




RESEARCH ARTICLE

Twenty-year trends in patient referrals throughout the creation and development of a regional memory clinic network

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*See Appendix A.

Abstract

Introduction: Memory clinics (MCs) are the main model for dementia diagnosis and care. Following the development of a MC network in Northern France, our objectives were to assess its impact on patient characteristics over 20 years.

Methods: The characteristics of new consultants were studied from 1997 to 2016.

Results: New consultants increased from 774 per year in 1997 to 26258 per year in 2016, as the number of MCs increased from 12 to 29. Over time, patients were progressively older and less educated, and more were living alone. A greater proportion of patients were referred by specialists. Referral delay and home-to-MC distance kept decreasing. The oldest patients were referred at a progressively less-severe stage. The proportion of young patients kept increasing in the tertiary referral center.

Discussions: The development of a region-wide MC network led to increased referral of vulnerable patients and differentiation of the tertiary referral center over time.

KEYWORDS

Alzheimer's disease, ambulatory care facilities, community, dementia, health networks, memory clinics, public health, public health policies, public health practice

1 | INTRODUCTION

In 2018, ≈50 million people were living with dementia worldwide. This number is expected to triple in 2050.¹ Previous studies have shown that even in developed countries the rate of underdiagnosis was ≈50%, especially in the mild dementia stage.^{2,3} Despite the absence of curative treatments for dementia, timely diagnosis is a preliminary step to provide adequate support.⁴ Timely diagnosis allows better comprehension and management of symptoms, prescription of

symptomatic drugs, and non-pharmaceutical interventions including in-home care and caregiver support, resulting in improved quality of life of patients and caregivers.⁵⁻⁷ It is probably a cost-effective approach, because early intervention contributes to delay cognitive decline, maintains functional abilities, and delays admission to institutional care.⁸ Later in the disease course, proper diagnosis and care allows institutional long-term care admission at the right time and place.⁹ Therefore, better access to diagnosis is a major challenge for all countries.¹⁰

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Memory clinics (MCs) are specialized health care facilities in which multidisciplinary teams provide diagnostic workup of neurocognitive disorders and appropriate management. The first MCs were set up in North America during the mid-1970s, and in the UK shortly thereafter.¹¹ MCs have ever since established themselves in developed countries as secondary referral care for people with dementia, mild cognitive impairment, and subjective cognitive complaint.¹² However, organization, working methods, and services of MCs remain heterogeneous from one country to another.¹³ The impact of these different practices on patient care remains largely unknown.

The first French multidisciplinary MC was founded in 1991 in the neurology department of Lille University Hospital, in Northern France, a region of 4 million inhabitants. Shortly after, an advanced MC opened in 1993 in Baillieu, a rural town of 15,000 inhabitants 25 km from the university hospital, run by the same medical team but in a different environment. The successful experience of this outpost MC led to the establishment of other MCs in the main general hospitals of the region from 1995.¹⁴ All MCs provided easy access to brain imaging and multidisciplinary assessment by neurologists, geriatricians, psychologists, and social workers; whenever necessary, patients could additionally be assessed by psychiatrists, speech therapists, and dedicated nurses. These MCs soon organized as a health care network, prompting harmonization of diagnostic workup, easy access to cerebrospinal fluid (CSF) biomarkers and organization of a regional brain donation program. Data on patient characteristics and health care resources are systematically collected in all MCs since 1997. All data are monitored and computerized by a data manager in Lille MC.

Within this network, Lille MC has the distinctive characteristic of being both a secondary and tertiary referral center. Acknowledged as a Memory Resource and Research Center (MRRC), Lille MC is the referral center for all MCs in the region. Since 2009, Lille MRRC is also acknowledged as a national reference center for young-onset dementia. Lille MRRC hosted a multidisciplinary meeting every 2 months for all MC professionals, providing continuing medical education, with clinical and clinicopathological case reports, scientific presentations, and sharing of professional information including updates on social services support.

The objective of our study was to assess the changes in the clinical characteristics of new patients referred to the MCs over 20 years, throughout the creation and development of our regional network, in the context of national public health policies and Alzheimer's disease plans. Our hypothesis was that referral would occur at an increasingly early stage and that patients referred to Lille MRRC would increasingly stand out from the ones referred to the other MCs.

2 | PATIENTS AND METHODS

2.1 | Patient selection

We included all consecutive new consultants attending one of the MCs of the Nord Pas-de-Calais region from January 1997 to December 2016. A new patient was defined as a patient referred for the first time

RESEARCH IN CONTEXT

1. Systematic review: We searched all articles published using PUBMED. Previous studies on memory clinics (MCs) focused mainly on their organization in each country. Data on the evolution of the characteristics of MC patients over time were scarce.
2. Interpretation: Our data suggest that the establishment of a regional MC network was associated with: (1) an increase in the number of referrals, particularly in the most vulnerable population; (2) a better use of the resources offered by the tertiary referral center; (3) a shortening of the referral delay and improved accessibility to the MC.
3. Future directions: Future work should study the impact of public information on referral delay and degree of cognitive impairment at the first consultation. Analyzing changes in diagnoses and management over time will be important to assess the impact of the network on quality of care.

to any of the MCs of the network. Data were prospectively collected in each MC and centralized in the regional database maintained by Lille MRRC, and declared to the National Commission for Informatics and Liberties (CNIL).

The following demographic characteristics of new patients were extracted from our database: age at first visit, sex, education level (illiteracy, primary (≤ 6 years of education), secondary (≤ 12 years), or tertiary education), distance between the dwelling place and the MC (≥ 50 or < 50 km) and type of dwelling place (private home, assisted living facility, nursing home, or others). If the patient was living in a private home, the civil status and family interactions were collected (living with partner or family, living alone with or without family support).

Referral source was classified into general practitioners (GPs), specialists (neurologists, geriatricians, and psychiatrists, or others) or self-referral (patients coming by themselves). The delay of referral was calculated from the estimated date of symptom onset according to the medical history provided by the patient, family, or referrer, to the date of the first visit in a MC.

Last, the Mini Mental State Examination (MMSE)¹⁵ and the clinical diagnosis at the first visit were extracted from the database. The clinical diagnosis was made according to the diagnostic criteria in effect at the time of referral: Clinical diagnoses of dementia and mild cognitive impairment (MCI) were set using consensus criteria.¹⁶⁻¹⁸ Etiological diagnoses were classified into Alzheimer's dementia with or without vascular lesions (AD),¹⁹⁻²² frontotemporal lobar degeneration (FTLD),²³⁻²⁵ Lewy body dementia (LBD),^{26,27} vascular dementia (VaD),^{28,29} alcohol-related disorders, psychiatric disorders, and others.

2.2 | Statistical analysis

Qualitative variables were expressed as frequencies and percentages. Quantitative variables were expressed as median and interquartile range.

The 20-year span of the study was separated into five periods: P1 (from 1997 to 2000), P2 (from 2001 to 2004), P3 (from 2005 to 2008), P4 (from 2009 to 2012), and P5 (from 2013 to 2016). The link between these periods and quantitative variables was analyzed using Spearman correlations. The correlation coefficient (r) was calculated to measure the effect size. Qualitative variables were analyzed by chi-square test or Fisher exact test. Cramer's V coefficient (V) was calculated to measure the effect size.

Supplemental analysis was performed by comparing quantitative and qualitative variables two-by-two using Mann-Whitney test and standardized difference (d), and chi-square test or Fisher exact test and Cramer's V coefficient (V), respectively. Specifically, data were compared between P1 and P5 or between the MRRC and the other MCs.

The French National Institute of Statistics (INSEE) provided demographic data of the regional residents (age and sex per year) from 1997 to 2015. We used the 2015 population as the standard reference to estimate standardized rates of new consultants per 100,000 inhabitants for the population, by direct standardization, in order to take into account the demographic change in the general population over time.

Statistical analysis was done at the two-tailed α level of 0.05. Data were analyzed using the SAS software package, release 9.4 (SAS Institute, Cary, NC).

2.3 | Ethics

The study protocol was considered as observational by the institutional review board of the Lille University Hospital. The database was declared to the Commission Nationale Informatique et Libertés (CNIL), the French committee responsible for protecting personal data. Privacy and confidentiality rules were respected.

3 | RESULTS

3.1 | Twenty-year trends in memory clinic referrals

From 1997 to 2016, a total of 93,617 new patients were referred to the MCs of our regional network. A 239% increase was observed from the first period P1 ($n = 7747$) to the last period P5 ($n = 26,258$) (Table 1). The increase of the rate of new consultants was confirmed after age and sex-standardization adjusted to the regional population (Figure 1A). In the meantime, the number of MCs rose from 12 in 1997 to 29 in 2016 (Figure 1B). No new MC was funded and labeled since 2015. In the MRRC, the number of new patients remained stable over time (Table 2).

More than half of the patients were referred by GPs and this proportion remained stable over time (56.1% in the first period vs 55.1%

in the last). Concomitantly, the proportion of patients referred by specialists increased by 9.7% over time, reaching 39.7% in the last period ($P < .0001$, $V = 0.09$). Very few patients were self-referred, and the proportion kept decreasing over time (from 13.9% in P1 to 3.9% in P5). In the first period, the majority (92.0%) of patients lived within a 50 km radius from the MC, and this proportion gradually increased over time (96.1% in the last period, $P < .0001$, $V = 0.06$). Detailed characteristics of patients from the whole network can be found in Table 1.

In the MRRC, a greater proportion of patients lived farther than 50 km from the clinic, and this proportion continued to increase over time (from 14.7% in P1 to 22.1% in P5, $P < .0001$, $V = 0.09$). Patients referred to the MRRC were more likely than patients from the MCs to be referred by a specialist (43.6% vs 39.7% in the last period, $P < .0001$, $V = 0.03$). Nevertheless, the proportion of MRRC patients referred by their GP increased over time (from 44.6% in P1 to 48.9% in P5, $P < .0001$, $V = 0.11$). The characteristics of MRRC patients are detailed in Table 2.

3.2 | Twenty-year trends in patient demographics at referral

The median age of the new patients increased from 72.0 years in P1 to 78.0 years in P5 ($P < .0001$, $r = 0.15$). In the whole network, the number of patients increased in all age categories. The highest increase from P1 to P5 was observed for the oldest patients (≥ 85 years), which increased by 14.7% (Figure 2A,B). In the MRRC, the increase was the highest in youngest categories, with a 3.0% raise in patients younger than 55 years of age, and a 7.8% increase for patients 55 to 64 years of age (Figure 2C,D).

Females accounted for almost two thirds of all patients and sex distribution remained stable over the different periods (from 63.1% female in P1 to 63.5% in P5, Table 1). In the MRRC, the proportion of female patients decreased gradually over time, reaching only 55.9% in the last period ($P < .0001$, $V = 0.04$; Table 2).

In all centers, the proportion of less-educated patients gradually increased with time, especially for illiterates (from 0.3% in P1 to 2.6% in P5, $P < .0001$, $V = 0.06$), at the expense of patients with secondary education. The proportion of patients with tertiary education remained stable in all centers (Table 1), whereas it increased over time in the MRRC (from 13.6% in P1 to 23.3% in P5; Table 2).

Patients living in nursing homes tended to be referred more to the MCs over time (from 7.5% in P1 to 8.7% in P5). Concomitantly, the proportion of patients living in private homes decreased over time (from 88.9% in P1 to 84.4% in P5). Among the latter, the proportion of patients living alone increased with time (from 28.2% in P1 to 33.6% in P5; $P < .0001$, $V = 0.05$).

3.3 | Twenty-year trends in referral delay

We observed a shortening of the referral delay (ie, the time from first symptom onset to the first consultation) over time. The referral delay

TABLE 1 Demographic and medical characteristics of patients recorded from 1997 to 2016 in all memory centers of the Nord-Pas-de-Calais Region

	P1 1997-2000	P2 2001-2004	P3 2005-2008	P4 2009-2012	P5 2013-2016	P	Effect size ^a
Total patient number per period	7747	12498	21994	25120	26258		
Patient number per year	1936.8	3124.5	5498.5	6280	6564.5		
Demographic characteristics							
Age, years; median (IQR)	72.0 (15.0)	74.0 (15.0)	76.0 (15.0)	77.0 (16.0)	78.0 (16.0)	<.0001	0.15
Age class; % (n)						<.0001	0.09
<55	14.7 (1138)	12.3 (1537)	9.8 (2159)	9.7 (2447)	8.1 (2126)		
≥55 and <65	12.4 (962)	11.4 (1433)	11.9 (2611)	12.1 (3055)	10.7 (2820)		
≥65 and <75	31.8 (2466)	27.7 (3458)	22.8 (5007)	19.3 (4844)	18.7 (4899)		
≥75 and <85	32.7 (2532)	39.2 (4896)	41.9 (9229)	40.0 (10037)	39.5 (10365)		
≥85	8.4 (649)	9.4 (1174)	13.6 (2988)	18.9 (4737)	23.0 (6048)		
Females; % (n)	63.1 (4889)	65.3 (8162)	65.8 (14474)	64.6 (16224)	63.5 (16671)	<.0001	0.02
Education level; % (n)						<.0001	0.06
Illiterate	0.3 (20)	0.7 (80)	2.1 (457)	4.4 (1064)	2.6 (648)		
Primary	74.8 (5508)	75.7 (9034)	77.6 (16556)	77.8 (18965)	77.0 (19133)		
Secondary	14.7 (1086)	14.3 (1704)	11.8 (2516)	8.7 (2123)	10.1 (2501)		
Tertiary	10.2 (748)	9.3 (1106)	8.5 (1819)	9.1 (2206)	10.3 (2571)		
Missing data; n	385	574	646	762	1405		
Dwelling place; % (n)						<0.0001	0.05
Private home with partner or family	60.6 (3676)	57.0 (5840)	55.2 (11401)	51.5 (12648)	50.8 (13286)		
Private home alone	28.2 (1712)	31.4 (3217)	32.0 (6593)	33.6 (8268)	33.3 (8699)		
Assisted living facility	2.5 (155)	3.0 (303)	3.1 (641)	2.2 (529)	2.1 (550)		
Nursing home	7.5 (452)	6.4 (662)	6.9 (1420)	9.4 (2308)	8.7 (2287)		
Others	1.2 (73)	2.2 (229)	2.8 (579)	3.3 (826)	5.1 (1342)		
Missing data; n	1679	2247	1360	541	94		
Referred by; % (n)						<.0001	0.10
GP	56.1 (4191)	59.5 (7294)	57.6 (12610)	53.6 (13479)	55.1 (14478)		
Specialist	30.0 (2242)	29.9 (3661)	36.8 (8043)	39.3 (9861)	39.7 (10421)		
Patient himself	13.9 (1040)	10.6 (1293)	5.6 (1228)	4.7 (1178)	3.9 (1013)		
Other	0.0 (1)	0 (0)	0.0 (7)	2.4 (601)	1.3 (345)		
Missing data; n	273	250	106	1	1		
Distance to memory center; % (n)						<0.0001	0.06
<50 km	92.0 (6893)	94.6 (11391)	96.4 (20095)	96.2 (24160)	96.1 (25245)		
≥50 km	8.0 (601)	5.4 (652)	3.6 (758)	3.8 (960)	3.9 (1013)		
Missing data; n	253	455	1141	0	0		
MMSE							
Numeric; median (IQR)	24.0 (10.0)	24.0 (9.0)	24.0 (8.0)	23.0 (9.0)	23.0 (9.0)	<.0001	-0.05
Class; % (n)							
<10	4.9 (322)	3.7 (380)	3.8 (693)	4.5 (934)	3.8 (845)	<.0001	0.03
≥10 and <20	24.3 (1596)	23.4 (2420)	23.7 (4378)	24.7 (5157)	25.9 (5721)		
≥20 and <27	35.9 (2353)	38.5 (3986)	40.3 (7424)	41.2 (8603)	42.4 (9381)		
≥27	34.9 (2288)	34.4 (3563)	32.2 (5936)	29.6 (6193)	27.9 (6173)		
Missing data; n	1188	2149	3563	4233	4138		

(Continues)

TABLE 1 (Continued)

	P1 1997-2000	P2 2001-2004	P3 2005-2008	P4 2009-2012	P5 2013-2016	P [*]	Effect size ^a
Delay to first visit (d); median (IQR)	835.0 (1137.5)	783.0 (1077)	738.0 (879)	565.0 (803)	644.0 (800.5)	<.0001	-0.10
Missing data; n	1215	2610	4576	8219	7778		

Note: Data provided are percentages (frequencies) or median (interquartile range) excluding missing data unless specified. Primary: ≤ 6 years of education); secondary: ≤ 12 years or tertiary education: college.

Abbreviations: GP, general physician; IQR, interquartile range, MMSE, Mini Mental State Examination.

^aSpearman correlation coefficient or Cramer's V.

^{*}P values are calculated with chi-square test for categorical variables or Spearman correlation test for numerical variables.

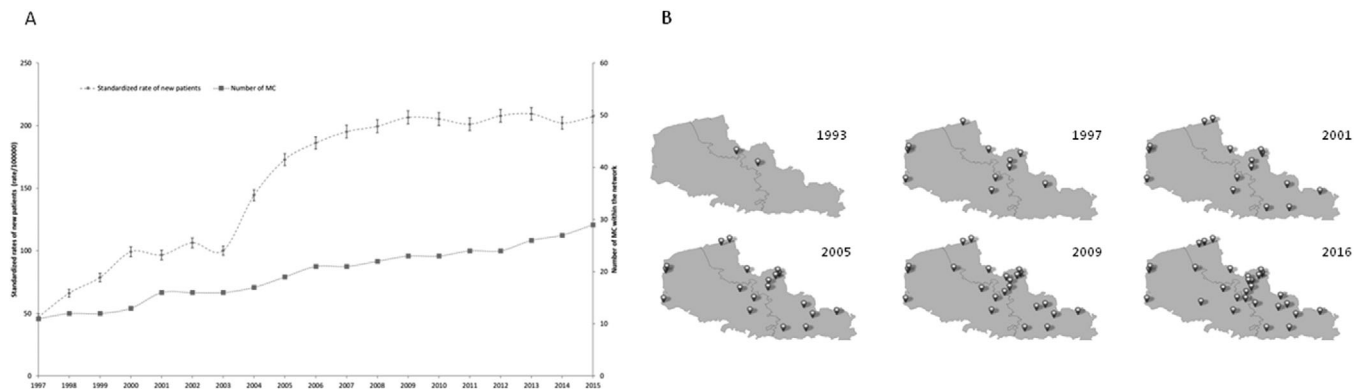


FIGURE 1 (A) Evolution over years of standardized rates of new patients for 100,000 residents in Nord Pas-de-Calais by age and sex, according to INSEE (French National Institute of Statistics). Left vertical axis values: standardized rates. Right vertical axis values: number of Memory clinic. Horizontal axis values: years. (B) Memory clinic distribution in the Nord Pas-de-Calais region across time

was 6.37 months shorter in the last period as compared to the first (644 days in P5 vs 835 days in P1, $P < .0001$, $d = 0.26$). Although the referral delay increased from the penultimate to the last period, referral delay was significant correlated with time ($P < .0001$, $r = -0.10$).

The referral delay decreased for all age categories, in particular for the oldest patients. Patients ≥ 85 years consulted 15.5 months earlier in the last period as compared to the first one (from a median 1108 days in P1 to 643 in P5; Figure 3A). Overall, there was a shortening of the referral delay independently of the level of education, which appeared to be more pronounced for less educated patients (illiterates and primary school level; Figure 3B).

The same shortening of the referral delay over time was observed for MRRC patients. The referral delay was 6.57 months shorter in the last period as compared to the first (787 days in P5 vs 984 days in P1, $P < .0001$, $d = 0.1502$), and there was a significant correlation with time ($P < .0001$, $r = -0.06$; Table 2).

3.4 | Twenty-year trends in clinical profiles

The median MMSE score was stable over time (Table 1). However, the proportion of patients at a mild (MMSE 20 to 26) stage gradually

increased (from 35.9% in P1 to 42.4% in P5, $P < .0001$, $V = 0.03$) at the expense of patients at severe (MMSE < 10) and very mild (MMSE 27-30) stages (Table 1). Accordingly, the proportion of MCI patients gradually increased over time (from 18.6% in P1 to 35.6% in P5; $P < .0001$, $V = 0.07$) at the expense of demented patients (from 67.5% in P1 to 52.5% in P5; Table 3). The proportion of MCI patients was the highest in the MMRC, and it continued to increase over time (from 21.7% in P1 to 45.1% in P5, $P < .0001$, $V = 0.11$; Table 3).

When looking into age subgroups, the oldest (75 to 84 years and ≥ 85 years) patients showed a 1-point increase in the median MMSE score at referral from P1 to P5, whereas the MMSE score was decreasing or stable in the younger age categories (Figure 4A). When classified according to education, the median MMSE score decreased mildly from the first to the last period for less-educated patients, from 21 to 15 for illiterate patients, and from 23 to 22 for patients with primary education level (Figure 4B).

Distribution of the first clinical diagnoses did not change much over time (Table 3). Noticeably, there was a gradual decrease in the proportion of AD in all centers (from 49.4% in P1 to 37.1% in P5, $P < .0001$, $V = 0.07$), particularly in the MRRC (from 41.3% in P1 to 19.7% in P5, $P < .0001$, $V = 0.11$). The diagnostic distribution was significantly different in the MMRC compared to the remaining MCs. There was

TABLE 2 Demographic and medical characteristics of patients recorded from 1997 to 2016 in the MRRC

	P1 1997-2000	P2 2001-2004	P3 2005-2008	P4 2009-2012	P5 2013-2016	P	Effect size ^a
Total patient number per period	3563	3608	3435	3657	3661		
Patient number per year	890.8	902	858.8	914.3	915.3		
<i>Demographic characteristics</i>							
Age, years; median (IQR)	70.0 (17.0)	70.0 (20.0)	69.0 (20.0)	67.0 (21.0)	66.0 (21.0)	<0.0001	-0.05
Age class; % (n)						<.0001	0.05
<55	19.8 (704)	19.7 (711)	20.3 (698)	22.8 (834)	22.8 (835)		
≥55 and <65	15.5 (552)	16.9 (609)	20.3 (695)	21.2 (776)	23.3 (851)		
≥65 and <75	31.5 (1123)	28.5 (1027)	25.0 (859)	24.2 (884)	23.6 (865)		
≥75 and <85	26.8 (955)	29.3 (1058)	29.0 (997)	24.8 (909)	22.7 (832)		
≥85	6.4 (229)	5.6 (203)	5.4 (186)	7.0 (254)	7.6 (278)		
Females; % (n)	60.9 (2169)	60.5 (2184)	59.4 (2041)	58.5 (2139)	55.9 (2047)	<.0001	0.04
Education level; % (n)						<.0001	0.07
Illiterate	0.5 (18)	1.3 (42)	2.2 (71)	2.6 (93)	2.6 (92)		
Primary	69.7 (2303)	69.3 (2299)	68.6 (2240)	61.6 (2178)	57.8 (2035)		
Secondary	16.1 (532)	15.4 (512)	12.8 (418)	15.1 (535)	16.4 (577)		
Tertiary	13.6 (450)	14.0 (465)	16.4 (535)	20.6 (729)	23.3 (820)		
Missing data; n	260	290	171	122	137		
Dwelling place; % (n)						<.0001	0.07
Private home with partner or family	62.8 (1746)	60.5 (1697)	64.0 (1727)	66.4 (2133)	66.9 (2407)		
Private home alone	25.1 (698)	28.0 (786)	26.4 (712)	24.2 (777)	23.3 (838)		
Assisted living facility	2.3 (64)	2.5 (71)	2.0 (54)	1.4 (47)	1.0 (38)		
Nursing home	7.7 (212)	3.7 (102)	3.5 (94)	3.0 (95)	2.7 (97)		
Others	2.1 (59)	5.3 (148)	4.1 (112)	5.0 (161)	6.1 (219)		
Missing data; n	784	804	736	444	62		
Referred by; % (n)						<0.0001	0.11
GP	44.6 (1511)	48.8 (1729)	48.2 (1646)	49.9 (1825)	48.8 (1788)		
Specialist	34.9 (1182)	33.5 (118)	41.6 (1421)	42.9 (1569)	43.6 (1597)		
Patient himself	20.5 (693)	17.7 (629)	10.1 (347)	6.9 (252)	6.9 (251)		
Other	0.0 (1)	0 (0)	0.1 (3)	0.3 (11)	0.7 (25)		
Missing data; n	176	62	18	0	0		
Distance to memory center; % (n)						<.0001	0.09
<50 km	85.3 (2829)	85.6 (2890)	84.4 (2848)	79.0 (2889)	77.9 (2853)		
≥50 km	14.7 (487)	14.4 (486)	15.6 (525)	21.0 (768)	22.1 (808)		
Missing data; n	247	232	62	0	0		
<i>MMSE</i>							
Numeric; median (IQR)	25.0 (9)	26.0 (7)	26.0 (6)	25.0 (7)	25.0 (7)	<.0001	0.03
Class; % (n)							
<10	5.1 (156)	2.8 (84)	2.7 (79)	3.1 (94)	3.2 (103)	<.0001	0.05
≥10 and <20	22.2 (688)	17.6 (534)	14.0 (408)	17.0 (524)	17.1 (559)		
≥20 and <27	34.1 (1055)	36.2 (1097)	39.9 (1164)	39.8 (1225)	36.5 (1189)		
≥27	38.6 (1192)	43.4 (1315)	43.4 (1266)	40.1 (1236)	43.2 (1410)		
Missing data; n	472	578	518	578	400		

(Continues)

TABLE 2 (Continued)

	P1 1997-2000	P2 2001-2004	P3 2005-2008	P4 2009-2012	P5 2013-2016	P ^a	Effect size ^b
Delay to first visit (d); median (IQR)	984 (1285)	881 (1169.5)	823 (1221)	786 (1135)	787 (1043)	<.0001	-0.06
Missing data; n	486	700	475	436	594		

Note: Data provided are percentages (frequencies) or median (interquartile range) excluding missing data unless specified. Primary: ≤ 6 years of education); secondary: ≤ 12 years or tertiary education: college.

Abbreviations: GP, general physician; IQR, interquartile range; MMSE, Mini Mental State Examination; MRRC, Memory Resource and Research Center.

^aSpearman correlation coefficient or Cramer's V.

^bP values are calculated with chi-square test for categorical variables or Spearman correlation test for numerical variables.

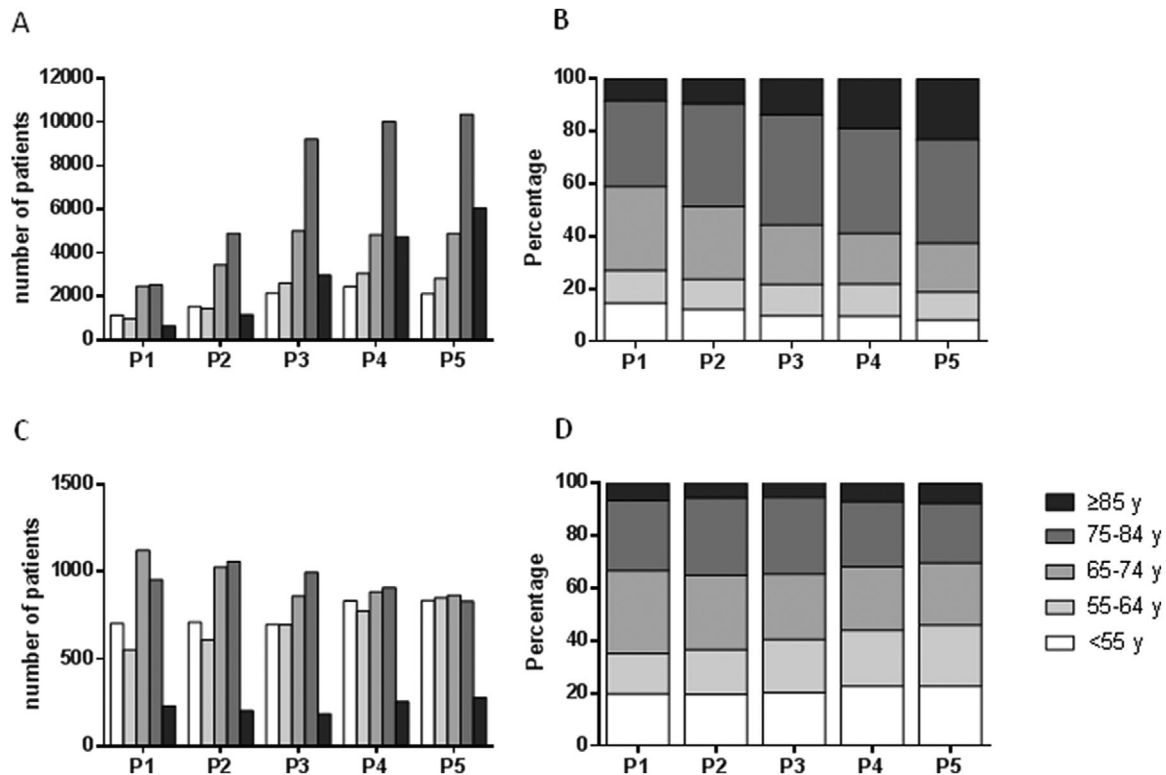


FIGURE 2 New patients according to age categories over the different periods. New patients in all centers: absolute (A) and relative (B) figures. New patients in the Memory Resource and Research Centre (MRRC): absolute (C) and relative (D) figures. P1: from 1997 to 2000, P2: from 2001 to 2004, P3: from 2005 to 2008, P4: from 2009 to 2012, and P5: from 2013 to 2016

a higher proportion of FTL in the MRRC (3.5% vs 0.9%, $P < .0001$, $V = 0.08$), which represented the third cause of dementia in the MRRC and the fourth in the whole network, where the third cause was LBD (Figure 5).

4 | DISCUSSION

This study analyzed the 20-year trends in referral following the creation and spreading of an MC network in a region of 4-million inhabitants. The development of the network was associated with: (1) an increased referral of vulnerable patients; (2) a shortening of the

referral delay (time from symptom onset to first consultation), especially in older patients; (3) an increased referral at an early stage; and (4) an increased differentiation of the patients referred to the tertiary referral center (MRRC), demonstrating a better use of resources.

Population-wide studies on MC networks are scarce, most of which being cross-sectional. They show a generalization of the MC model for dementia diagnosis and care in the Western world (Europe, Australia, New Zealand, etc).³⁰⁻³⁴ Heterogeneity of practices and organizations within countries is often underscored,^{32,34-36} reflecting the lack of national standards defining memory clinics.³⁷ Depending on the country or settings, MCs have variable access to neuropsychological assessment,³⁵ which is not harmonized.³⁸ Quality indicators for MCs

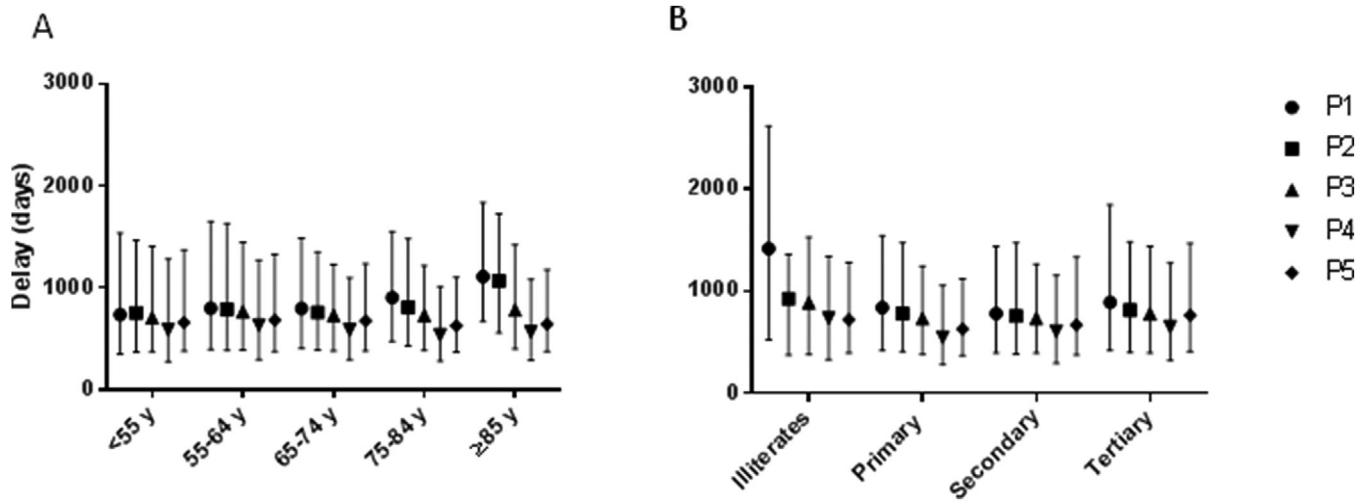


FIGURE 3 (A) Evolution of delay from first symptoms to first visit in a memory clinic over periods according to age categories. (B) Evolution of delay from first symptoms to first visit in a memory clinic over periods according to educational level. P1: from 1997 to 2000, P2: from 2001 to 2004, P3: from 2005 to 2008, P4: from 2009 to 2012, and P5: from 2013 to 2016

had been suggested to increase homogeneity of care.^{39,40} In this study, we showed the impact of the creation and spreading of a regional MC network with a defined organization¹⁴ in the course of 20 years. We reached a considerable number of new patients per year, equivalent to the numbers of nationwide MC networks.^{41,42}

Few studies have analyzed the impact of MCs. An Australian study evaluated the impact of MCs on the caregiver burden over 1 year.⁴³ A Canadian survey in Ontario showed that the development of primary care-based proximity MCs facilitated diagnosis and management of dementia in remote areas.⁴⁴ Because of their positive impact, the number of MCs was raised to 100 in a follow-up report.⁴⁵ However, the evolution of the characteristics of MC patients over time is rarely analyzed. Whether and how MCs organized into a network to harmonize care for patients according to their profile (typical or atypical dementia, late or young-onset dementia, appropriate management, or vulnerable patients) has seldom been described.

One of the most noticeable results of our study is the increased and faster referral of vulnerable patients throughout the development of our MC network. As the distance to MCs shortened due to a better territory coverage, the establishment of proximity MCs was associated with increased referral of older patients, patients with a lower level of education and patients living alone or in nursing homes. In our region, illiterate patients or patients with a very low level of education are mostly immigrants or older individuals who were raised during the Second World War. Access to MC and cognitive assessment is a challenge in such populations.⁴⁶ Likewise, the setup of proximity MCs was shown to increase the referral of older patients in Ontario.^{44,45} Such organizations combining proximity care and accessibility to specialists when necessary are needed to improve timely care and equitable access for all patients.

Although older, our study showed that patients came at an increasingly earlier stage, with the greatest proportion of MCI patients in the last period. This observation suggests a delay in the onset of cogni-

tive decline, which could be due to better education and better control of vascular risk factors.^{47,48} The Alzheimer's COoperative Valuation in Europe (ALCOVE) recommendations state that citizens should have access to an accurate diagnosis at a time when it can be of most benefit to them.⁴ This implies the early referral of patients to discard curable causes and engage in the diagnostic process when appropriate. A recent survey in The Netherlands showed that half of patients at first referral were at the MCI stage in 2016, whereas most were at the dementia stage in 1998.⁴² Although efforts should be pursued to encourage earlier referral, our organization also contributed to facilitate the early detection of cognitive difficulties. Our study and others will contribute to understanding the factors associated with late referral and allow improving our practice. Nurses are being trained in dementia care are being formed currently in France and should improve the screening of cognitive disorders in primary care.

The diagnosis distribution in all centers in our study was in line with that of previously published registries. In particular, the proportion of AD and VaD patients were quite similar in the Swedish National dementia registry (Sweden).⁴¹ Of interest, the longitudinal design of our study showed that our organization contributed to an increasingly specific referral of rare dementias to the MRRC, that strengthened its position as a tertiary referral center for proximity MCs. Accordingly, the proportion of patients with FTLD or AD-related disorders increased in the MRRC over 20 years, as well as the proportion of younger patients. Because female preponderance is more pronounced in AD, the increase in related disorders certainly contributed to the diminishing proportion of female patients in the MRRC over time. Similarly, in Dutch University-based MCs, patients were younger on average than in non-academic MCs (35% vs 18% were <65).⁴² Clinical research and clinical trials in particular were a strong incentive as well to refer rare and young-onset dementia cases as well as patients at prodromal or mild dementia stages to the MRRC. The inclusion criteria of the ongoing studies were advertised throughout the network, and MCs

TABLE 3 Diagnostics of patients recorded from 1997 to 2016 in all MCs (up) and in the MRRC (tertiary memory center)

In all MCs							
	P1	P2	P3	P4	P5		
	1997-2000	2001-2004	2005-2008	2009-2012	2013-2016	P	Cramer's V
						<.0001	0.07
MCI: % (n)	18.6 (1377)	23.7 (2789)	31.7 (6775)	33.3 (8239)	35.6 (9228)		
<i>Diagnosis; % (n)</i>							
AD	49.5 (3660)	47.0 (5528)	40.3 (8596)	34.9 (8610)	37.1 (9612)		
FTLD	3.4 (251)	2.1 (241)	1.2 (248)	0.9 (229)	1.1 (300)		
LBD	3.2 (237)	3.7 (436)	4.1 (886)	3.2 (796)	2.9 (746)		
VaD	11.5 (849)	10.8 (1271)	10.2 (2186)	13.9 (3428)	11.4 (2948)		
Psy	10.1 (751)	8.7 (1024)	8.6 (1831)	9.0 (2228)	8.4 (2185)		
ARD	1.3 (97)	1.5 (177)	1.6 (338)	2.2 (544)	2.0 (517)		
Others	2.4 (181)	2.5 (293)	2.3 (482)	2.6 (642)	1.5 (398)		
Missing data; n	344	739	652	404	324		
In MRRC							
	P1	P2	P3	P4	P5		
	1997-2000	2001-2004	2005-2008	2009-2012	2013-2016	P	Cramer's V
						<.0001	0.11
MCI: % (n)	21.7(728)	28.8 (930)	33.6 (1027)	39.1 (1330)	45.1 (1589)		
<i>Diagnosis; % (n)</i>							
AD	41.3 (1384)	33.9 (1093)	26.4 (807)	23.4 (794)	19.7 (692)		
FTLD	4.3 (143)	3.7 (121)	2.9 (88)	2.6 (89)	3.8 (133)		
LBD	3.9 (131)	4.5 (147)	4.0 (121)	2.8 (96)	2.3 (82)		
VaD	13.6 (455)	11.0 (355)	13.0 (396)	11.1 (377)	10.7 (377)		
Psy	10.4 (349)	12.2 (393)	12.4 (379)	13.5 (460)	12.7 (447)		
ARD	1.3 (45)	2.0 (64)	2.1 (64)	2.8 (94)	2.7 (96)		
Others	3.5 (117)	3.9 (126)	5.6 (171)	4.7 (161)	3.0 (106)		
Missing data; n	211	379	382	256	139		

Abbreviations: AD, Alzheimer's dementia; ARD, alcohol-related disorders; FTLD, frontotemporal lobar degeneration; LBD, Lewy body dementia; MC, memory clinics; MCI, mild cognitive impairment; MRRC, Memory Resource and Research Center; Psy, psychiatric disorders; VaD, vascular dementia.

began to participate in clinical studies and trials under the supervision of the MRRC,⁴⁹ in order to encourage participation to research and thus third referral.

The main strength of this study is its reliance on longitudinal data collected in the course of 20 years in a regional prospective multicenter registry, which was developed as MCs were established. From the start, MCs in our network used the same procedures and diagnostic workup, and data were recorded and checked by a data manager. Hence our data also reflects the evolution of medical practices following the creation of MCs in a region-wide setup. We did not find in the literature any such example of a population-wide study assessing the impact of health policies for dementia management.

Missing data, which may affect the reliability of the results, represent the main limitation of our survey. Missing data reflect the difficulties of to supplement databases in real-life clinical settings. Most missing data concerned the first MMSE score and the delay to first refer-

ral. However, the rate of missing data was quite homogeneous among centers. The other limitation is the descriptive nature of the study, which forbids determining a causal relationship between the trends we observed and the development of the MC network. Other factors may have intervened to explain earlier and broader referral, such as public awareness of dementia diagnosis and care, or cultural changes in the elderly population in the time span of the study.

In conclusion, our study showed the benefits of a region-wide MC network. Our results may contribute to guide health policy for dementia care. According to another WHO report on dementia, a public health approach is essential "to improve the care of patients with dementia and to give equitable access to resources for all members of society, including raising awareness, timely diagnosis, commitment to good quality continuing care and services, caregiver support, workforce training prevention and research."⁵⁰ Our study supported that a network organization allows reaching some of these objectives and favors harmonization of

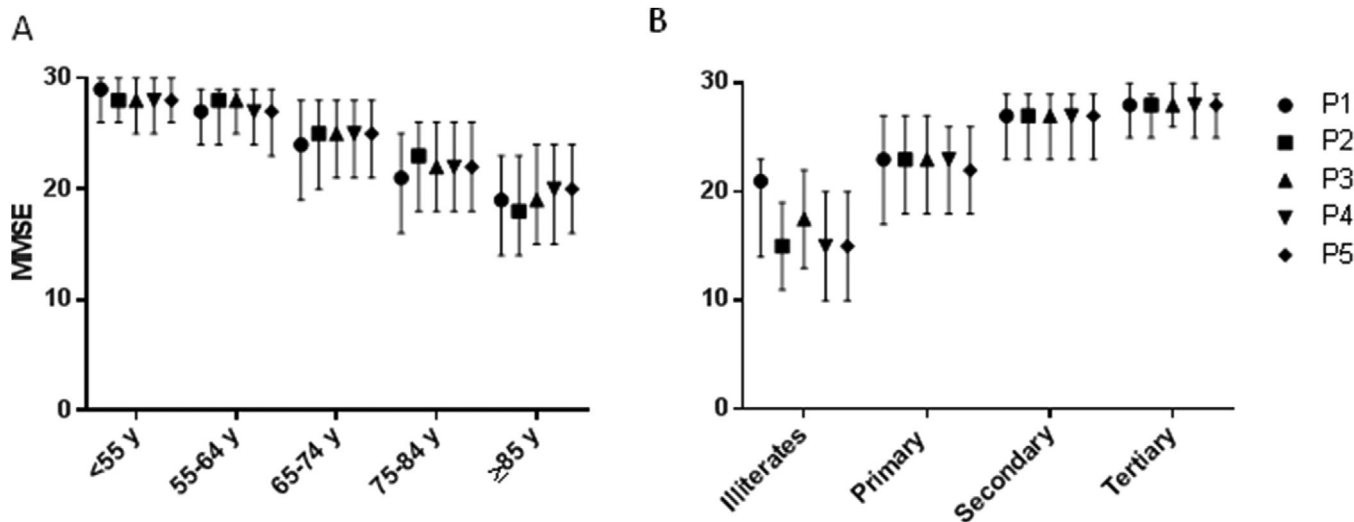


FIGURE 4 (A) MMSE score at referral according to age categories. (B) MMSE score at referral according to educational level

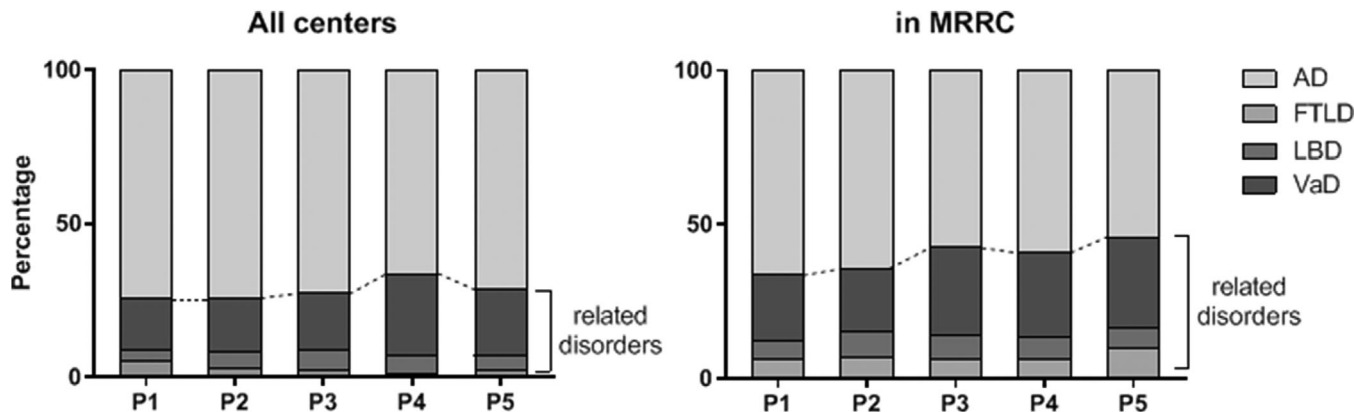


FIGURE 5 Diagnostic distribution among patients with Alzheimer's disease (AD) with or without vascular lesions, LBD (Lewy body dementia), FTLD (frontotemporal lobar degeneration), and VaD (vascular dementia). (A) distribution in all centers; (B) distribution in MRRC

care across MCs. However, continuing efforts are needed to target the vulnerable population and prompt referral at an earlier stage, to plan some secondary protective measures, and to prepare the venue of future disease-modifying and efficient preventive strategies. Increasing public awareness and understanding the social and medical factors that contribute to delay of first referral will be keys to improve our practice.

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CONFLICT OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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APPENDIX A

The MEOTIS network. Dr Abied Rachid, Dr Adnet Catherine, Barois Arnaud, Baude Stéphanie, Dr Berriot Véronique, Dr Boyer Gloria, Dr Brique Didier, Dr Calais Gauthier, Dr Chekroud Hacène, Dr Cliche Joël, Dr Dachy Valérie, Debock Valérie, Dr Deprez Anne, Dr Dereeper Olivier, Dr Devos Philippe, Dr Elazouzi Abdelghani, Dr Enderle Adeline, Dr Fanjaud Nicolas, Dr Forzy Pierre, Dr Gallouj Karim, Dr Garcon Karine, Dr Honore Marie, Dr Huvent Dominique, Dr Idiri Houria, Ladeiro Annabelle, Dr Lavenu Isabelle, Dr Le Coz Patrick, Dr Leclercq Eugénie, Dr Lefebvre Denis, Dr Maciejasz Pierre, Dr Messin Rémi, Dr Petit Valérie, Plichon Christine, Ponthieu Sandrine, Dr Quievre Cécile, Dr Roche Jean, Dr Rosolacci Thierry, Dr Senechal Olivier, Dr Taillez Nathalie, Dr Tison Frédéric, Tollot Sarah, Dr Trocmet Marie, Verpoort Charlotte.