM SPSS Statistics for Windows, Version 25.0.* Armonk, NY: IBM Corp) and analyzed with Stata version 18 (StataCorp. 2023. *Stata Statistical Software: Release 18.* College Station, TX: StataCorp LP). The significance level was set at 0.05, and all tests were two-sided.

3. Results

The age-standardized rate of dementia within one year of diabetes onset among incident cases aged ≥ 65 years in 2016 and 2017 was 22.0 per 1,000 person-years (95 % CI 17.4–27.5). This rate is significantly higher than the overall incidence rate of dementia reported for the same age group in the region of Emilia-Romagna in 2017 (16.7 per 1,000 person-years, 95 % CI 16.5–17.0).

The baseline characteristics of the type 2 diabetes cohort aged ≥ 55 (n = 40,159) are summarized in Table 1. Among these individuals, 19,681 (49.0 %) were female, 13,686 (34.5 %) were aged ≥ 75 years, 1,835 (4.6 %) were non-Italian citizens, 6,062 (15.1 %) lived in rural areas, 3,080 (7.7 %) had an MCS of ≥ 15, and 6,119 (15.2 %) had an initial therapy consisting of ≥ 2 medications. During a median follow-up period of 7.0 years [interquartile range [IQR] 4.1–9.9], spanning up to 13.0 years, a total of 2,725 new cases of dementia were observed, accounting for 6.8 % of the cohort. This corresponds to an incidence rate of dementia equal to 9.8 per 1,000 person-years (95 % CI 9.5–10.2), with a median age at onset of 84 years [IQR 79–89]. All-cause deaths, including those occurring after dementia, totaled 11,759 (29.3 %), corresponding to an incidence rate of 41.8 per 1,000 person-years (95 % CI 41.0–42.5).

Table 1
Baseline Characteristics of the Residents in the LHA of Romagna, Italy, With an Estimated Onset of Type 2 Diabetes in 2008–2017, Overall and by Post-Diabetes Dementia up to December 31, 2020.

Characteristics	All (n = 40,159)	Post-Diabetes Dementia	
		Yes (n = 2,725)	No (n = 37,434)
Sex			
Male	20,478 (51.0 %)	1,124 (41.2 %)	19,354 (51.7 %)
Female	19,681 (49.0 %)	1,601 (58.8 %)	18,080 (48.3 %)
Age Group, y			
55–64	12,620 (31.4 %)	122 (4.5 %)	12,498 (33.4 %)
65–74	13,671 (34.0 %)	590 (21.7 %)	13,081 (34.9 %)
≥ 75	13,868 (34.5 %)	2,013 (73.9 %)	11,855 (31.7 %)
Diabetes Duration as Median [IQR], y	7.0 [4.1–9.9]	4.3 [1.8–7.0]	7.2 [4.3–10.0]
Citizenship			
Italian	38,324 (95.4 %)	2,704 (99.2 %)	35,620 (95.2 %)
Non-Italian	1,835 (4.6 %)	21 (0.8 %)	1,814 (4.8 %)
Degree of Urbanization			
City	14,949 (37.2 %)	957 (35.1 %)	13,992 (37.4 %)
Town or suburb	19,148 (47.7 %)	1,267 (46.5 %)	17,881 (47.8 %)
Rural area	6,062 (15.1 %)	501 (18.4 %)	5,561 (14.9 %)
MCS Class*			
≤ 4	26,554 (66.1 %)	1,404 (51.5 %)	25,150 (67.2 %)
5–9	7,453 (18.6 %)	718 (26.3 %)	6,735 (18.0 %)
10–14	3,072 (7.6 %)	337 (12.4 %)	2,735 (7.3 %)
≥ 15	3,080 (7.7 %)	266 (9.8 %)	2,814 (7.5 %)
Initial Treatment†			
One oral antidiabetic	34,040 (84.8 %)	2,257 (82.8 %)	31,783 (84.9 %)
Two or more antidiabetics, incl. insulin	6,119 (15.2 %)	468 (17.2 %)	5,651 (15.1 %)

Abbreviations: LHA, Local Healthcare Authority, IQR, Interquartile Range, MCS, Multisource Comorbidity Score.
* Diabetes and dementia were not included in the MCS calculation.
† Within 30 days of diabetes onset.

The Kaplan–Meier estimates of dementia-free survival (DFS) (Fig. 1 and Supplementary Table 1) revealed significant differences across the three age groups (log-rank chi-squared test = 3,347.95, p-value < 0.001). DFS for the oldest group (≥75 years) declined to below 90 % (88.0 %, 95 % CI 87.3–88.6) within five years of diabetes onset and then continued to linearly decrease to 68.8 % (95 % CI 66.7–70.8) until the end of follow-up (up to 13 years since onset). In contrast, DFS for the youngest group (aged 55 to 64) showed only a marginal decrease, reaching 97.4 % (95 % CI 96.4–98.1) at the end of the follow-up.

Table 2 shows the results of the multivariable competing-risks analysis. Consistent with the Kaplan–Meier plot, individuals aged ≥ 75 (SHR 14.72, 95 % CI 12.24–17.70) and 65–74 (SHR 4.32, 95 % CI 3.56–5.25) had a higher risk of dementia compared to those aged 55–64 years. Being female (SHR 1.25, 95 % CI 1.16–1.34), residing in rural areas (SHR 1.26, 95 % CI 1.13–1.40), receiving two or more antidiabetic medications as initial treatment (SHR 1.24, 95 % CI 1.13–1.37), and

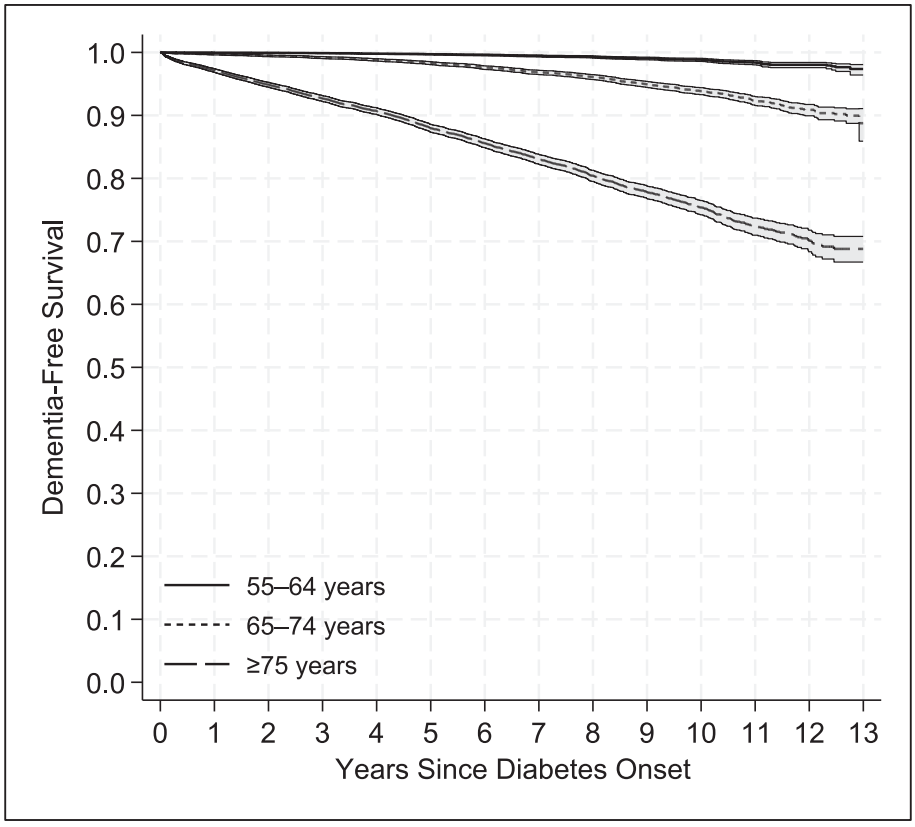

Fig. 1. Kaplan–Meier Dementia-Free Survival by Age Group at Type 2 Diabetes Onset. *Notes:* Pointwise estimates are presented along with 95% confidence intervals.

Table 2
Multivariable Competing-Risks Regression Model for Dementia-Free Survival After Type 2 Diabetes Onset.

Characteristics	Sub-Hazard Ratio		*p*-value
	Estimate	95 % CI	
Sex			
Male	Ref.		
Female	1.25	1.16, 1.34	< 0.001
Age Group, y			
55–64	Ref.		
65–74	4.32	3.56, 5.25	< 0.001
≥ 75	14.72	12.24, 17.70	< 0.001
Citizenship			
Italian	Ref.		
Non-Italian	0.34	0.22, 0.52	< 0.001
Degree of Urbanization			
City	Ref.		
Town or suburb	1.04	0.96, 1.13	0.362
Rural area	1.26	1.13, 1.40	< 0.001
MCS Class*			
≤ 4	Ref.		
5–9	1.17	1.07, 1.28	0.001
10–14	1.29	1.15, 1.45	<0.001
≥ 15	1.00	0.88, 1.14	0.979
Initial Treatment†			
One oral antidiabetic	Ref.		
Two or more antidiabetics, incl. insulin	1.24	1.13, 1.37	< 0.001

Abbreviations: CI, Confidence Interval; MCS, Multisource Comorbidity Score.
* Diabetes and dementia were not included in the MCS calculation.
† Within 30 days of diabetes onset.

having higher MCS values were also significantly associated with elevated dementia risk. Finally, non-Italian citizens had a lower risk compared to Italians (SHR 0.34, 95 % CI 0.22–0.52).

4. Discussion

The primary findings from this study are three-fold. First, we found that the one-year incidence of dementia among individuals aged ≥ 65 with type 2 diabetes was higher than the general population residing in the region of Emilia-Romagna in 2016 and 2017. Second, conditional on having diabetes, the most important risk factor for developing dementia was the older age of diabetes onset, with a particularly elevated risk for those whose diabetes occurred after age 65. Third, when examining demographic and clinical predictors for dementia, we found that risk was higher for women, for those living in rural areas, for those with greater comorbidity at baseline, and for those who were taking more than one antidiabetic medication as their initial treatment. In sum, in this sample of adults with type 2 diabetes of typical (i.e., 50 s–70 s) onset, older age of diabetes onset was associated with substantially elevated risk of developing dementia over an approximately 10-year follow-up period. These findings have implications for both understanding the epidemiology of dementia risk and planning health services for older adults with diabetes.

Several prior studies have reported results indicating that a younger age of diabetes onset is independently associated with an increased risk of dementia [13–15]. However, our study's first finding suggests that the relative increase in dementia risk for patients with type 2 diabetes persists even at older ages (≥65 years). Moreover, our study's second finding reveals that, although a younger age at diabetes onset is associated with a significantly higher *relative* risk of dementia compared to normoglycemia [13–15], this does not translate into significantly large *absolute* numbers of dementia cases over more than ten years of follow-up. This likely reflects that older age is a preeminent determinant of dementia risk, alongside diabetes status. Indeed, while there are *meta*-analyses that indicate a robust association between lifetime diabetes status and dementia risk [25–27], their contrasting interpretations regarding the importance of age of diabetes onset suggest that more

longitudinal studies are needed to clarify the nature of diabetes–dementia relationship.

Other predictors of dementia onset in this study included sex, living in a rural area, being an Italian citizen, and clinical characteristics at baseline. Our findings regarding sex are in line with a previous systematic review [28] which found that women have a higher risk of developing vascular dementia compared with men. Similarly, other studies have also found that dementia risk is greater for older adults who live in rural areas [29]. The reasons for elevated risk in rural communities are unclear, but studies suggest that both compositional (e.g., people in these areas may have lower education and/or less cognitively demanding occupations) and contextual (e.g., fewer opportunities for social engagement) factors may be relevant [30]. Italian citizens had a higher dementia risk relative to immigrants; given that these data are all healthcare records, this potentially reflects that the latter may have less access to and/or use of specialist care where cognitive impairment would be detected [31]. Finally, greater medical comorbidity at baseline and more intense initial diabetes treatment were associated with dementia risk; both findings are consistent with prior work showing that disease severity is associated with a worse prognosis for older adults with diabetes, including subsequent risk of dementia [13].

4.1. Implications for healthcare services

Comprehensive management of diabetes requires a multidisciplinary approach, addressing not only glycemic control but also associated comorbidities, complications, and psychosocial aspects. Common comorbidities include cardiovascular diseases, kidney disorders, and mental health issues [17,18], which themselves are risk factors for cognitive and functional decline. The relationship between diabetes and these comorbidities is often bidirectional, with each condition potentially exacerbating the other. Multiple clinical trials have shown that this type of complexity is best managed by a multidisciplinary team approach, such as the Collaborative Care Model (CCM) [32]. In addition, a recent study found that diabetes management in the primary care setting by a multidisciplinary team was associated with a lower risk of subsequent dementia incidence compared to usual care [33]. Finally, the CCM has also been applied to dementia care and is associated with better quality of life for patients and caregivers, irrespective of diabetes status [34]. Collectively, these studies emphasize the need for approaching diabetes care for older adults in a manner that reflects the multiple ways in which this condition impacts psychological, cognitive, and physical functioning [35]. Identifying the risk factors for developing dementia may also have implications on type 2 diabetes treatment: sodium-glucose cotransporter-2 (SGLT-2) inhibitors have been found to be associated with lower dementia risk in older patients [36], while preclinical models have shown a relationship between glucagon-like peptide-1 (GLP-1) receptor agonists and improved cognitive functioning [37]. Moreover, ADA guidelines emphasize the importance of simplifying diabetes treatment plans to minimize the risk of hypoglycemia [16].

Clinical guidelines in diabetes have recently begun to emphasize the importance of cognitive impairment in diabetes and its management. However, common cognitive screening instruments have low sensitivity for identifying mild cognitive impairment, and, given the low incidence of dementia before age 65, there is no evidence that it is clinically net-beneficial to screen middle-aged adults for cognitive decline [38]. Accordingly, consistent with our findings, recent practice recommendations advise annual cognitive screening for adults with diabetes aged $\geq$ 65 years [15]. However, age alone is likely not a sufficient criterion for monitoring cognitive functioning for adults with diabetes. Srikanth et al. [39] suggest also incorporating specific clinical characteristics when considering whether to screen for dementia, including self-reported or informant-reported concerns about cognitive functioning, history of falls, history of recurrent hypoglycemia, difficulty with diabetes self-management (e.g., errors in self-administration of medications), and symptoms of depression or emotional distress.

4.2. Strengths and limitations

Findings should be interpreted considering the study's strengths and limitations. We made use of a large cohort of adults with diabetes, with nearly complete identification of diabetes and dementia cases that were treated in a large catchment area. Moreover, given the high risk of mortality in late life, we used a competing-risks model to ensure robust inference. However, this study relied on healthcare administrative records, which reflect clinical ascertainment rather than the true incidence of disease; in addition, these records lack information on socioeconomic status, health behaviors, and lifestyles (e.g. alcohol consumption and smoking status) that are relevant to the diabetes–dementia relationship and the prognosis of type 2 diabetes [40]. We acknowledge that prior studies that examined diabetes age of onset and dementia risk [13–15] used survey assessments (e.g., neurocognitive screeners) to identify probable dementia cases, which likely resulted in those cases being identified by the study protocol at earlier ages relative to health administrative records; as a result, our study designs are not directly comparable. Finally, we limited our sample to type 2 diabetes cases that onset at ages $\geq$ 55 years, reflecting the typical age of type 2 diabetes onset; thus, it is possible that earlier age of diabetes onset (in the 30 s or 40 s) may be associated with elevated dementia risk relative to typical age.

4.3. Conclusion

Later age at the onset of diabetes is strongly associated with dementia. This finding has significant implications for appropriate healthcare planning. With population aging, clarity regarding the nature of the diabetes–dementia relationship is needed to inform strategies for promoting overall well-being and specific healthcare pathway planning for older adults with diabetes.

CRediT authorship contribution statement

Rossella Messina: Writing – original draft, Conceptualization. **Briana Mezuk:** Writing – original draft, Conceptualization. **Simona Rosa:** Data curation. **Marica Iommi:** Data curation. **Maria Pia Fantini:** Writing – review & editing, Supervision, Conceptualization. **Jacopo Lenzi:** Writing – original draft, Methodology, Funding acquisition, Formal analysis. **Paolo Di Bartolo:** Writing – review & editing, Supervision.

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 material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.diabres.2024.111760.

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