JAMDA xxx (2017) 1–6

JAMDA

journal homepage: www.jamda.com

Original Study

Diabetes Care and Dementia Among Older Adults: A Nationwide 3-Year Longitudinal Study

Matthieu Wargny MD, MSc [a,b,c,*], Adeline Gallini PharmD, PhD [a,b,d], Hélène Hanaire MD, PhD [e], Fati Nourhashemi MD, PhD [b,f], Sandrine Andrieu MD, PhD [a,b,d], Virginie Gardette MD, PhD [a,b,d]

[a] *Department of Epidemiology, University Hospital of Toulouse, Toulouse, France*
[b] *INSERM, UMR 1027 Epidemiology and Analyses in Public Health, Toulouse, France*
[c] *Clinical Investigation Center, Departement of Diabetology, Metabolic diseases and Nutrition, University Hospital of Nantes, Nantes, France*
[d] *Université de Toulouse III, Faculty of Medicine, Department of Epidemiology and Public Health, Toulouse, France*
[e] *Department of Diabetology, Metabolic Disease and Nutrition, University Hospital of Toulouse-Rangueil, Toulouse, France*
[f] *Gérontopole, University Hospital of Toulouse, Toulouse, France*

Keywords:
Dementia
diabetes mellitus
comorbidities
Alzheimer's disease
chronic diseases
public health

A B S T R A C T

Objectives: To compare diabetes monitoring and the incidence of acute diabetic complications between patients with and without incident Alzheimer's Disease and Related Syndromes (ADRS).
Design: Longitudinal observational study from 2010 to 2014.
Setting: Data from the French national health system database.
Participants: The France-Démence cohort: individuals aged 65 years or older suffering from incident ADRS, based on long-term disease registry, hospitalization for dementia, or antidementia drug delivery. They were matched (1:1) to a pair free of ADRS on age, sex, residence area, and insurance scheme. This study included France-Démence population with known diabetes for at least 2 years.
Measurements: Data related to diabetes control and complications: biological monitoring such as glycated hemoglobin A_{1c} (HbA_{1c}, ≥1/y, ≥2/y), lipid profile, microalbuminuria; eye examination; hospitalization for diabetes-related complications such as coma with ketoacidosis; and hospitalization for hypoglycemia were studied between the year prior to ADRS identification (Y_{-1}) and the 2 following years (Y_0; Y_1). Incidences between the 2 groups (ADRS/non-ADRS) were compared using age-standardized incidence ratios (SIR).
Results: The studied population included 87,816 individuals. HbA1c determination was less frequent in ADRS group, no matter the study period and the minimal annual threshold used. Respectively, 82.6% and 88.5% of ADRS and non-ADRS group had at least 1 HbA_{1c} testing during Y_{-1} [SIR = 0.94, 95% confidence interval (CI) 0.93–0.95], 73.4% and 89.0% during Y_0 (SIR = 0.83, 95% CI 0.82–0.84), and 75.4% and 89.3% during Y_1 (SIR = 0.85, 95% CI 0.83–0.86). Subjects with ADRS were also consistently more hospitalized than non-ADRS peers. The gap was maximal in the year following the diagnosis, as observed for hospitalizations for any cause related to diabetes (SIR Y_{-1}: 2.04, Y_0: 3.14, Y_1: 1.67), diabetes mellitus with coma (SIR Y_{-1}: 3.84, Y_0: 9.30, Y_1: 3.06), and hypoglycemia (SIR Y_{-1}: 4.20, Y_0: 5.25, Y_1: 2.27).
Conclusions: Incident ADRS is associated with a less frequent diabetes monitoring and an increased risk of diabetes complications compared with older people without ADRS. Our study questions healthcare quality offered to participants with ADRS in comorbidity control. Further investigations are required to explain the mechanisms underlying our results and to propose actions to improve care of patients with ADRS.

The prevalence of Alzheimer's Disease and Related Syndromes (ADRS) is growing worldwide.[1] This increase is largely driven by population aging, resulting from continuous improvement in the management of chronic affections such as cardiovascular and metabolic diseases. The prevalence of ADRS among older people with diabetes mellitus is especially likely to rise, as diabetes is a risk factor for vascular dementia and Alzheimer's disease.[2–4] In 2011, a

This study was funded by a grant from Toulouse University Hospital (local bidding, AOL 2016).
The authors declare no conflicts of interest.
* Address correspondence to Matthieu Wargny, MD, MSc, INSERM, UMR 1027 Epidemiology and Analyses in Public Health, 37 Allées Jules Guesde, Toulouse 31 000, France.
E-mail address: matthieu.wargny@univ-nantes.fr (M. Wargny).

https://doi.org/10.1016/j.jamda.2017.12.006
1525-8610/

nationwide study found a 8.5% prevalence of ADRS in people with diabetes older than 75 years.[5] From another angle, the prevalence of diabetes varied from 6% to 39% in patients with ADRS[6–15] and was about 14% in a large cohort study carried out between 1990 and 2007 in the United Kingdom.[16] Therefore, clinicians frequently have to take care of older adults with multiple comorbidities,[17] compelled to make the best of a complex situation.

ADRS makes diabetes monitoring more challenging by[18,19] compromising the patient's self-management abilities and threatening diabetes control. According to a comorbidity model developed by Piette and Kerr,[20] ADRS may be considered as a discordant comorbidity toward diabetes because it may introduce competing demands and lower diabetes prioritization. When dealing with diabetes control and monitoring of complications, clinicians resort to guidelines applicable to the general population suffering from diabetes,[21] but there is no systematic approach to the management of diabetes and dementia.[22] In particular, no specific guidelines are available regarding the frequency of glycated hemoglobin A_{1c} (HbA_{1c}) test in older adults with ADRS. However, HbA_{1c} still needs to be regularly assessed to avoid acute and chronic diabetic complications.

Few studies have evaluated diabetes monitoring regarding ADRS status. Some suggested lower frequencies of HbA1c test[23–25] or eye examination[24,25] among diabetic patients with prevalent ADRS compared with counterparts who did not suffer from ADRS. Others reported similar diabetes monitoring according to ADRS status.[26] Conversely, some studies found that the presence of comorbidities, even discordant, could be associated with a better healthcare quality among vulnerable older adults.[27] To our knowledge, no study has used a longitudinal approach to examine diabetes monitoring in conjunction to ADRS progression.

This study assessed whether incident ADRS affects the frequency of diabetes-related health services use: biological monitoring (HbA_{1c}, lipid profile and microalbuminuria tests), eye examination, and hospitalization for diabetes-related complications in French older adults during the year preceding ADRS diagnosis and the 2 following years.

Methods

Data Source

We used administrative data from the French national health system database, SNIIRAM (Système National d'Information Inter-Régimes de l'Assurance Maladie),[28] which covers 97% of the French population in 2011.[29] Reimbursed ambulatory healthcare are exhaustively collected: ambulatory visits to various healthcare providers, laboratory tests (without their results), and drug reimbursements. Every hospital stay is recorded, providing patient diagnoses as well as major procedures performed during the stay. Each hospitalization is associated with 1 main diagnosis (mandatory), 1 related diagnosis, and several potential associated diagnoses that could affect length and cost of stay. Moreover, chronic conditions are registered through the Long-Term Disease (LTD) system. It allows free full healthcare coverage for care related to several costly chronic diseases, including diabetes mellitus and ADRS, granted upon a demand made by the patient's physician to the French Healthcare System. Therefore, it is expected to facilitate an equal financial access to care. Lastly, vital status, including date of death, is also available.

Population — The DIA-FRA-DEM (Diabète-France-Démence) Cohort

FRA-DEM (for France-Démence) is a dynamic exposed/unexposed cohort exhaustively gathering incident cases of ADRS identified through the SNIIRAM since January 2011, paired to people free of ADRS. In this study, dementia was defined by the first recording of one of the following criteria: (1) LTD registration for ADRS [*International Classification of Diseases, 10th Revision* (ICD-10) codes: F00-F03, G30, G31]; (2) hospital stay reporting a diagnosis code of ADRS (similar ICD-10 codes); or (3) reimbursement for at least 1 acetylcholinesterase inhibitor (rivastigmine, galantamine or donepezil) or memantine. Each incident ADRS case was randomly paired (1:1) to a beneficiary without any ADRS criteria, matched on age, sex, residence area, and insurance scheme. For each pair, the first date of ADRS identification in the SNIIRAM defined the index date. In both groups, a 5-year period free of ADRS criteria was required before the index date.

In the DIA-FRA-DEM study, we selected individuals aged 65 years or older with a first ADRS criterion in 2011 or 2012 and with prevalent diabetes mellitus, defined by a LTD registration with ICD-10 codes E10 to E14. Diabetes identification had to have preceded ADRS identification for at least 2 years.

Follow-up

We defined for each participant a 3-year follow-up period: the year before the index date (Y_{-1}) and the 2 following years (Y_0 and Y_1), up to December 31, 2014 (Figure 1). A participant was censored when one of the following events occurred: (1) death, (2) loss to follow-up (6-month period without any ambulatory reimbursement, for ambulatory monitoring exclusively), or (3) incidence of ADRS (in the non ADRS group).

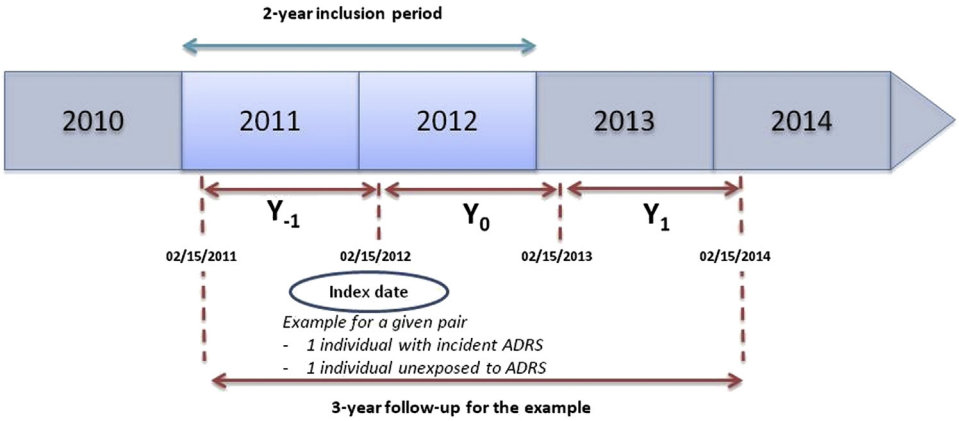

Fig. 1. DIA-FRA-DEM study: 3 years of follow-up of a pair. Example of an individual diagnosed with an incident ADRS identified on February 15, 2012 in the French national health insurance system. Y_{-1}, the year preceding the index date; Y_0 and Y_1: the next 2 years.

Outcomes

Diabetes-related health services use was studied. We defined conservative thresholds for ambulatory biological monitoring: ≥1 (primary endpoint) and ≥2 annual HbA_{1c} tests; ≥1 annual lipid profile; ≥1 annual microalbuminuria test; ≥1 annual eye examination, defined by a visit to an ophthalmologist or a dilated fundus examination, in or out of the hospitals.

Diabetes-related hospitalizations and complications as well as several other conditions of interest were collected: ≥1 annual hospitalization for hypoglycemia, ketoacidosis without coma, diabetic coma (with ketoacidosis, hyperosmolar or hypoglycemia), diabetic nephropathy, and diabetic neuropathy; ≥1 annual hospitalization for any diabetes-related cause; ≥1 annual hospitalization for falls and femur fracture, regarding their potential link with diabetes control, dementia, and their frequency in this population.

Please refer to the supplementary materials for more information on endpoints definition. The ICD-10 codes used are given in Supplementary Table S1. Additional measured endpoints, such as medical appointments (Supplementary Table S3) and ambulatory drug reimbursement (Supplementary Table S4) are also provided.

Other collected data included sex, age at index date, and other chronic conditions recorded through LTD registrations.

Statistical Analyses

Characteristics of the population are described at the index date. Proportions between the 2 groups (ADRS/without ADRS) were compared using standardized incidence ratios (SIR) with 95% confidence interval (CI), with an indirect standardization on age using 5-year age classes. Censoring was handled with incidence estimates using person-years to define incidence denominators. The data of censored individuals were used until their date of censoring.

We conducted 2 sensitivity analyses: (1) among persons with a minimum life expectancy of 2 years, we performed the analysis among the population uncensored at the end of the study; (2) to limit the bias induced by the fact that ADRS could be identified during a hospitalization, which tended to overestimate the hospitalization rate in ADRS group, we conducted a subgroup analysis among the ADRS population for whom ADRS identification was not based on hospitalization.

Analyses were performed using SAS (v 9.4; SAS Institute Inc, Cary, NC) and R (v 3.0.1; R Foundation for Statistical Computing, Vienna, Austria) software.

Ethical Committee

The project received approval from the French data protection authority (CNIL, authorization n°1631786, 2013).

Results

Follow-up and Characteristics of the Population

The FRA-DEM cohort included 352,595 individuals with incident ADRS and their pair between January 2011 and December 2012. In the ADRS group, 11.4% (n = 40,117) presented a diabetes history; in the group without ADRS, 13.5% (n = 47,699). Incident ADRS was first identified through hospitalization (72.3%, n = 28,991), antidementia drugs initiation (17.8%, n = 7130), and initiation of LTD registration for ADRS (11.2%, n = 4481). In the ADRS group, 36,323 person-years were followed during Y_0 and 28,583 during Y_1 compared with 46,256 and 41,131 in the non-ADRS group. Respectively 35.6% of the ADRS group (n = 14,312) against 19.0% of the non-ADRS group (n = 9068) were censored before the end of the follow-up.

Table 1
Characteristics of the DIA-FRA-DEM Population at Index Date (N = 87,816)

Characteristics	ADRS N = 40,117	Non-ADRS N = 47,699
Age at index date, in y (mean ± SD)	81.6 ± 6.7	82.1 ± 6.7
Women (n, %)	22,678 (56.5)	27,876 (58.4)
Diabetes type (n, %)		
Type 1	4703 (11.7)	5756 (12.1)
Type 2	34,433 (85.8)	40,907 (85.8)
Others or unknown	981 (2.4)	1036 (2.2)
Long-term diseases (n, %)		
Diabetes mellitus	40,117 (100)	47,699 (100)
Circulatory system disease	20,176 (50.3)	24,949 (52.3)
Cancer	6677 (16.6)	9411 (19.7)
Psychiatric condition	2642 (6.6)	1846 (3.9)
Parkinson disease	1602 (4.0)	775 (1.6)
Number of different registrations for LTD other than ADRS or diabetes mellitus (n, %)		
0	12,785 (31.9)	14,634 (30.7)
1	13,316 (33.2)	15,562 (32.6)
2	8435 (21.0)	10,288 (21.6)
3	3624 (9.0)	4665 (9.8)
4 or more	1957 (4.9)	2550 (5.3)
Number of different drugs delivered during the last trimester before index date (mean ± SD)	12.6 ± 7.2	13.7 ± 6.5

SD, standard deviation.
ICD-10 codes related to the different LTDs: Circulatory system diseases: I; Cancer, malignant neoplasms C, in situ neoplasms D00-D09, and neoplasms of uncertain or unknown behavior D37-D48; Psychiatric condition, mental and behavioral disorders F, with the exclusion of dementia-related disorders F00-F03 and alcohol-related disorders F10; Parkinson disease, F02.3, G20-G22, and G23.2.

At the index date, women represented 56.5% and 58.4% of the population in the ADRS and non-ADRS groups, respectively (Table 1). Mean age ± standard deviation was 81.6 ± 6.7 years in ADRS group and 82.1 ± 6.7 years in non-ADRS group. Around two- thirds of the population presented at least 1 LTD for other conditions than diabetes or ADRS, with about 50% suffering from cardiovascular diseases.

Biological Analyses and Eye Examination

Fewer individuals received ≥1 annual HbA_{1c} test in the ADRS group than in the non-ADRS group, during each yearly period (Figure 2). During Y_{-1}, 82.6% and 88.5% of ADRS and non-ADRS group had at least 1 HbA1c test, respectively (SIR = 0.94, 95% CI 0.93–0.95). During Y_0, this difference worsened, with 73.4% in ADRS group compared with 89.0% in the non-ADRS group (SIR = 0.83, 95% CI 0.82–0.84) and remained stable during Y_1 (75.4% vs 89.3%, SIR = 0.85, 95% CI 0.83–0.86).

Patterns for ≥2 annual HbA1c tests were similar: Y_{-1} SIR = 0.89 (95% CI 0.88–0.90), Y_0 SIR = 0.74 (95% CI 0.73–0.75), Y_1 SIR = 0.78 (95% CI 0.77–0.80).

The prevalence of ≥1 LDL-cholesterol test during Y_{-1} was 56.0% in ADRS group and 63.2% among the non-ADRS group, with Y_{-1} SIR= 0.89 (95% CI 0.88–0.90), Y_0 SIR = 0.68 (95% CI 0.67–0.69), and Y_1 SIR = 0.72 (95% CI 0.71–0.74).

Screening for microalbuminuria was less frequent in both groups, with only 16.1% and 21.8% had ≥1 annual screening during Y_{-1} in ADRS and non-ADRS group, respectively (Y_{-1} SIR = 0.72 (95% CI 0.70–0.74), Y_0 SIR = 0.48 (95% CI 0.47–0.50) and Y_1 SIR= 0.52 (95% CI 0.50—0.53)).

Finally, ≥1 eye examination during the year was mostly unperformed in the population: 38.4% of the ADRS group and 49.9% of the non-ADRS group during Y_{-1} (Y_{-1} SIR = 0.77 (95% CI 0.75–0.78), Y_0 SIR = 0.67 (95% CI 0.66–0.68), and Y_1 SIR = 0.63 (95% CI 0.61–0.64)).

Sensitivity analyses excluding individuals censored during the follow-up period showed similar trends over time (Figure 2), despite a decreased magnitude of the differences observed between groups.

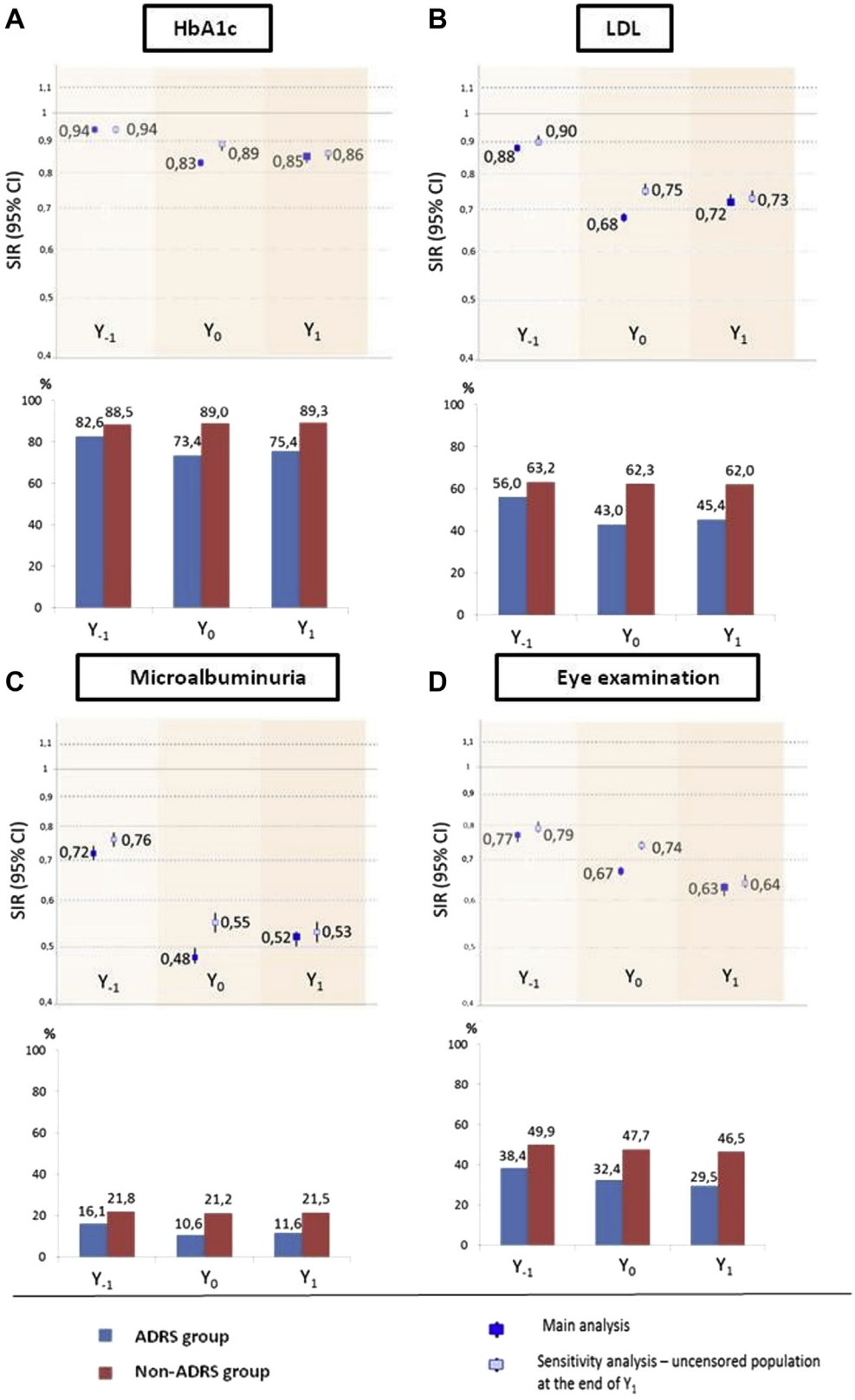

Fig. 2. Biologic and eye examination monitoring in the DIA-FRA-DEM cohort (N = 87,816). Prevalence (*bar charts*) and SIR with 95% CI comparing groups with and without ADRS are presented for the 3 years of follow-up (Y_{-1}, Y, and Y_1), (A) for at least 1 HbA1c test, (B) at least 1 low-density lipoprotein (*LDL*)-cholesterol test, (C) at least 1 test for microalbuminuria, and (D) at least 1 eye examination during the studied year. SIR estimations are presented using logarithmic axis for both main (*full dark blue rectangle*) and sensitivity (*pale blue rectangle*) analyses. Sensitivity analyses are performed for populations uncensored at the end of follow-up (N = 64,449).

Hospitalizations

During Y_{-1}, 72/1000 person-years in the ADRS group went through at least 1 hospitalization related to diabetes, against 35/1000 in the non-ADRS group (SIR = 2.04, 95% CI 1.97–2.12) (Table 2). This SIR rose to 3.14 (95% CI 3.04–3.24) during Y_0 and decreased to 1.67 (95% CI 1.59–1.76) during Y_1.

Regarding hospitalizations for ketoacidosis without coma, Y_{-1} incidence was 3.1/1000 for ADRS groups and 0.6/1000 for non-ADRS group, with successive SIRs values of 4.70 (95% CI 3.91–5.60), 7.78 (95% CI 6.72–8.96), and 2.66 (95% CI 1.97–3.51) during Y_0 and Y_1, respectively. Similar trends were seen for hospitalizations for diabetes-related coma, incidence during Y_{-1} was 4.9/1000 for ADRS groups vs 3.2/1000 for non-ADRS group, and the SIRs values were 3.84 (95% CI 3.14–4.65), 9.30 (95% CI 8.08–10.64), and 3.06 (95% CI 2.38–3.88) for Y_{-1}, Y_0 and Y_1, respectively.

Incidence rates of hospitalization for hypoglycemia, fall, or femur fracture followed similar patterns (Table 2).

In the sensitivity analysis excluding individuals with ADRS for whom ADRS was first identified during a hospital stay, the magnitude of SIRs was reduced, especially for Y_0, but individuals with ADRS remained significantly more likely to undergo every studied hospitalization than individuals without ADRS (Supplementary Table S2).

Discussion

Our study has 4 main findings. First, adherence to diabetes monitoring guidelines was low for both groups in this cohort of older individuals without, theoretically, any financial barrier to diabetes healthcare use. Second, individuals with ADRS were significantly less likely to receive recommended monitoring than counterparts without ADRS. Third, the magnitude of the differences on diabetes monitoring between groups tended to increase over time. Fourth, individuals with ADRS were significantly more likely to be hospitalized for diabetes complications than individuals without ADRS.

For all outcomes and studied years, we found that individuals with ADRS were less likely to receive minimal diabetes monitoring than individuals without ADRS. This is in accordance with an Australian study reporting an adjusted risk ratios (RRs) of 0.83 (95% CI 0.77–0.90) for ≥1 annual HbA_{1c}, and 0.72 (95% CI 0.63–0.83) for ≥1 annual microalbuminuria test.[23] A US study, using a wider adjustment on multiple sociodemographic criteria and comorbidities, also reported a lesser extent of receipt of ≥1 annual HbA_{1c} test among people with dementia (adjusted RR = 0.96, 95% CI 0.96–0.97) or ≥1 annual LDL-C test (adjusted RR = 0.91, 95% CI 0.90–0.91).[24] This is also in line with the literature suggesting a lower access to comorbidities prevention[30,31] and a worse management of comorbidities[32,33] among individuals with dementia. However, our results are discordant with a German study finding similar general practitioners' (GPs) practice for diabetes medication, regardless of the dementia status of the patients, that may be explained by differences in the population studied and limited sample size (n = 138).[26]

We observed a lower receipt of recommended examinations in the year preceding ADRS identification, which worsened over the subsequent years. This difference remained in conservative sensitivity analyses excluding the frailest individuals, and cannot be explained by differences in the number of GPs' consultations per year, which were similar in both groups (47.4 % of the ADRS group had at least 12 annual visits in ADRS group, against 46.2% in the non-ADRS group; SIR = 1.04, 95% CI 1.02–1.05). This particularly low receipt of diabetes monitoring in individuals with ADRS raises some concerns in France, where 3 successive national plans for Alzheimer's disease have been implemented since 2001.[34] Unfortunately, the present study cannot disentangle whether this low monitoring could be explained by patients' characteristics, or GPs', relatives and informal caregivers' attitudes. French GPs have financial incentives to prescribe biological diabetes monitoring, but they report a lack of training in the management of patients with dementia.[35] In Germany, an analysis of the health insurance database found that nursing home residents with dementia received lower diabetes-related medical examination than recommended, this effect being greater for higher dependency.[36] It points out a possible inappropriate monitoring.

Individuals with ADRS were more frequently hospitalized for diabetes-related conditions than individuals without ADRS, particularly for coma and ketoacidosis, but also for nephropathy and neuropathy. The results concerning hospitalizations for life-threatening and preventable events such as diabetic coma are particularly alarming, with a 3- (Y_{-1} and Y_1) to 9-fold (Y_0) increased risk in individuals with ADRS. An increased risk of diabetes-related hospitalizations among individuals with ADRS has already been suggested in other studies, including for the risk of hypoglycemia.[37,38] These results were confirmed in sensitivity analyses excluding the frailest subpopulation.

This study presents several strengths. To our knowledge, it is the first to adopt a dynamic perspective to study the effect of ADRS on diabetes care, showing that health services use was temporarily affected around ADRS diagnosis. Diabetes was identified using LTD registration, which is widely prevalent among individuals with diabetes and is expected to be very specific. The nationwide dimension of this study allows to report representative practice of patients and their practitioners. Furthermore, using administrative data allowed an exhaustive capture of all reimbursed care related to diabetes.

Table 2
Comparison of Hospitalization Rates Between Groups With and Without ADRS During Follow-Up (Y_{-1}, Y_0, and Y_1)

Groups (PY)	Y_{-1}			Y_0			Y_1		
	ADRS (40,149 PY)	Non-ADRS (47,699 PY)	SIR [95% CI]	ADRS (38,063 PY)	Non-ADRS (46,754 PY)	SIR [95% CI]	ADRS (34,863 PY)	Non-ADRS (44,109 PY)	SIR [95% CI]
	Rate (/1000 PY)			Rate (/1000 PY)			Rate (/1000 PY)		
Diagnoses associated with hospitalization, specific to diabetes									
Diabetes − any cause	72.3	34.8	2.04 [1.97; 2.12]	97.6	30.5	3.14 [3.04; 3.24]	42.9	25.1	1.67 [1.59; 1.76]
Ketoacidosis (without coma)	3.1	0.6	4.70 [3.91; 5.60]	5.1	0.7	7.78 [6.72; 8.96]	1.4	0.5	2.66 [1.97; 3.51]
DM with coma	2.6	0.7	3.84 [3.14; 4.65]	5.5	0.6	9.30 [8.08; 10.64]	2.0	0.6	3.06 [2.38; 3.88]
DM with nephropathy	4.9	3.2	1.48 [1.28; 1.70]	7.1	2.7	2.51 [2.22; 2.83]	3.8	1.7	2.15 [1.80; 2.55]
DM with neuropathy	5.1	2.8	1.79 [1.55; 2.05]	7.4	2.4	3.06 [2.71; 3.44]	2.6	2.2	1.15 [0.92; 1.41]
Other diagnoses associated with hospitalization, nonspecific to diabetes									
Hypoglycemia	10.7	2.6	4.20 [3.81; 4.61]	14.6	2.8	5.25 [4.82; 5.70]	5.4	2.4	2.27 [1.96; 2.62]
Falls	15.8	1.9	8.64 [7.98; 9.34]	25.4	2.5	10.70 [10.03; 11.39]	10.0	2.2	4.60 [4.13; 5.11]
Fracture of femur	27.7	6.7	4.32 [4.07; 4.58]	37.0	7.6	5.14 [4.88; 5.42]	20.9	7.4	2.99 [2.78; 3.22]

DM, diabetes mellitus; PY, person-years.
Please refer to Supplementary Table S1 for ICD-code details.

However, our study presents some limitations. First, diabetes and ADRS diagnoses were not clinically ascertained, but derived from claims data. Regarding ADRS identification, it is likely that the index date may not represent the date of the first ADRS symptoms[39–41] but rather ADRS diagnosis. This latter is of great interest because it represents a milestone in the individual's illness trajectory. Second, health insurance data did not include all procedures performed for inpatients. Therefore, we cannot exclude the possibility that some biological tests or eye examinations could have been performed without being registered in the database. This may have overestimated the differences because individuals with ADRS were more frequently hospitalized. Third, we could not distinguish between community-dwelling individuals or individuals living in nursing homes. It would have been interesting to study a potential difference in the monitoring of individuals with ADRS between the 2 settings, with possible differences in standards of care. Fourth, we lacked information about ADRS and diabetes severity. Lastly, our study did not aim at identifying the factors associated with diabetes monitoring. Further studies, both quantitative and qualitative, are needed to assess the reasons of the lower receipt we evidenced.

Conclusions

In this nationwide study, diabetic older adults with ADRS were significantly less likely to receive basic monitoring for diabetes mellitus and more likely to experience diabetes-related complications than older adults without ADRS. This monitoring is easy to perform, refers to accessible and acceptable healthcare, and has an impact on the future course of ADRS and the patient's autonomy. Our study, therefore, questions healthcare quality offered to people with dementia.

Acknowledgments

The authors thank the CNAMTS (*Caisse Nationale d'Assurance Maladie des Travailleurs Salariés*) for data extraction (DEMEX team: Mehdi Gabbas, Brice Dufresne, David Dias); Dr Charlotte Vaurs for her help during protocol writing; Dr Agnès Sommet for her helpful critic of this work; Dr Robert Bourrel and Dr Didier Fabre for their informed advice on SNIIRAM data.

References

1. World Alzheimer Report 2015: The Global Impact of Dementia. London, England: Alzheimer's Disease International; 2015.
2. Biessels GJ, Staekenborg S, Brunner E, et al. Risk of dementia in diabetes mellitus: A systematic review. Lancet Neurol 2006;5:64–74.
3. Lu F-P, Lin K-P, Kuo H-K. Diabetes and the risk of multisystem aging phenotypes: A systematic review and meta-analysis. PloS One 2009;4:e4144.
4. Cheng G, Huang C, Deng H, Wang H. Diabetes as a risk factor for dementia and mild cognitive impairment: A meta-analysis of longitudinal studies. Intern Med J 2012;42:484–491.
5. Cosker K, Denis P, Tala S, et al. Pathologies associées, états de santé et traitements des personnes diabétiques en France: Les données du Sniiram 2011. Bull Epidémiol Hebd 2014:507–514.
6. Barnett K, Mercer SW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: A cross-sectional study. Lancet Lond Engl 2012;380:37–43.
7. Bunn F, Burn A-M, Goodman C, et al. Comorbidity and dementia: A scoping review of the literature. BMC Med 2014;12:192.
8. McCormick WC, Kukull WA, van Belle G, et al. Symptom patterns and comorbidity in the early stages of Alzheimer's disease. J Am Geriatr Soc 1994;42:517–521.
9. Löppönen MK, Isoaho RE, Räihä IJ, et al. Undiagnosed diseases in patients with dementia—A potential target group for intervention. Dement Geriatr Cogn Disord 2004;18:321–329.
10. Zamrini E, Parrish JA, Parsons D, Harrell LE. Medical comorbidity in black and white patients with Alzheimer's disease. South Med J 2004;97:2–6.
11. Lyketsos CG, Toone L, Tschanz J, et al. Population-based study of medical comorbidity in early dementia and "cognitive impairment, no dementia (CIND)": Association with functional and cognitive impairment: The Cache County Study. Am J Geriatr Psychiatry 2005;13:656–664.
12. Schubert CC, Boustani M, Callahan CM, et al. Comorbidity profile of dementia patients in primary care: are they sicker? J Am Geriatr Soc 2006;54:104–109.
13. Zekry D, Herrmann FR, Grandjean R, et al. Demented versus non-demented very old inpatients: the same comorbidities but poorer functional and nutritional status. Age Ageing 2008;37:83–89.
14. Sakurai H, Hanyu H, Kanetaka H, et al. Prevalence of coexisting diseases in patients with Alzheimer's disease. Geriatr Gerontol Int 2010;10:216–217.
15. Heun R, Schoepf D, Potluri R, Natalwala A. Alzheimer's disease and comorbidity: increased prevalence and possible risk factors of excess mortality in a naturalistic 7-year follow-up. Eur Psychiatry J 2013;28:40–48.
16. Rait G, Walters K, Bottomley C, et al. Survival of people with clinical diagnosis of dementia in primary care: Cohort study. BMJ 2010;341:c3584.
17. van Oostrom SH, Picavet HSJ, van Gelder BM, et al. Multimorbidity and comorbidity in the Dutch population–Data from general practices. BMC Public Health 2012;12:715.
18. Hewitt J, Smeeth L, Chaturvedi N, et al. Self-management and patient understanding of diabetes in the older person. Diabet Med 2011;28:117–122.
19. Feil DG, Zhu CW, Sultzer DL. The relationship between cognitive impairment and diabetes self-management in a population-based community sample of older adults with type 2 diabetes. J Behav Med 2012;35:190–199.
20. Piette JD, Kerr EA. The impact of comorbid chronic conditions on diabetes care. Diabetes Care 2006;29:725–731.
21. American Diabetes Association. Standards of Medical Care in Diabetes-2016, 2016.
22. Sinclair AJ, Hillson R, Bayer AJ, National Expert Working Group. Diabetes and dementia in older people: A Best Clinical Practice Statement by a multidisciplinary National Expert Working Group. Diabet Med J Br Diabet Assoc 2014;31:1024–1031.
23. Zhang Y, Vitry A, Roughead E, et al. Comorbidity and the utilization of health care for Australian veterans with diabetes. Diabet Med J 2010;27:65–71.
24. Thorpe CT, Thorpe JM, Kind AJH, et al. Receipt of monitoring of diabetes mellitus in older adults with comorbid dementia. J Am Geriatr Soc 2012;60:644–651.
25. Connolly A, Campbell S, Gaehl E, et al. Under-provision of medical care for vascular diseases for people with dementia in primary care: A cross-sectional review. Br J Gen Pract J R Coll Gen Pract 2013;63:e88–e96.
26. Müther J, Abholz H-H, Wiese B, et al. Are patients with dementia treated as well as patients without dementia for hypertension, diabetes, and hyperlipidaemia? Br J Gen Pract J R Coll Gen Pract 2010;60:671–674.
27. Min LC, Wenger NS, Fung C, et al. Multimorbidity is associated with better quality of care among vulnerable elders. Med Care 2007;45:480–488.
28. Moulis G, Lapeyre-Mestre M, Palmaro A, et al. French health insurance databases: What interest for medical research? Rev Med Interne 2015;36:411–417.
29. Polton D, Ricordeau P. Le SNIIR-AM et les bases de données de l'Assurance Maladie en 2011. 2011.
30. Rodriguez EG, Dodge HH, Birzescu MA, et al. Use of lipid-lowering drugs in older adults with and without dementia: A community-based epidemiological study. J Am Geriatr Soc 2002;50:1852–1856.
31. Shah SM, Carey IM, Harris T, et al. The impact of dementia on influenza vaccination uptake in community and care home residents. Age Ageing 2012;41:64–69.
32. Lopponen M, Raiha I, Isoaho R, et al. Dementia associates with under medication of cardiovascular diseases in the elderly: A population-based study. Dement Geriatr Cogn Disord 2006;22:132–141.
33. Saposnik G, Cote R, Rochon PA, et al. Care and outcomes in patients with ischemic stroke with and without preexisting dementia. Neurology 2011;77:1664–1673.
34. Devos P, Haeffner-Cavaillon N, Ledoux S, et al. Assessing the French Alzheimer plan. Lancet Lond Engl 2014;383:1805.
35. Somme D, Gautier A, Pin S, Corvol A. General practitioner's clinical practices, difficulties and educational needs to manage Alzheimer's disease in France: Analysis of national telephone-inquiry data. BMC Fam Pract 2013;14:81.
36. Schwarzkopf L, Holle R, Schunk M. Effects of nursing home residency on diabetes care in individuals with dementia: An explorative analysis based on German claims data. Dement Geriatr Cogn Disord Extra 2017;7:41–51.
37. Kim HM, Seong J-M, Kim J. Risk of hospitalization for hypoglycemia among older Korean people with diabetes mellitus: Interactions between treatment modalities and comorbidities. Medicine (Baltimore) 2016;95:e5016.
38. Prinz N, Stingl J, Dapp A, et al. High rate of hypoglycemia in 6770 type 2 diabetes patients with comorbid dementia: A multicenter cohort study on 215,932 patients from the German/Austrian diabetes registry. Diabetes Res Clin Pract 2016;112:73–81.
39. Cattel C, Gambassi G, Sgadari A, et al. Correlates of delayed referral for the diagnosis of dementia in an outpatient population. J Gerontol A Biol Sci Med Sci 2000;55:M98–M102.
40. Knopman D, Donohue JA, Gutterman EM. Patterns of care in the early stages of Alzheimer's disease: Impediments to timely diagnosis. J Am Geriatr Soc 2000;48:300–304.
41. Nourhashemi F, Andrieu S, Gillette-Guyonnet S, et al. Effectiveness of a specific care plan in patients with Alzheimer's disease: Cluster randomised trial (PLASA study). BMJ 2010;340:c2466.

Supplementary Table S1
Codes Defining Biological Analyses, Medical Acts, and Causes of Hospitalizations, Specific or Nonspecific to Diabetes

Outcomes	Coding Specification
Biological analyses	NMBA codes
HbA1c determination	1577
LDL-cholesterol determination	996, 2001
Microalbuminuria testing	1133
Medical act	CCMA and Medical Specialty codes
Realization of an eye examination	• CCMA: BGQP, EBQF • Medical Specialty: 15
Cause of hospitalization specific to diabetes mellitus	ICD-10 codes
Diabetes-related (any cause)	E10-E14, E16.0-E16.2, G59.0, G63.2, G99.0, H28.0, H36.0, N08.3, M14.2, M14.6
Diabetic coma	
• Diabetic coma with or without ketoacidosis	(E10-E14)-.0
• Hyperosmolar coma	
• Hypoglycemic coma	
• Hyperglycemic coma NOS	
Diabetes with ketoacidosis without mention of coma	
• Diabetic acidosis	(E10-E14)-.1
• Diabetic ketoacidosis	
Diabetes with renal complications	
• Diabetic nephropathy	(E10-E14)-.2, N08.3
• Intracapillary glomerulonephrosis	
• Kimmelstiel-Wilson syndrome	
Diabetes with ophthalmic complications	
• Cataract	(E10-E14)-.3, H28.0, H36.0
• Retinopathy	
Diabetes with neurologic complication	
• Diabetic neuropathy	(E10-E14)-.4, G59.0, G63.2, G99.0
• Diabetic mononeuropathy	
• Diabetic polyneuropathy	
• Autonomic neuropathy in endocrine and metabolic diseases	
Cause of hospitalization nonspecific to diabetes	ICD-10 codes
Hypoglycemia	
• Drug-induced hypoglycemia without coma	E16.0-E16.2
• Other hypoglycemia	
• Hypoglycemia, unspecified	
Falls	
• Tendency to fall, not elsewhere classified	R29.6
Fracture of femur	
• Fracture of femur	S72

CCMA, Common Classification for Medical Acts; NMBA, Nomenclature of Medical Biology Acts; NOS, not otherwise specified.
Medical Specialty codes are codes used to specify the specialty of a given practitioner in the French National Health Insurance Database (SNIIRAM).

Supplementary Table S2
Sensitivity Analyses: Comparison of Hospitalization Rates Between Groups With and Without ADRS During Follow-Up (Y_{-1}, Y_0, and Y_1)

	Y_{-1}			Y_0			Y_1		
	ADRS (14,721 PY)	Non-ADRS (47,699 PY)	SIR [95% CI]	ADRS (14,251 PY)	Non-ADRS (46,754 PY)	SIR [95% CI]	ADRS (13,373 PY)	Non-ADRS (44,109 PY)	SIR [95% CI]
	Rate (/1000 PY)			Rate (/1000 PY)			Rate (/1000 PY)		
Diagnoses associated with hospitalization, specific to diabetes									
Diabetes – any cause	61.1	34.8	1.70 [1.59; 1.81]	47.2	30.5	1.50 [1.39; 1.62]	36.2	25.1	1.39 [1.27; 1.52]
Ketoacidosis (without coma)	2.8	0.6	4.23 [3.03; 5.73]	1.9	0.7	3.00 [1.98; 4.37]	1.6	0.5	2.92 [1.80; 4.46]
DM with coma	1.8	0.7	2.50 [1.63; 3.66]	1.8	0.6	3.13 [2.05; 4.59]	1.7	0.6	2.71 [1.71; 4.06]
DM with nephropathy	3.6	3.2	1.07 [0.80; 1.40]	3.2	2.7	1.14 [0.83; 1.52]	2.5	1.7	1.35 [0.93; 1.89]
DM with neuropathy	3.8	2.8	1.31 [0.99; 1.70]	2.9	2.4	1.19 [0.86; 1.61]	1.7	2.2	0.73 [0.47; 1.10]
Other diagnoses associated with hospitalization, nonspecific to diabetes									
Hypoglycemia	7.5	2.6	2.99 [2.46; 3.60]	6.7	2.8	2.41 [1.95; 2.95]	3.7	2.4	1.56 [1.15; 2.06]
Falls	16.6	1.9	9.35 [8.21; 10.60]	10.0	2.5	4.25 [3.58; 5.01]	7.9	2.2	3.71 [3.03; 4.48]
Fracture of femur	37.6	6.7	6.05 [5.56; 6.58]	22.7	7.6	3.31 [2.96; 3.69]	20.5	7.4	3.03 [2.68; 3.41]

DM, diabetes mellitus; PY, person-years.
The ADRS for whom the criteria of identification for incident dementia was a dementia-related hospitalization was excluded (remaining population N = 62,420).
Please refer to Supplementary Table S1 for ICD code details.

Supplementary Table S3
Comparison of Medical Consultations With GPs and Cardiologists Between Groups With and Without ADRS During Follow-Up (Y_{-1}, Y_0, and Y_1)

Groups (PY)	Y_{-1}			Y_0			Y_1		
	ADRS (40,117 PY)	Non-ADRS (47,699 PY)	SIR [95% CI]	ADRS (36,323 PY)	Non-ADRS (46,256 PY)	SIR [95% CI]	ADRS (28,583 PY)	Non-ADRS (41,131 PY)	SIR [95% CI]
	Rate (%)			Rate (%)			Rate (%)		
Medical appointments									
GP (≥12 visits/y)	47.4	46.2	1.04 [1.02; 1.05]	43.3	44.2	1.00 [0.98; 1.01]	40.8	42.0	0.99 [0.97; 1.01]
Cardiologist (≥1 visit(s)/y)	36.5	44.8	0.81 [0.80; 0.82]	31.3	43.2	0.72 [0.71; 0.74]	27.0	42.5	0.63 [0.62; 0.64]

PY, person-years.

Supplementary Table S4
Main Diabetes Medication During Follow-Up (Y_{-1}, Y_0, and Y_1) Regarding to the ADRS Status

Groups	Y_{-1}		Y_0		Y_1	
	ADRS	Non-ADRS	ADRS	Non-ADRS	ADRS	Non-ADRS
PY	40,117	47,699	36,323	46,256	28,583	41,131
Diabetes medication: ≥2 delivery/y (%)						
Oral medication						
Metformine	42.7	41.5	30.1	38.3	31.0	37.0
Sulfonylurea	33.4	34.7	19.1	30.0	17.7	27.3
Any insulin	34.8	43.7	34.0	44.2	35.0	43.3
Insulin glargin	18.7	23.4	19.7	24.2	21.0	24.4
Insulin detemir	4.5	5.5	5.1	5.7	5.4	5.8
Rapid acting insulin	16.8	20.7	16.2	21.1	16.6	20.9

PY, person-years.
At least 2 deliveries a year were needed to be considered as under treatment.