



French organization of care for patients with Young Onset Dementia to meet their specific needs

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Disclosures

- Participation in many pharmaceutical trials and academic studies in dementia
- Occasional participation in scientific advisory boards
- No specific disclosure for the present communication

Introduction

- **Early or Young Onset dementia** = usually **onset before 65**.
 - For some authors “**Early Onset**” means **diagnosed** before 65
 - Early dementia ≠ early onset dementia
 - “**Young Onset**” sometimes means < **60** or even **45**

Prevalence and incidence doubles every 5 years from 35 years

Numbers depend on settings and data collection, size of the studied population; inclusion/exclusion of causes (alcohol, stroke, TBI, HD, psychosis, mental disabilities, AIDS, MS ...), age < 65 years at **onset**, at **diagnosis** or at **entry**

Woodburn & Johnstone, Health Bull (Edinb) 1999,
Kelley et al Arch Neurol 2008; Harvey et al JNNP 2003

Epidemiology

- **Prevalence of YOD : 50-80 [CI95: 39-98] per 100,000 inhab. < 65 y. Incidence : 10-15 new cases per 100,000 inhab. /y;**
As many men as women
- **Extrapolation of number of YOD patients in UK** for a population of 59 millions inhabitants: **18,319** [CI 95%: 15,296 – 21,758]

| | |
|-------------------------|--|
| Alzheimer's disease | 6,000 [4,254-7,989] 550 new cases/y |
| Vascular dementia | 3,000 [1,832-4,526] |
| Frontotemporal dementia | 2,500 [1,502-4,008] 460 new cases/y |
| Alcoholic dementia | 2,200 [1,290-3,654] |

Mercy et al Neurology 2008; Ikejima et al, Stroke 2009;
Ratnavalli et al, Neurology 2012; Harvey et al, JNNP 2003;
Vieira et al, Clin Pract Epidemiol Ment Health 2013; Sanchez-Abraham et al, Neurologia 2014
Lambert et al, Eur J Neurol 2014; Ikejima et al, Psychiatr Clin Neurosci 2014

Progression and survival of patients with YOD

- Shorter survival in some old studies
- Actually **more rapid decline** in young than in old demented patients although no difference in MMSE score at first visit (because of delayed diagnosis and cognitive reserve?) **but longer survival.**
- Longer survival (except for genetic cases) **but higher impact of the disease on mortality in young patients**

Koedam et al, Dement Geriatr Cog Disord 2008; Van der Vlies Psychol Med 2009;
Rountree et al, Alz Res Ther 2012, Go et al, Dement Geriatr Cogn Disord 2013

Distinctive features of YOD

Delay in establishing a proper diagnosis

- Time between 1st symptoms and diagnosis 5 years versus 3 years (personal data)
- Illness often considered by the general public –and many professionals - as a disease of the elderly
- Many differential diagnosis
- Atypical features
 - difficult diagnosis → expertise mandatory

A number of different causes of dementia

- **Degenerative** : **AD, FTLD**, DLB (including Parkinson), Huntington's disease...
- **Vascular** (including genetic like CADASIL)
- Autoimmune or inflammatory (MS...)
- Traumatic
- Toxic (alcohol)
- Infectious (including AIDS)
- Metabolic (including inborn errors of metabolism)
- Other

Harvey et al, JNNP 2003; Panegyre & Frencham, Am J Alz Dis Other Dement 2007; Shinagawa et al, Dement Geriatr Cogn Disord 2007; Fujihara et al, Arq Neuropsiquiatr 2004; McMurtry et al, Int J Geriatr Psychiatry 2006; Kelley et al., Arch Neurol 2008

Diagnostic distribution in the Memory clinics

Nord – Pas-de-Calais 2013 (4 millions inhabitants)

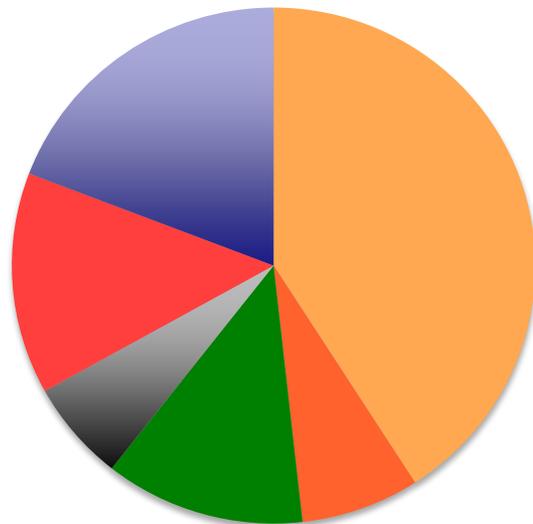
New patients with onset before 65 y = 1756 out of 6497 (27%)

Higher proportion of related/associated disorders
in young patients

New patients < 65 y

With dementia n=396 (23%)

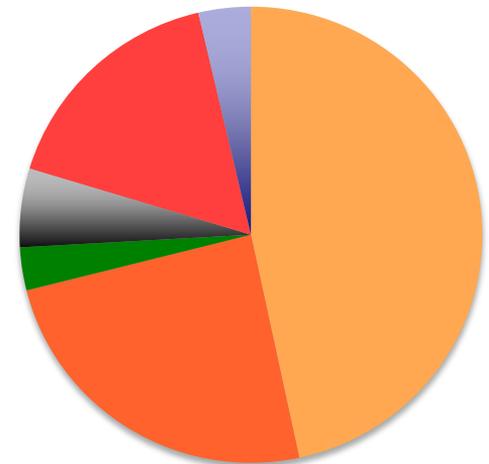
11% of all dementias



- Alzheimer
- Alzheimer+ Vascular
- FTLD
- DLB
- Vascular dementia
- Other dementia

All new patients

With dementia n=3443 (53%)



Importance of psychiatric symptoms

- Frequent history of depression
- Apathy, Delusion, hallucinations, aggression
- **Frontal lobe syndrome** (FTLD and some EOAD)
- In addition to atypical age, and awareness of cognitive problems
 - Psychiatric misdiagnoses (depression +++ and psychosis) → diagnostic delay if no denial

Harvey et al., 1998 www.dementia.ion.ac.uk; Alzheimer's Australia report 2007; Garre-Olmo et al, Neurology 2010; van Vliet et al, Dement Geriatr Cogn Disord 2012

Atypical clinical features in YO-AD:

- **Predominant instrumental cognitive deficits** : visuospatial functions, language, praxis... disconcerting if amnesia does not seem severely impaired
- **Focal atrophies** (Primary Progressive Aphasia, Posterior Cortical Atrophy...) Rarer with ApoE4
- **Less anosognosia**
- **Genetic forms** of AD (10% vs 2%), with possible neurological symptoms e.g. spastic paraparesia, Lobar haemorrhages, extra-pyramidal symptoms
 - contribute to misleading

Imamura et al, Neuropsychologia 1998;
Rossor MN et al, Lancet Neurology 2010;9: 793-806;
van der Flier et al, Lancet Neurol 2011
Mendez et al, Am J Alz Dis & Other Dement 2012

Imaging

Structural imaging :

Global atrophy may be severe, but **hippocampal atrophy may be relatively less severe in young patients** compared to older patients (should not exclude the diagnosis of AD)

However : Molecular Imaging

- **FDG-PET and HmPA0- SPECT** : differences according to age : more diffuse and severe hypometabolism in YOD, especially in posterior regions, posterior cingulate
- **PIB-PET** : no difference according to age or higher PIB retention, similar burden in posterior cortical atrophy and diffuse Alzheimer's disease

Cerebrospinal Fluid (CSF)

- **No difference according to age :**
 - ↳ $A\beta$ Total, ↗ Tau and Phospho-Tau
even more discriminant in young patients
 - No difference according to clinical features :
instrumental predominance and focal atrophy or
amnesic and spread
- Young patients should be referred to tertiary centres

Bouwman et al, Neurobiol Aging 2009; Dumurgier et al, Neurobiol Dis 2013;
Van de Flier et al, Lancet Neurol 2011; Moore et al, Can Fam Physician 2014

Medico-social characteristics of YOD

Caregivers of Young patients

- Observation:

- Stunned by an unexpected diagnosis, often denied
- « Sandwich generation »: caregivers sometimes responsible not only for their ill-spouse but also for their children, and their parents (or parents in law).
- Often suffer from health problems
- Exhausted, depressive, often under antidepressants and/or hypnotics
- Have few respite
- Anxious about heredity of the disease and end of life

Caregivers of Young patients

- **Main complaints:**
 - **Behavioural changes** : excessive spending, addiction, impulsivity, apathy → professional, financial, social difficulties, dangerous driving, sometimes violence against spouse or children.
 - **Difficult communication.**
- **Expressed needs :**
 - **Early recognition and referral**
 - **Dedicated** day-care, temporary respite care or long term care facilities, and **financial support.**

Thomas et al, Int J Geriatr Psychiatr 2005; Arail et al Int J Geriatr Psy 2007
Alzheimer's Australia report 2007; Bakker et al, Am J Alz Dis & Other Dement 2010
Aramari et al AmJAlzDis & OtherDement 2012

- **Two** measures of the French Alzheimer plan 2008-2012 dedicated to YOD (<60)
 - **Measure 19**: Setting a reference center for YOD
 - **Measure 18**: Accommodations for YOD

Measure 19: **Multisite Reference Centre**

Call for proposal, independent international committee

- **Complementarities**
 - **LILLE-BAILLEUL**: Coordinator
Clinic, Management, Biology (CSF, plasma): ePLM network
 - **ROUEN** : Genetics of monogenic forms of AD: AD network
 - National coordinator for DIAN
 - **PARIS-SALPETRIERE**: Imaging, rare dementias, and national FTD network
- **Linked with the 26 Memory Resources and Research Centres** (follow-up of patients both by MRRCs and GP \pm local specialists)



AIMS: care, management / public health, research, int. collaborat.

I - CARE

- **Raising awareness in professionals & general public**
 - Conferences, media, communications, reviews...
 - www.centre-alzheimer-jeunes.fr, <http://www.alzheimer-genetique.fr>
- **Improvement of diagnosis and genetic testing**
 - Identification of a **referent specialist** (neurologist) for YOD in each MRRC (n=26)
 - Continuous training, educational publications, ethics meetings (EREMA = Ethics in AD)
 - **Implementation of procedures in genetics** → 150 AD families and FTD families → DIAN GENFI, new mutations
 - In **CSF** sampling, in **imaging**
 - And in **neuropathology** AD-PATH



II - Management

- **Identification of a referent** in each MRRC, social worker, psychologist, or nurse
- **Training of professionals (with France Alzheimer)**
Publications for professionals, www.centre-alzheimer-jeunes.fr,
<http://www.alzheimer-genetique.fr>
- **Support for caregivers**
 - Support groups, thematic day cares, specific programs, Week-ends for YOD patients and caregivers (UTB foundation), Web site, Brochure on YOD, Photographic work to de-stigmatize YOD and point out the specificity of different causes of dementia: “I still exist”,
- **Procedures:** Mobiqual, Parcours, Long Visit (for GPs), Welcome in facilities
- **Measure 18:** Accommodations and facilities for YOD

II - Management

• Measure 18: Accommodations for YOD

- To evaluate quantitative and qualitative needs – if specificities have been detected for accommodations for young patients (< 60 years)
To synthesize propositions

Course of actions :

- **Epidemiological context**
- **National survey:** questionnaire sent to all collective accommodations possibly receiving individuals with YOD (including nursing home for people aged > 60 allowing special dispensation for younger patients) and psychiatric yards (n > 10,000)
 - Out of 2,400 young patients (<60 y) living in collective accommodations at that time, 220 suffered from ADAD

AIMS : II - Management

- **Accommodations for YOD: Course of actions**
 - **Documentary** filmed in places spotted by the survey as having an experiment in managing patient with YOD (support for raising awareness, discussion and training)
 - **Questioning:** Does the number of beds occupied by YOD patients meet the needs? Difficulties to enter such services? Inadequate offer?
 - Questionnaires analyses, visits and meetings on site (nurses, directors and practitioners), survey of services allowing dispensations, longitudinal survey of 110 YOD patients /caregivers
 - 2-day seminar with professionals experimented in caring YOD
 - 1 day meeting with YOD patients able to express their needs in public and who wished to be “actors of their life”
 - Literature analysis, other countries experience
- Synthesis of the needs for YOD patients presented at a national meeting



Accommodations for YOD

- **Observations and synthesis of the needs**
 - YOD specificities disconcert and worry relatives as well as professionals
 - YOD patients are scarce and dispersed in nursing homes
 - Difficult relationship between the young patient(s) and the staff (distress, painful projection). **Need for training and support +++**
 - Before 60 y: very few patients, many with frontal lobe syndrome or severe behavioural disorders

Accommodations for YOD

• Observations and synthesis of the needs

- 3 situations needing an entry in a collective setting:
 - 1) Loss of autonomy (socially isolated or wish to protect the family) ; New needs, a lot of expectations
 - 2) “Behavioural crisis” whatever the cause (depression, delirium, inappropriate behaviour/ exhaustion of the family, social issues...) need for medical and social services, revised care plan
 - 3) Long term accommodation for severe behavioural troubles or somatic problems (difficulties with swallowing...), and too many interventions impossible at home
- Many services already appropriate, however age was often the cause of supplementary distress
- Limitations: focused on Alzheimer’s disease and related disorders
- Specific situation of patients with mental retardation i.e. Down syndrome



Accommodations for YOD

• Orientations

- Help and support for life at home
- Conciliate specialisation and proximity
- Remove barriers at entry in close existing facilities willing to welcome a young patient
- Spread care practices to all teams facing this unusual situation : role for the reference centre: running an expert network of duos (doctor + nurse) and social workers
- A few specific accommodations for a small number of very specific patients (resource centre as well as place for training professionals from other teams) – + a few experimentations
- Identification of facilities welcoming YOD patients: a list is available on www.centre-alzheimer-jeunes.fr and regularly updated
- Participative training meetings, sharing of practices, regional and national once a year (project of an internet forum)

Accommodations for YOD

- **5 points to be given priority in nursing homes that welcome young patients:**
 - Need for a precise diagnosis (collaboration with tertiary memory clinics)
 - How to accompany a young patient with a frontal lobe syndrome?
 - Activities to be offered to young patients in a nursing home
 - Support to families and relatives of young patients in nursing homes
 - End of life of young patients in nursing homes



III - Research

- **Cohorts : COMAJ** (n= 270)
 - and G-MAJ, Parcours, IMAP+, AMABIO3
- **Identification of new genes, ANR on imaging**
- **Identification of risk factors**
- **Participation in studies in Social and Human Sciences** including an economic survey with Médéric Alzheimer Foundation www.fondation-mederic-alzheimer.org/content/download/18759/83735/file/RAPPORT%20ESEMAJ%20FINAL.pdf



IV – International collaborations

- **DIAN** Dominant Inherited Alzheimer's disease Network
- **GENFI-2** : Genetic FTD Initiative
- **EADC** European Alzheimer's Disease Consortium
 - European Early-Onset Dementia consortium
- **ANR/FRSQ** programme: **AMAJ** Aide aux Malades Alzheimer jeunes
- **JPND** Joint Programming on Neurodegenerative Diseases
 - CSF, PPI (Patient Public Involvement)
- **Task Force of the IPA** (international Psychogeriatric Association)

Conclusions

- Long delay between 1st symptoms and diagnosis made at a more severe stage
- Socio-professional, family and financial impact
- Lack of specific facilities (nursing home, respite care) and trained professionals
- Genetic concerns: 10% in EOAD (vs < 2% in LOAD) ; \approx 40% in FTLD
- Important research challenge
 - Target of disease-modifying treatments, wilful population to participate in research
- **The needs of young patients of today are those of older patients in the future**




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Advocacy for research in YOD
(and not only familial YOD)

Young patients usually:

- Have no other disease, co-morbidities, other medications
 - Especially have no (or less) vascular disorders, and cerebrovascular lesions
- Are willing to participate in research programmes, as well as their family, mainly spouse, often pro-active, well organised
 - YOD patients are actually overrepresented in patients participating in clinical research
- Can be a lobby, because they are still in active life (even if they have ceased working)
- Are not afraid of new examinations, or technologies
- Move, are not reluctant to travelling (e.g. to go to an expert centre)
- Are not resigned, are not accepting the disease
- Are less at risk of attrition in longitudinal studies (do not give up) and so far are **excluded from clinical and pharmaceutical studies because of their young age!**

- **Autosomal dominant forms of AD** are a great model to develop disease-modifying drugs (cf. DIAN, GENFI), but:
 - Is the pathophysiology the same whatever the mutations and similar to sporadic multifactorial cases?
 - Ethical issues
- Monogenic mutations account for 10% of EOAD (< 2% of LOAD) and 20-40% of FTD
- Important to understand why **sporadic cases** have a large range of onset. It would lead to strategies to delay the disease(s).
- Important not to miss atypical phenotypes
- Need for research in Human and Social Sciences

Difficult diagnosis ?

- Biological and imaging studies give confidence in the diagnosis of AD, even when clinical features and age at onset (before 60) are not typical
- Young patients (and families) often in favour of autopsy to confirm diagnosis and to help research → helpful to validate biomarkers.
- Neuropathology does not differ in EOAD and LOAD
 - vascular burden higher in LOAD and genetic burden higher in EOAD

Role of young patients

- The (relatively rare) young patients of today are representative of what will be the much more numerous 'old' patients of tomorrow in terms of habits, likes and dislikes, abilities and skills (e.g. transportation mastering, information technology, communication, electronic devices...).
- In studying this population we could anticipate the future needs the society will have to face.
- International collaborations mandatory!