Gruppo di ricerca geriatrica

Journal Club - Aggiornamenti in Geriatria

11 agosto 2017

L'importanza della diagnosi precoce di demenza

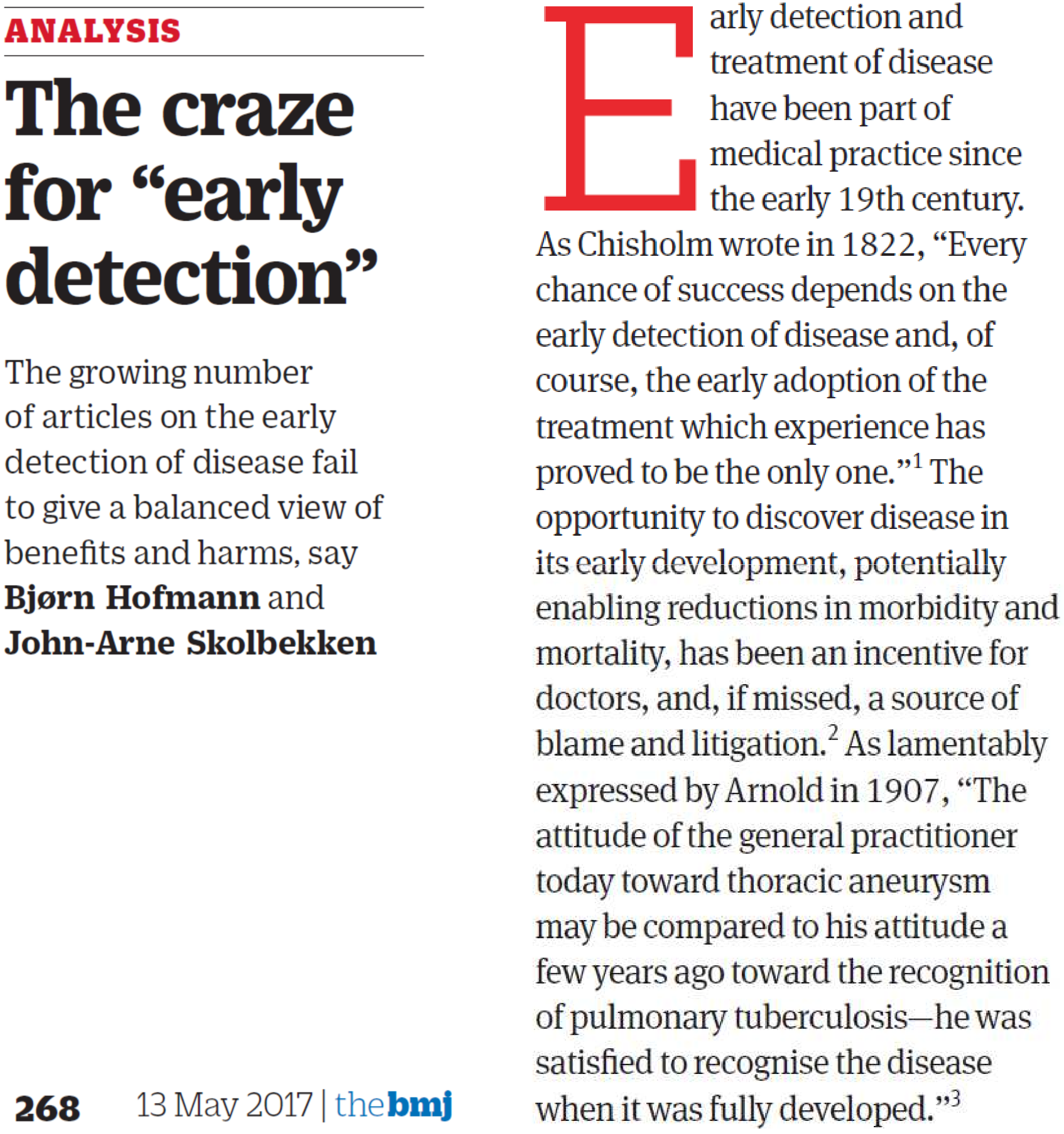
Marco Trabucchi

Ancient Babylonia

A Babylonian medical textbook, the *Diagnostic Handbook* written by Esagil-kin-apli (fl. 1069-1046 BC), introduced the use of empiricism, logic and rationality in the diagnosis of an illness or disease.

The book made use of logical rules in combining observed symptoms on the body of a patient with its diagnosis and prognosis.

He described the symptoms for many varieties of epilepsy and related ailments along with their diagnosis and prognosis which both played significant roles in the practice of Babylonian medicine.



ANALYSIS

The craze for "early detection"

The growing number of articles on the early detection of disease fail to give a balanced view of benefits and harms, say **Bjørn Hofmann** and **John-Arne Skolbekken**

Early detection and treatment of disease have been part of medical practice since the early 19th century. As Chisholm wrote in 1822, "Every chance of success depends on the early detection of disease and, of course, the early adoption of the treatment which experience has proved to be the only one."[1] The opportunity to discover disease in its early development, potentially enabling reductions in morbidity and mortality, has been an incentive for doctors, and, if missed, a source of blame and litigation.[2] As lamentably expressed by Arnold in 1907, "The attitude of the general practitioner today toward thoracic aneurysm may be compared to his attitude a few years ago toward the recognition of pulmonary tuberculosis—he was satisfied to recognise the disease when it was fully developed."[3]

Gruppo di ricerca geriatrica

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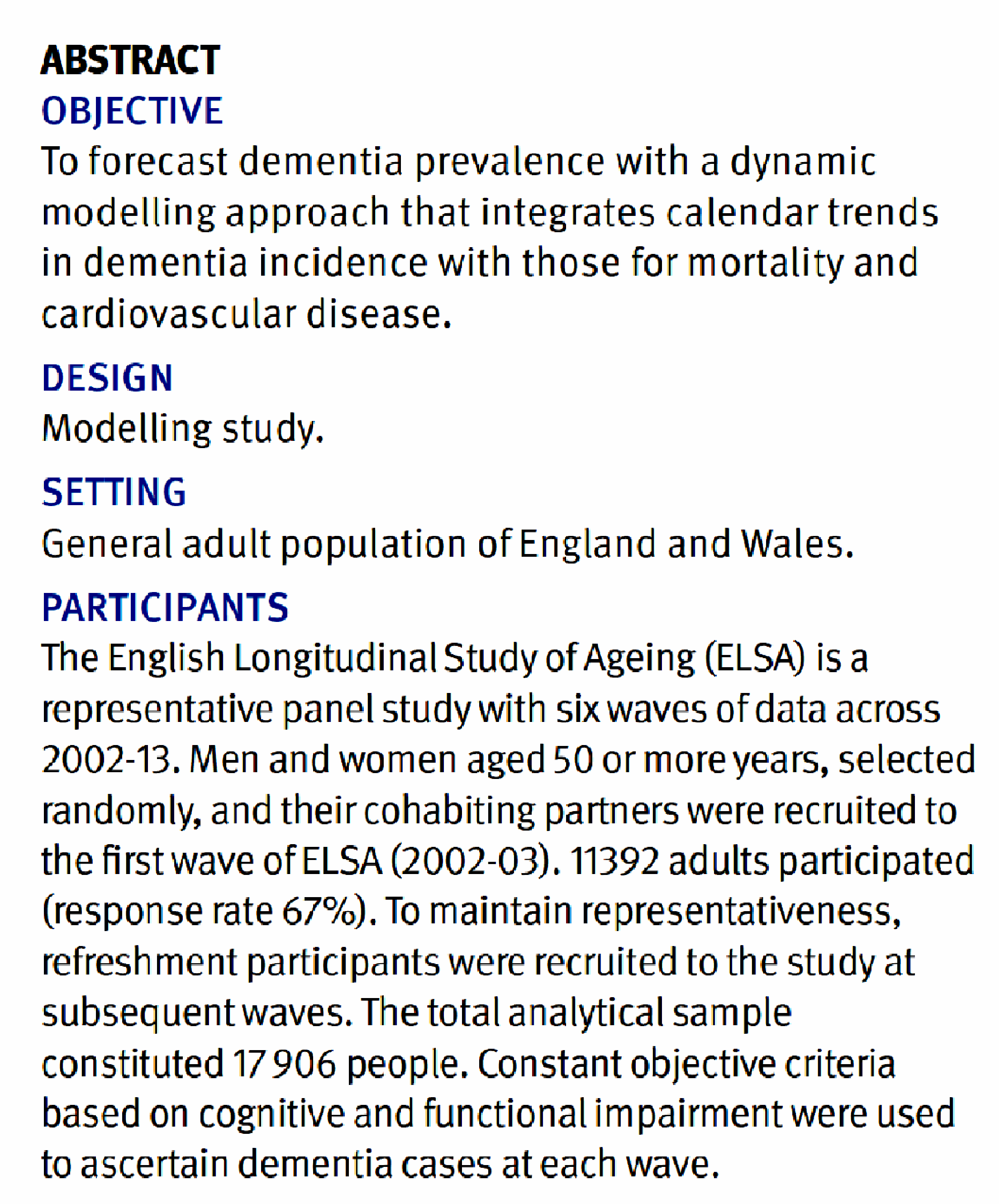
La demenza: sempre più diffusa e per ora… sempre più incomprensibile.



ABSTRACT

OBJECTIVE

To forecast dementia prevalence with a dynamic modelling approach that integrates calendar trends in dementia incidence with those for mortality and cardiovascular disease.

DESIGN

Modelling study.

SETTING

General adult population of England and Wales.

PARTICIPANTS

The English Longitudinal Study of Ageing (ELSA) is a representative panel study with six waves of data across 2002-13. Men and women aged 50 or more years, selected randomly, and their cohabiting partners were recruited to the first wave of ELSA (2002-03). 11392 adults participated (response rate 67%). To maintain representativeness, refreshment participants were recruited to the study at subsequent waves. The total analytical sample constituted 17 906 people. Constant objective criteria based on cognitive and functional impairment were used to ascertain dementia cases at each wave.

Temporal trend in dementia incidence since 2002 and projections for prevalence in England and Wales to 2040: modelling study

Sara Ahmadi-Abhari, Maria Guzman-Castillo, Piotr Bandosz, Martin J Shipley, Graciela Muniz-Terrera, Archana Singh-Manoux, Mika Kivimäki, Andrew Steptoe, Simon Capewell, Martin O'Flaherty, Eric J Brunner

Segue…

thebmj | *BMJ* 2017;358:j2856 | doi: 10.1136/bmj.j2856

Temporal trend in dementia incidence since 2002 and projections for prevalence in England and Wales to 2040: modelling study

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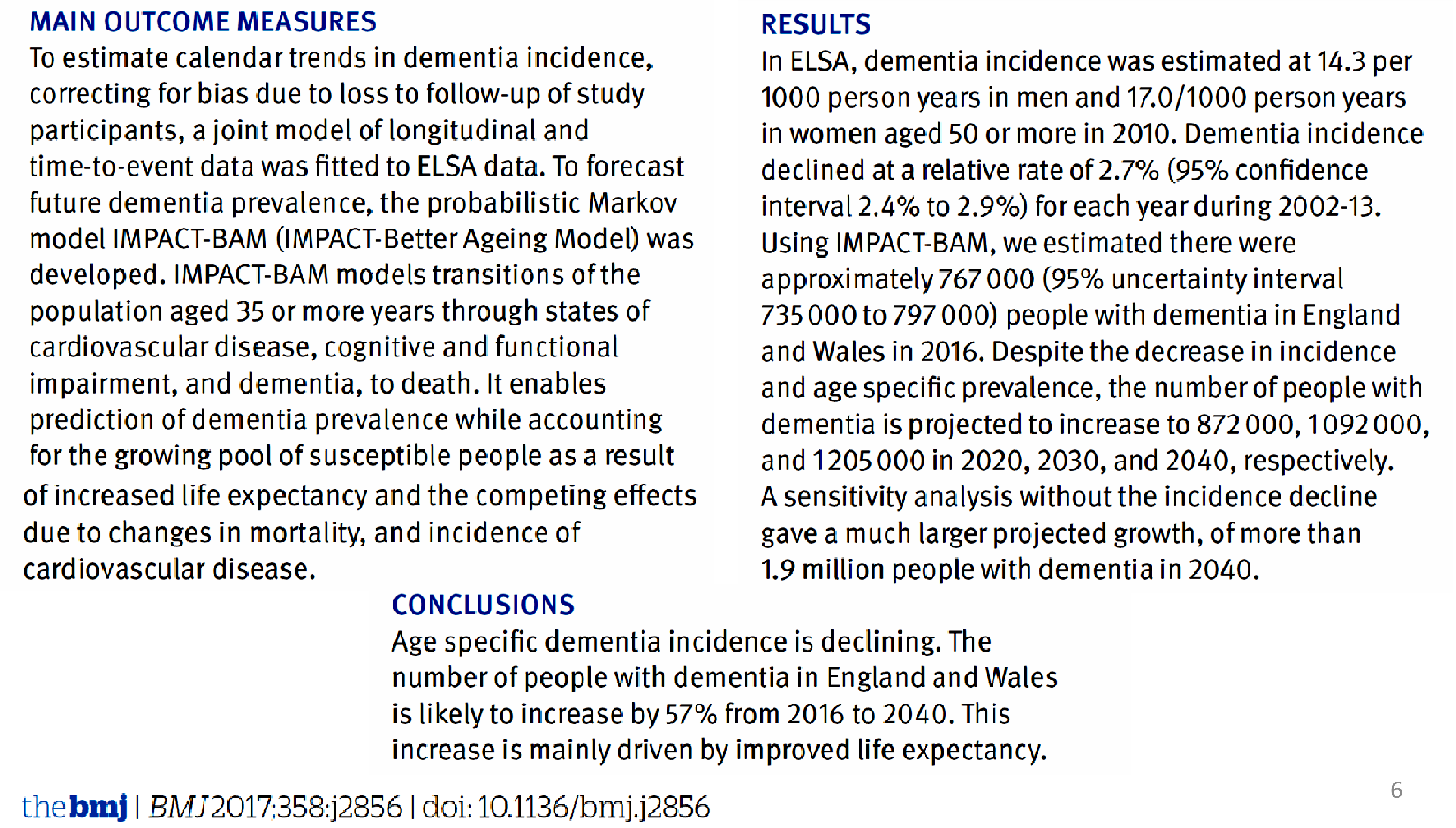


MAIN OUTCOME MEASURES

To estimate calendar trends in dementia incidence, correcting for bias due to loss to follow-up of study participants, a joint model of longitudinal and time-to-event data was fitted to ELSA data. To forecast future dementia prevalence, the probabilistic Markov model IMPACT-BAM (IMPACT-Better Ageing Model) was developed. IMPACT-BAM models transitions of the population aged 35 or more years through states of cardiovascular disease, cognitive and functional impairment, and dementia, to death. It enables prediction of dementia prevalence while accounting for the growing pool of susceptible people as a result of increased life expectancy and the competing effects due to changes in mortality, and incidence of cardiovascular disease.

RESULTS

In ELSA, dementia incidence was estimated at 14.3 per 1000 person years in men and 17.0/1000 person years in women aged 50 or more in 2010. Dementia incidence declined at a relative rate of 2.7% (95% confidence interval 2.4% to 2.9%) for each year during 2002-13. Using IMPACT-BAM, we estimated there were approximately 767 000 (95% uncertainty interval 735 000 to 797 000) people with dementia in England and Wales in 2016. Despite the decrease in incidence and age specific prevalence, the number of people with dementia is projected to increase to 872 000, 1 092 000, and 1 205 000 in 2020, 2030, and 2040, respectively. A sensitivity analysis without the incidence decline gave a much larger projected growth, of more than 1.9 million people with dementia in 2040.

CONCLUSIONS

Age specific dementia incidence is declining. The number of people with dementia in England and Wales is likely to increase by 57% from 2016 to 2040. This increase is mainly driven by improved life expectancy.

the**bmj** | *BMJ* 2017;358:j2856 | doi: 10.1136/bmj.j2856

TECH & SCIENCE

THE NEW OFFENSIVE ON ALZHEIMER'S DISEASE: STOP IT BEFORE IT STARTS

BY **ELIE DOLGIN** ON 2/16/17 AT 9:00 AM

NEWSWEEK

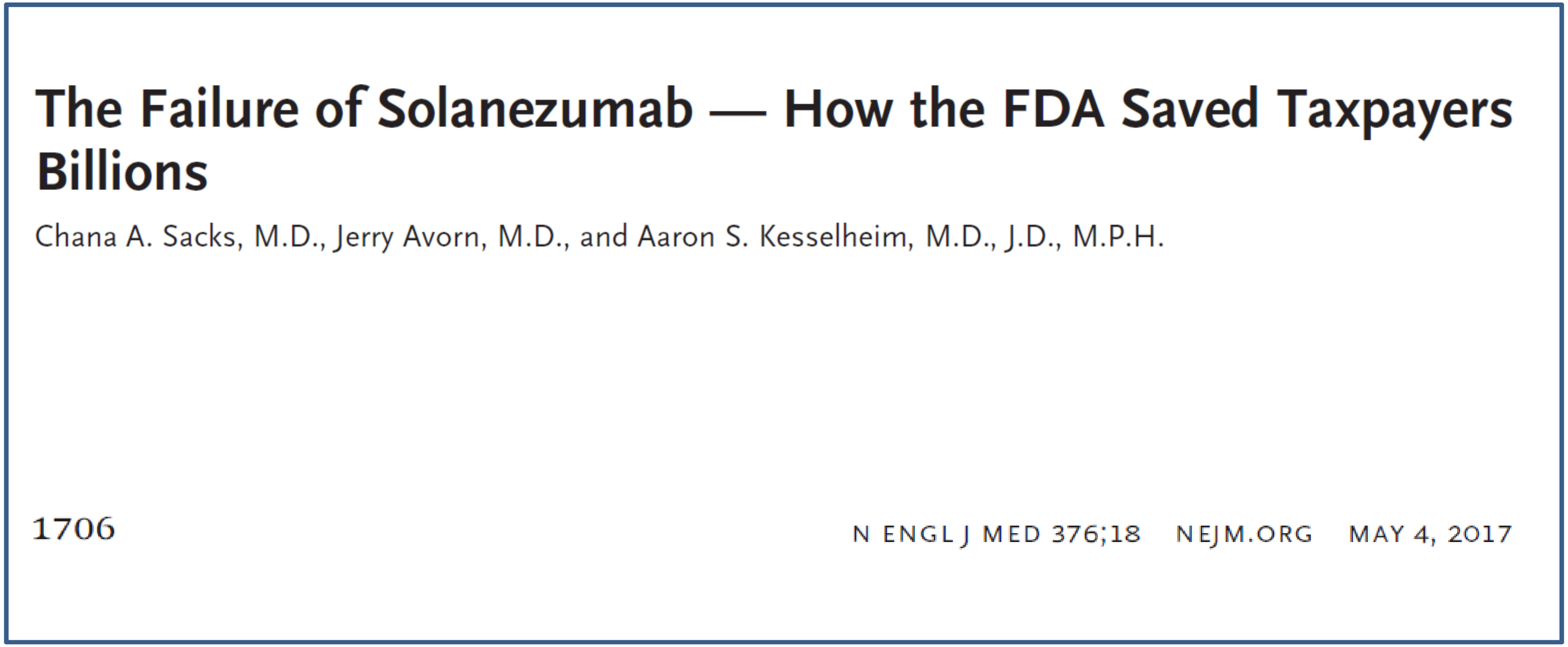
Brain Amyloid Pathology and Cognitive Function

Alzheimer Disease Without Dementia?

Pieter Jelle Visser, MD, PhD; Betty Tijms, PhD

If there ever was an exciting time for Alzheimer disease (AD) research, it is now. The discovery of biomarkers beginning 20 years ago, for example, positron emission tomography (PET) tracers that bind to plaques, the core pathological hallmark of the disease, unlocked new research fields. Together with increasing amounts of longitudinal data, it now is possible to study how the disease unfolds. This will transform the way AD is conceptualized, diagnosed, and treated.

JAMA June 13, 2017 Volume 317, Number 22 2285



The Failure of Solanezumab — How the FDA Saved Taxpayers Billions

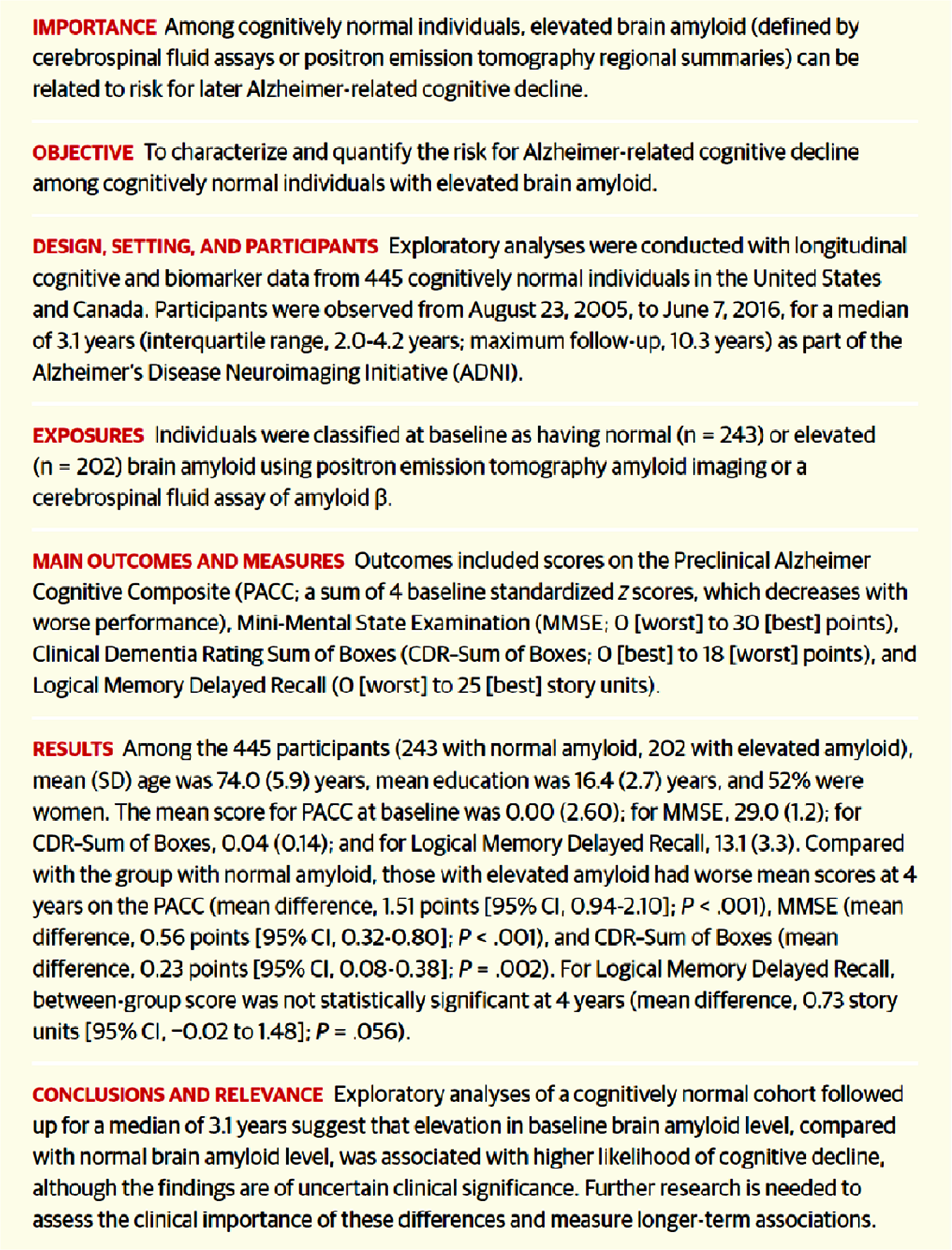
Chana A. Sacks, M.D., Jerry Avorn, M.D., and Aaron S. Kesselheim, M.D., J.D., M.P.H.

1706 N ENGL J MED 376;18 NEJM.ORG MAY 4, 2017

Association Between Elevated Brain Amyloid and Subsequent Cognitive Decline Among Cognitively Normal Persons.

Michael C. Donohue, Reisa A. Sperling, Ronald Petersen, Chung-Kai Sun, Michael W.Weiner, Paul S. Aisen, for the Alzheimer’s Disease Neuroimaging Initiative.

JAMA. 2017;317(22):2305-2316.



IMPORTANCE Among cognitively normal individuals, elevated brain amyloid (defined by cerebrospinal fluid assays or positron emission tomography regional summaries) can be related to risk for later Alzheimer-related cognitive decline.

OBJECTIVE To characterize and quantify the risk for Alzheimer-related cognitive decline among cognitively normal individuals with elevated brain amyloid.

DESIGN, SETTING, AND PARTICIPANTS Exploratory analyses were conducted with longitudinal cognitive and biomarker data from 445 cognitively normal individuals in the United States and Canada. Participants were observed from August 23, 2005, to June 7, 2016, for a median of 3.1 years (interquartile range, 2.0-4.2 years; maximum follow-up, 10.3 years) as part of the Alzheimer’s Disease Neuroimaging Initiative (ADNI).

EXPOSURES Individuals were classified at baseline as having normal (n = 243) or elevated (n = 202) brain amyloid using positron emission tomography amyloid imaging or a cerebrospinal fluid assay of amyloid β.

MAIN OUTCOMES AND MEASURES Outcomes included scores on the Preclinical Alzheimer Cognitive Composite (PACC; a sum of 4 baseline standardized *z* scores, which decreases with worse performance), Mini-Mental State Examination (MMSE; 0 [worst] to 30 [best] points), Clinical Dementia Rating Sum of Boxes (CDR–Sum of Boxes; 0 [best] to 18 [worst] points), and Logical Memory Delayed Recall (0 [worst] to 25 [best] story units).

RESULTS Among the 445 participants (243 with normal amyloid, 202 with elevated amyloid), mean (SD) age was 74.0 (5.9) years, mean education was 16.4 (2.7) years, and 52% were women. The mean score for PACC at baseline was 0.00 (2.60); for MMSE, 29.0 (1.2); for CDR–Sum of Boxes, 0.04 (0.14); and for Logical Memory Delayed Recall, 13.1 (3.3). Compared with the group with normal amyloid, those with elevated amyloid had worse mean scores at 4 years on the PACC (mean difference, 1.51 points [95% CI, 0.94-2.10]; $P < .001$), MMSE (mean difference, 0.56 points [95% CI, 0.32-0.80]; $P < .001$), and CDR–Sum of Boxes (mean difference, 0.23 points [95% CI, 0.08-0.38]; $P = .002$). For Logical Memory Delayed Recall, between-group score was not statistically significant at 4 years (mean difference, 0.73 story units [95% CI, −0.02 to 1.48]; $P = .056$).

CONCLUSIONS AND RELEVANCE Exploratory analyses of a cognitively normal cohort followed up for a median of 3.1 years suggest that elevation in baseline brain amyloid level, compared with normal brain amyloid level, was associated with higher likelihood of cognitive decline, although the findings are of uncertain clinical significance. Further research is needed to assess the clinical importance of these differences and measure longer-term associations.

Gruppo di ricerca geriatrica

… perché la diagnosi si deve fare …

Psicogeriatria

ANNO X - SUPPLEMENTO - NUMERO 1 - GENNAIO-APRILE 2015

Raccomandazioni dell'Associazione Italiana di Psicogeriatria (AIP) e della Società Italiana Neurologia delle Demenze (SINDEM) sulla diagnosi precoce della Malattia di Alzheimer

Documento dell'Associazione Italiana di Psicogeriatria

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Gruppo di ricerca geriatrica

Oggi non vi sono terapie in grado di mettere pienamente a frutto i vantaggi di una diagnosi precoce, nè è noto quando saranno disponibili. Ma ciò non può essere il pretesto per una visione pessimistica o per una resa sul fronte dell'impegno a favore dei malati e dei loro familiari. Una maggiore accuratezza diagnostica sin dalle fasi precoci della Malattia di Alzheimer, attraverso un utilizzo "intelligente" e appropriato dei vari marcatori, permette una migliore cura delle comorbidità somatiche e psicologiche, unitamente ad una più tempestiva gestione delle problematiche assistenziali e legali.

Raccomandazioni dell'Associazione Italiana di Psicogeriatria (AIP) e della Società Italiana Neurologia delle Demenze (SINDEM) sulla diagnosi precoce della Malattia di Alzheimer. **Psicogeriatria**, anno X, supplemento, numero 1, gennaio-aprile 2015.

La eterogeneità genetica dell’Alzheimer impone iter diagnostici sempre più accurati, sia per motivazioni intrinseche, sia perché il futuro metterà in luce l’esigenza di collegare specifici asset biologici con specifici farmaci.

PSICOGERIATRIA 2017; 1: 29-37

Il demone nella mente di mio marito[1]

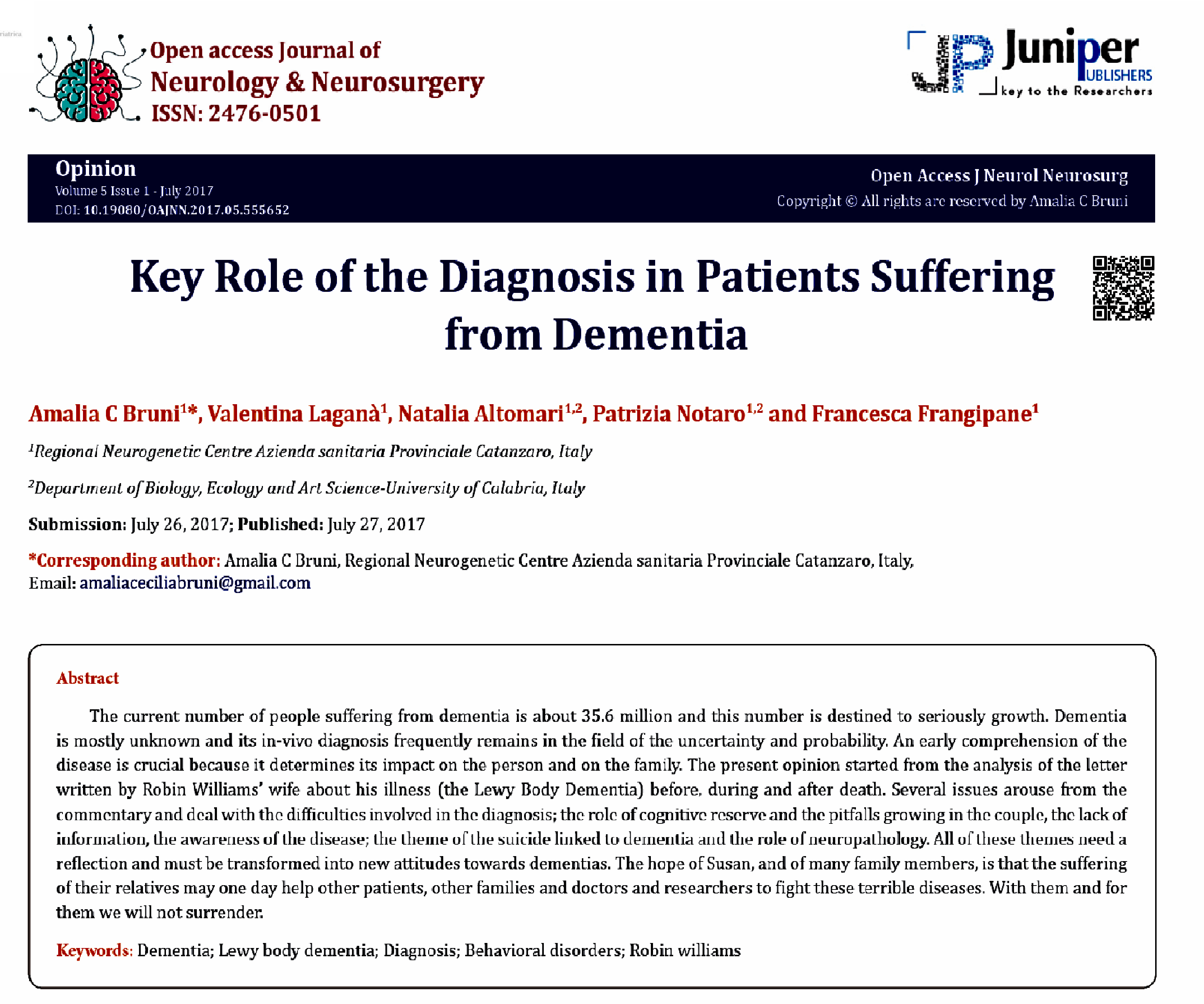
Amalia Cecilia Bruni, Valentina Laganà, Francesca Frangipane

Ti scrivo per condividere una storia con te, appositamente per te. La mia speranza è che questo possa aiutarti a capire un po' di più i tuoi pazienti, con i loro compagni di vita e chi si prende cura di loro. Forse questo aggiungerà un altro paio di volti dietro ai perché del tuo agire da professionista. Sono sicura che ne hai già tanti.

Si tratta di una storia personale, purtroppo tragica e straziante, ma attraverso la condivisione di queste informazioni con te so che posso contribuire a fare la differenza nella vita di altri.

Come forse saprai, mio marito Robin Williams aveva la malattia a Corpi di Lewy (LBD), una patologia ancora poco conosciuta, ma mortale. Si è tolto la vita nel 2014 al termine di una "persecuzione" intensa, destabilizzante e relativamente rapida determinata dai sintomi di questo morbo. Lui non era solo a vivere l'esperienza traumatica: come saprai, circa 1.5 milioni di connazionali in questo momento stanno soffrendo allo stesso modo. Anche se non era solo, il suo caso era particolare. Fino al rapporto del coroner, 3 mesi dopo la sua morte, non seppi che era affetto da LBD diffusa. Tutti e 4 i medici che ho incontrato, ai quali ho consegnato i risultati, dissero che quello di mio marito era uno dei casi peggiori che avessero mai visto. Lui aveva perso circa il 40% dei neuroni dopaminergici e quasi nessun neurone era libero dai corpi di Lewy, sia nel cervello, sia nel tronco encefalico.

[1] Schneider Williams S. The terrorist inside my husband's brain. Neurology 2016;87:1308-11.



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Neurology & Neurosurgery
ISSN: 2476-0501

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key to the Researchers

Opinion
Volume 5 Issue 1 - July 2017
DOI: 10.19080/OAJNN.2017.05.555652

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Key Role of the Diagnosis in Patients Suffering from Dementia

Amalia C Bruni[1]*, Valentina Laganà[1], Natalia Altomari[1,2], Patrizia Notaro[1,2] and Francesca Frangipane[1]

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[2]*Department of Biology, Ecology and Art Science-University of Calabria, Italy*

Submission: July 26, 2017; **Published:** July 27, 2017

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Abstract

The current number of people suffering from dementia is about 35.6 million and this number is destined to seriously growth. Dementia is mostly unknown and its in-vivo diagnosis frequently remains in the field of the uncertainty and probability. An early comprehension of the disease is crucial because it determines its impact on the person and on the family. The present opinion started from the analysis of the letter written by Robin Williams' wife about his illness (the Lewy Body Dementia) before, during and after death. Several issues arouse from the commentary and deal with the difficulties involved in the diagnosis; the role of cognitive reserve and the pitfalls growing in the couple, the lack of information, the awareness of the disease; the theme of the suicide linked to dementia and the role of neuropathology. All of these themes need a reflection and must be transformed into new attitudes towards dementias. The hope of Susan, and of many family members, is that the suffering of their relatives may one day help other patients, other families and doctors and researchers to fight these terrible diseases. With them and for them we will not surrender.

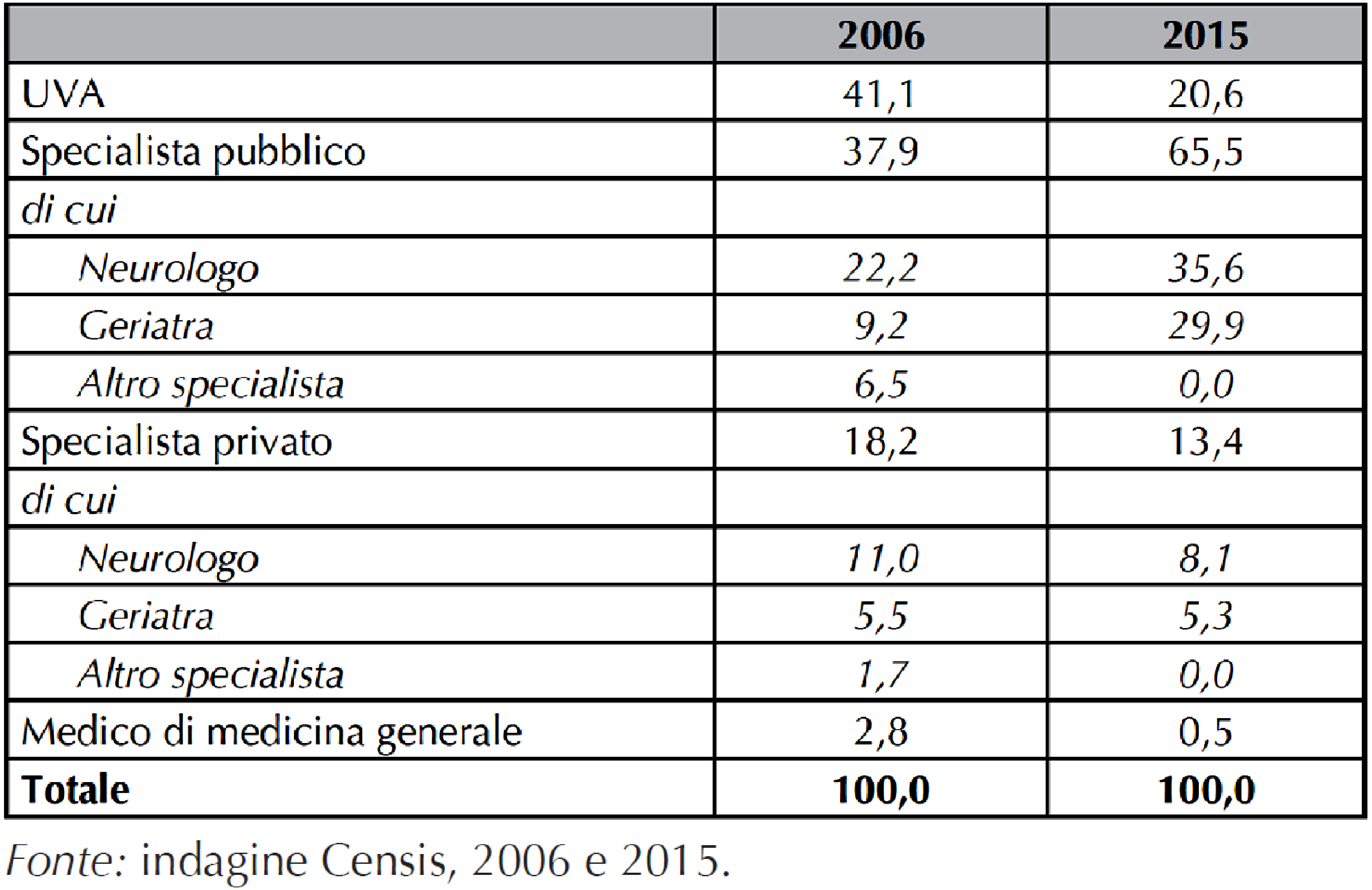
Keywords: Dementia; Lewy body dementia; Diagnosis; Behavioral disorders; Robin williams

La diagnosi si deve fare anche se vi è il rischio che la mancanza di cure diffonda sul tema demenza uno scetticismo diffuso, una "morte dell'esperto", stimolata in particolare dai social.
Anche l'insistenza della letteratura sugli stili di vita che prevengono la demenza potrebbe portare ad una sfiducia nella medicina tecnologica,
per affidarsi ad un modello aspecifico di benessere, aperto a qualsiasi banalità.

Gruppo di ricerca geriatrica

La diagnosi come "diritto civile" di ogni persona, un segno di rispetto della dignità dell'individuo.

Chi ha effettuato la diagnosi *(valori percentuali)*



	2006	2015
UVA	41,1	20,6
Specialista pubblico	37,9	65,5
di cui		
Neurologo	*22,2*	*35,6*
Geriatra	*9,2*	*29,9*
Altro specialista	*6,5*	*0,0*
Specialista privato	18,2	13,4
di cui		
Neurologo	*11,0*	*8,1*
Geriatra	*5,5*	*5,3*
Altro specialista	*1,7*	*0,0*
Medico di medicina generale	2,8	0,5
Totale	**100,0**	**100,0**

Fonte: indagine Censis, 2006 e 2015.

(Vaccaro K. In: Le demenze. La cura e le cure, Maggioli, 2016, p. 283-91)

Lo scenario della diagnosi è caratterizzato da una forte mobilità, effetto destinato ad accentuarsi con l’introduzione progressiva (e disomogenea) delle nuove tecnologie.
Il rischio di creare ambiti diagnostici di serie A e B in base alle disponibilità di tecnologie (imaging e biochimiche).
Una discussione ancora aperta nelle varie regioni.

Importance of an early diagnosis

1. Your symptoms might be reversible.
2. It may be treatable.
3. With treatments, the sooner the better.
4. Diagnoses are more accurate early in the disease process.
5. It's empowering.
6. You can focus on what's important to you.
7. You can make your best choices.
8. You can use the resources available to you.
9. Participate or advocate for research.
10. You can further people's understanding of the disease.
11. It will help your family.
12. It will help you, too.

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alzheimer's association®
policybrief
DECEMBER 2015 alz.org®

Early Detection and Diagnosis of Alzheimer's Disease

Barriers to early detection and diagnosis

For early detection to occur – and subsequent diagnosis and disclosure awareness – patients and physicians must overcome several barriers. Patients face barriers such as low public awareness of the early signs of Alzheimer's, including notable differences in diverse populations; perceived emotional distress of Alzheimer's and other dementias on family members; and misperceptions about Alzheimer's and other dementias. For example, a recent survey of 12 countries found 59 percent of respondents incorrectly believed that Alzheimer's is a typical part of aging, and 40 percent believed that Alzheimer's is not fatal. These barriers can lead to stigma, delays in seeking medical assistance or reluctance to communicate with health care providers. Data from the 2012 BRFSS showed only 23 percent of adults age 45 and older who reported subjective cognitive decline in the previous 12 months had talked with a health care provider about it.

Nel mondo la mancata diagnosi di demenza riguarda due terzi degli ammalati.
In Italia, anche in aree ad alta intensità di servizi, si suppone che vi sia un 20% dei cittadini affetti da demenza che non hanno ricevuto una diagnosi.

Gruppo di ricerca geriatrica

Sistema Socio Sanitario

Regione Lombardia

ATS Brescia

PERCORSO
DIAGNOSTICO-TERAPEUTICO-ASSISTENZIALE
DECADIMENTO COGNITIVO/DEMENZA

3° edizione dicembre 2016

(precedenti 2011 – 2013)

Fase pre-diagnostica, prima verifica ed eventuale invio al CDCD

***Obiettivo**:* pervenire ad una diagnosi precoce di decadimento cognitivo attraverso lo sviluppo di capacità di sospetto diagnostico e l'applicazione di strumenti di prima conferma in modo più omogeneo nel territorio ATS

***Attori principali**:* MMG

***Compiti**:* individuazione dei soggetti con sospetto di decadimento cognitivo attraverso lo screening effettuato secondo modalità ben definite

***Strumenti**:* in caso di sospetto diagnostico il MMG effettua lo screening delle funzioni cognitive raccogliendo dai familiari/caregiver precise informazioni anamnestiche attraverso un questionario.

In caso di lieve anomalia (un solo item positivo, che presenta però un impatto con l’attività quotidiana), il questionario può essere nuovamente somministrato dal MMG a breve distanza di tempo (3 mesi) per meglio valutare l'evoluzione delle performance del paziente.

E' facoltà del MMG somministrare al paziente anche il MMSE – Mini Mental State Examination, in particolare quando lo screening tramite questionario evidenzia criticità.

In caso di risultato patologico, il MMG avvia il processo di esclusione diagnostica/diagnosi differenziale attraverso la prescrizione e la valutazione dei risultati degli esami strettamente necessari.

(ATS Brescia, 2016)

Gruppo di ricerca geriatrica

Conferma diagnostica, diagnosi differenziale ed eventuale avvio del trattamento

Obiettivo: pervenire ad una diagnosi certa e decidere l'eventuale avvio dell'intervento terapeutico (farmacologico o non farmacologico)
Attori principali: CDCD
Compiti: corretto inquadramento diagnostico anche attraverso richiesta diretta di esami strumentali di secondo livello, somministrazione di test neuropsicologici, utilizzo di strumenti diagnostici complessi (es.: RMN, PET/SPECT, esame liquorale); eventuale avvio del trattamento farmacologico (secondo quanto alla nota 85 CUF/AIFA); comunicazione della diagnosi; informazione e supporto ai familiari
Strumenti: nel territorio di ATS di Brescia, l'attività dei CDCD è sviluppata con comune riferimento alle Linee guida per le demenze della Società Italiana di Neurologia - anno 2004 e della Società Italiana di Psicogeriatria - anno 2006.

(ATS Brescia, 2016)

Gruppo di ricerca geriatrica

La diagnosi precoce di demenza e:
le terapie, l'autonomia e la dignità del paziente,
l'uso delle risorse.
Riduce l'incertezza indotta dai sintomi; permette
una cura più adeguata della patologia somatica.

Piano Nazionale Demenze

Nuovi scenari di cura

Psicogeriatria

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SUPPLEMENTO
ANNO XI
NUMERO 2
MAGGIO-AGOSTO 2016

Rivista ufficiale
ASSOCIAZIONE
ITALIANA
PSICOGERIATRIA

Dementia: timely diagnosis and early intervention

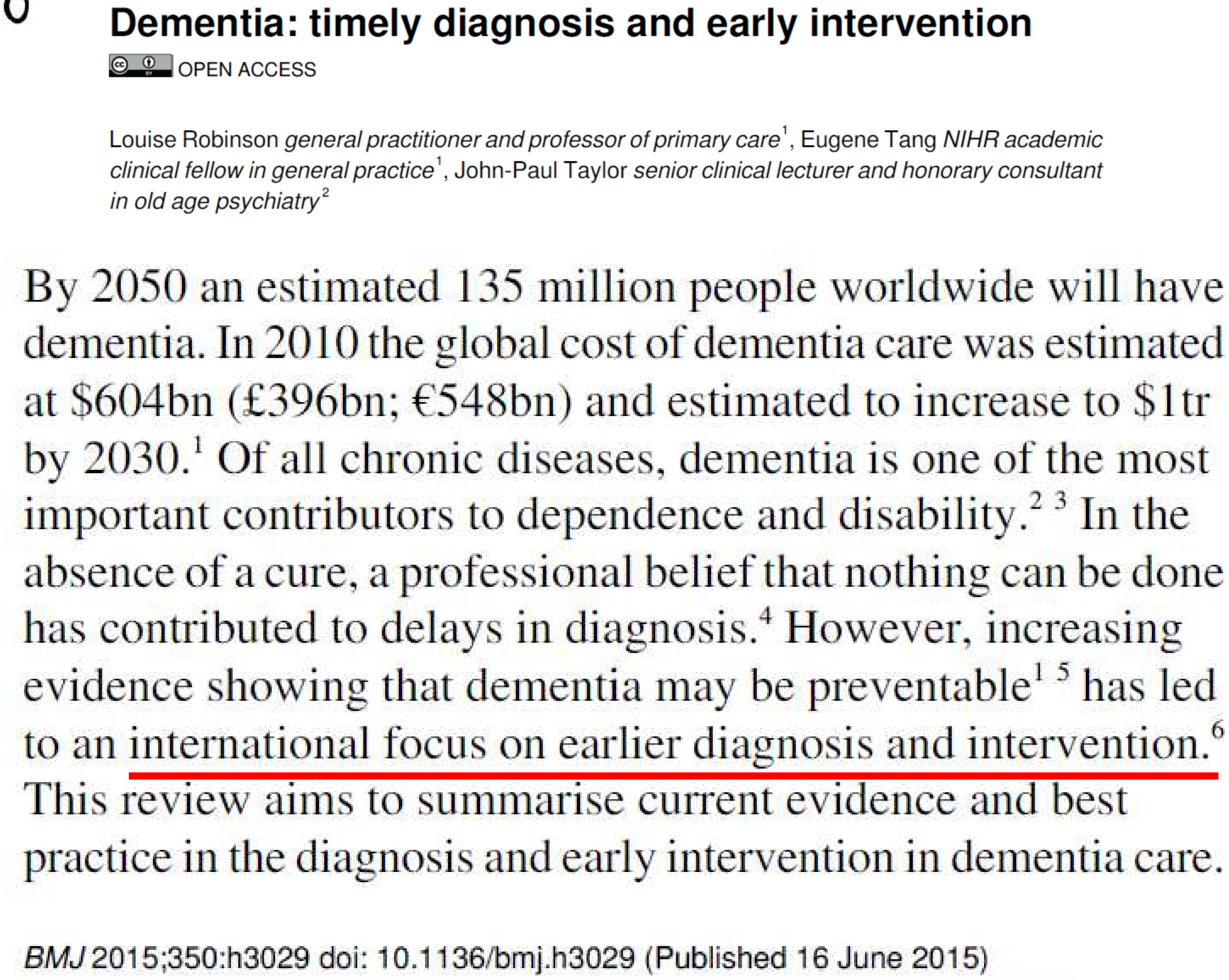
OPEN ACCESS

Louise Robinson *general practitioner and professor of primary care*[1], Eugene Tang *NIHR academic clinical fellow in general practice*[1], John-Paul Taylor *senior clinical lecturer and honorary consultant in old age psychiatry*[2]

Dementia describes a clinical syndrome that encompasses difficulties in memory, language, and behaviour that leads to impairments in activities of daily living. Alzheimer's disease is the most common subtype of dementia, followed by vascular dementia, mixed dementia, and dementia with Lewy bodies. Because the global population is rapidly ageing, dementia has become a concern worldwide[1]; the illness places considerable burden on individuals and their families and also on health and social care provision.

Segue…

BMJ 2015;350:h3029 doi: 10.1136/bmj.h3029 (Published 16 June 2015)



Dementia: timely diagnosis and early intervention

OPEN ACCESS

Louise Robinson *general practitioner and professor of primary care*[1], Eugene Tang *NIHR academic clinical fellow in general practice*[1], John-Paul Taylor *senior clinical lecturer and honorary consultant in old age psychiatry*[2]

By 2050 an estimated 135 million people worldwide will have dementia. In 2010 the global cost of dementia care was estimated at \$604bn (£396bn; €548bn) and estimated to increase to \$1tr by 2030.[1] Of all chronic diseases, dementia is one of the most important contributors to dependence and disability.[2 3] In the absence of a cure, a professional belief that nothing can be done has contributed to delays in diagnosis.[4] However, increasing evidence showing that dementia may be preventable[1 5] has led to an international focus on earlier diagnosis and intervention.[6] This review aims to summarise current evidence and best practice in the diagnosis and early intervention in dementia care.

BMJ 2015;350:h3029 doi: 10.1136/bmj.h3029 (Published 16 June 2015)

Dalla diagnosi alla sua comunicazione.
Un passaggio delicato, ma indispensabile

Gruppo di ricerca geriatrica

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policybrief

DECEMBER 2015

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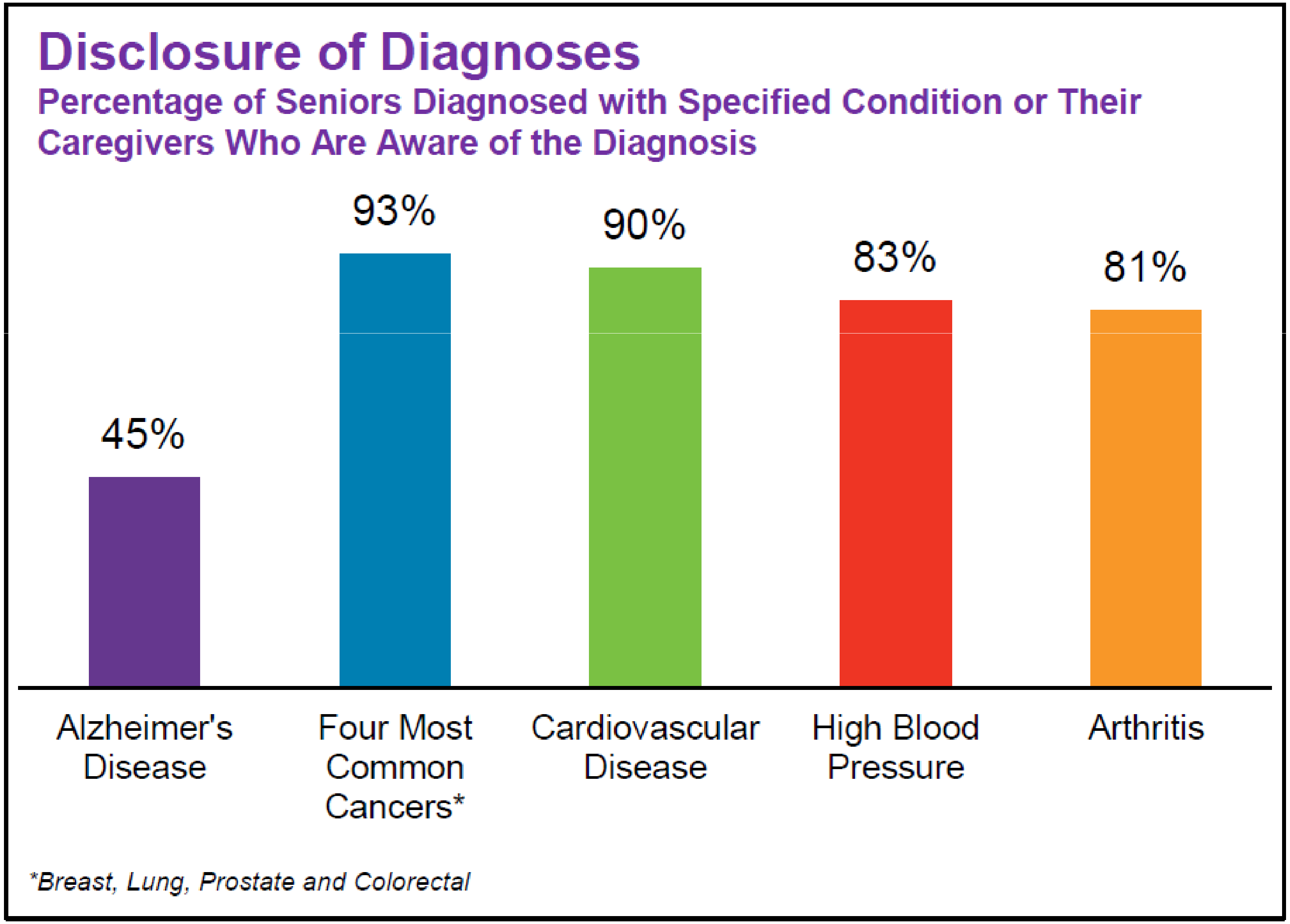
Early Detection and Diagnosis of Alzheimer's Disease



Disclosure of Diagnoses

Percentage of Seniors Diagnosed with Specified Condition or Their Caregivers Who Are Aware of the Diagnosis

**Breast, Lung, Prostate and Colorectal*

Attenzione alla "diagnosi fatte in casa": non danno alcuna indicazione seria e stimolano la comparsa di sintomi indotti dall'ansia e dall'incertezza.

Gruppo di ricerca geriatrica

«Being diagnosed with something like this absolutely devastates you, but for me diagnosis – and this is going to sound really strange – was probably the best news I had at the time. Because... I thought I was losing my mind.
I thought there was a conspiracy against me. I was right and everybody else was wrong.
An early diagnosis of dementia is so, so important. Once diagnosed, I knew what I was up against. As they say: know your enemy. If I hadn't been diagnosed early and I hadn't been seen by consultants on a regular basis, I wouldn't be as well as I am today. I don't know what my future holds, but at least I'm prepared for it. »

(Norman McNamara, 2015)

http://www.scie.org.uk/dementia/symptoms/diagnosis/early-diagnosis.asp

Le incertezze tecnologiche, in particolare riguardo all'imaging, si riflettono direttamente sulla possibilità di una diagnosi certa, indirettamente sul vissuto dei medici, dei pazienti e dei famigliari.

Il problema dei marker di malattia

Imaging the ageing brain: identifying early disease or opening Pandora's box?

Aside from accurately identifying brain pathology in vivo, ultimately what matters is whether any biomarker-based classification can reliably predict clinically relevant outcomes. For now, at least, this evidence is limited and accordingly, caution is recommended before equating pathologies determined on the basis of biomarkers to disease states in cognitively unimpaired individuals. These caveats notwithstanding, this landmark study is an important staging post on a journey that will hopefully lead to a personalised approach to prevention of dementia.

Jonathan M Schott

www.thelancet.com/neurology **Vol 16 June 2017**

The high proportion of cognitively unimpaired elderly individuals defined as having one or more pathologies in this study was striking. Although an age-related increase in the prevalence of these pathologies is not unexpected, for MRI measures of neurodegeneration and tau PET in particular, the exact proportions will be affected by the decision to define cutoff points on the basis of data from healthy younger individuals. Determining these cutoffs raises fundamental questions about the definition of normal ageing. Is it the absence of any pathology, or should allowance be given, for example, for some volume loss or tau accumulation as part of the natural ageing process—and if so, how much? This discussion is not unique to neurology, as highlighted by controversies surrounding recent guidelines proposing different cutoffs for treating systolic hypertension at different ages.

Jonathan M Schott

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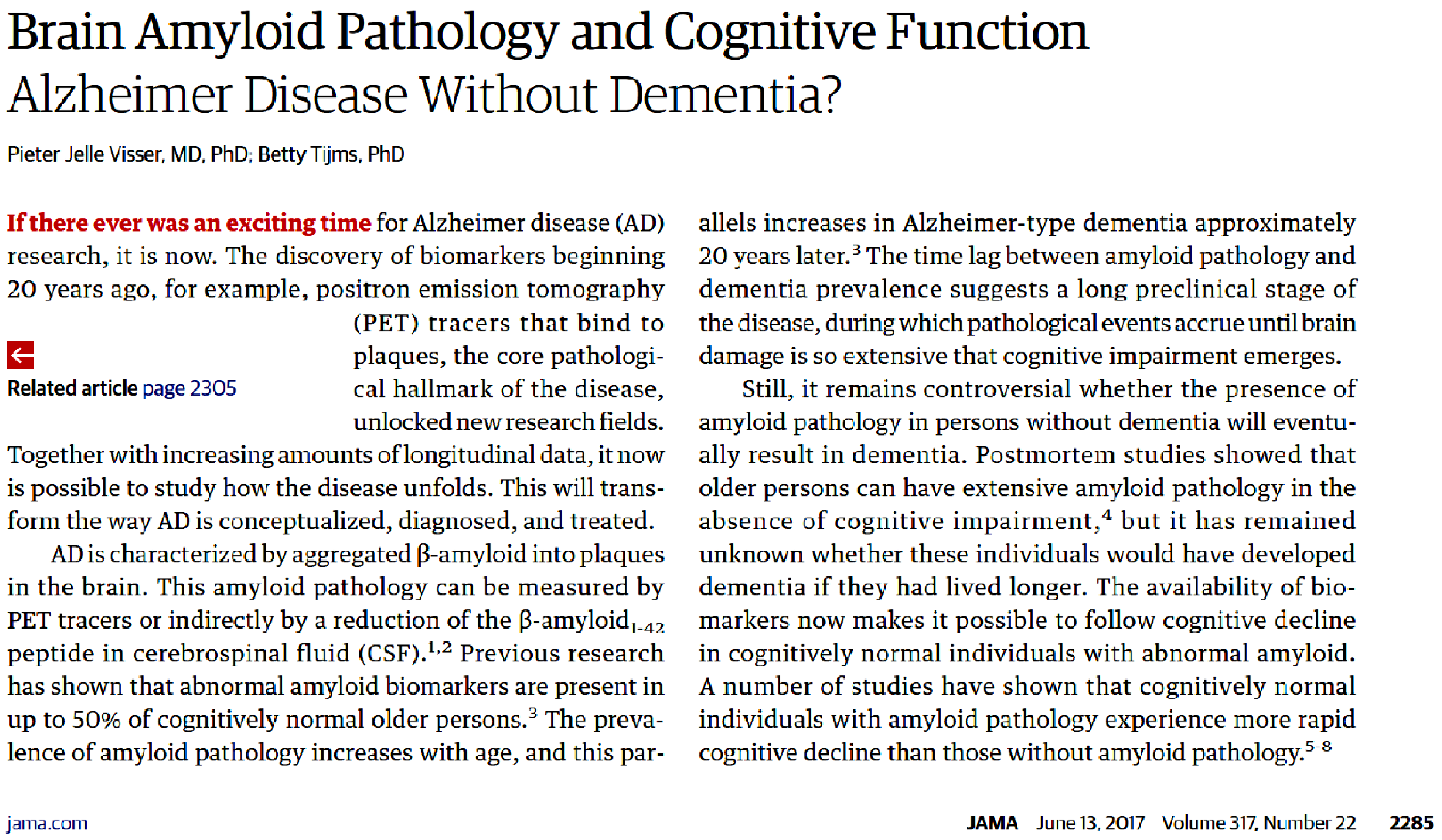


Brain Amyloid Pathology and Cognitive Function
Alzheimer Disease Without Dementia?

Pieter Jelle Visser, MD, PhD; Betty Tijms, PhD

If there ever was an exciting time for Alzheimer disease (AD) research, it is now. The discovery of biomarkers beginning 20 years ago, for example, positron emission tomography (PET) tracers that bind to plaques, the core pathological hallmark of the disease, unlocked new research fields. Together with increasing amounts of longitudinal data, it now is possible to study how the disease unfolds. This will transform the way AD is conceptualized, diagnosed, and treated.

Related article page 2305

AD is characterized by aggregated β-amyloid into plaques in the brain. This amyloid pathology can be measured by PET tracers or indirectly by a reduction of the β-amyloid$_{1-42}$ peptide in cerebrospinal fluid (CSF).[1,2] Previous research has shown that abnormal amyloid biomarkers are present in up to 50% of cognitively normal older persons.[3] The prevalence of amyloid pathology increases with age, and this parallels increases in Alzheimer-type dementia approximately 20 years later.[3] The time lag between amyloid pathology and dementia prevalence suggests a long preclinical stage of the disease, during which pathological events accrue until brain damage is so extensive that cognitive impairment emerges.

Still, it remains controversial whether the presence of amyloid pathology in persons without dementia will eventually result in dementia. Postmortem studies showed that older persons can have extensive amyloid pathology in the absence of cognitive impairment,[4] but it has remained unknown whether these individuals would have developed dementia if they had lived longer. The availability of biomarkers now makes it possible to follow cognitive decline in cognitively normal individuals with abnormal amyloid. A number of studies have shown that cognitively normal individuals with amyloid pathology experience more rapid cognitive decline than those without amyloid pathology.[5-8]

Normalità – patologia: il ruolo della clinica e quello della biologia.

Lewis Houghton/Science Photo Library

Detection of neurodegenerative disease using olfaction

Michael S Xydakis, Leonardo Belluscio

www.thelancet.com/neurology **Vol 16 June 2017**

Age-specific and sex-specific prevalence of cerebral β-amyloidosis, tauopathy, and neurodegeneration in cognitively unimpaired individuals aged 50–95 years: a cross-sectional study

Clifford R Jack Jr, Heather J Wiste, Stephen D Weigand, Terry M Therneau, David S Knopman, Val Lowe, Prashanthi Vemuri, Michelle M Mielke, Rosebud O Roberts, Mary M Machulda, Matthew L Senjem, Jeffrey L Gunter, Walter A Rocca, Ronald C Petersen

Summary

Background A new classification for biomarkers in Alzheimer's disease and cognitive ageing research is based on grouping the markers into three categories: amyloid deposition (A), tauopathy (T), and neurodegeneration or neuronal injury (N). Dichotomising these biomarkers as normal or abnormal results in eight possible profiles. We determined the clinical characteristics and prevalence of each ATN profile in cognitively unimpaired individuals aged 50 years and older.

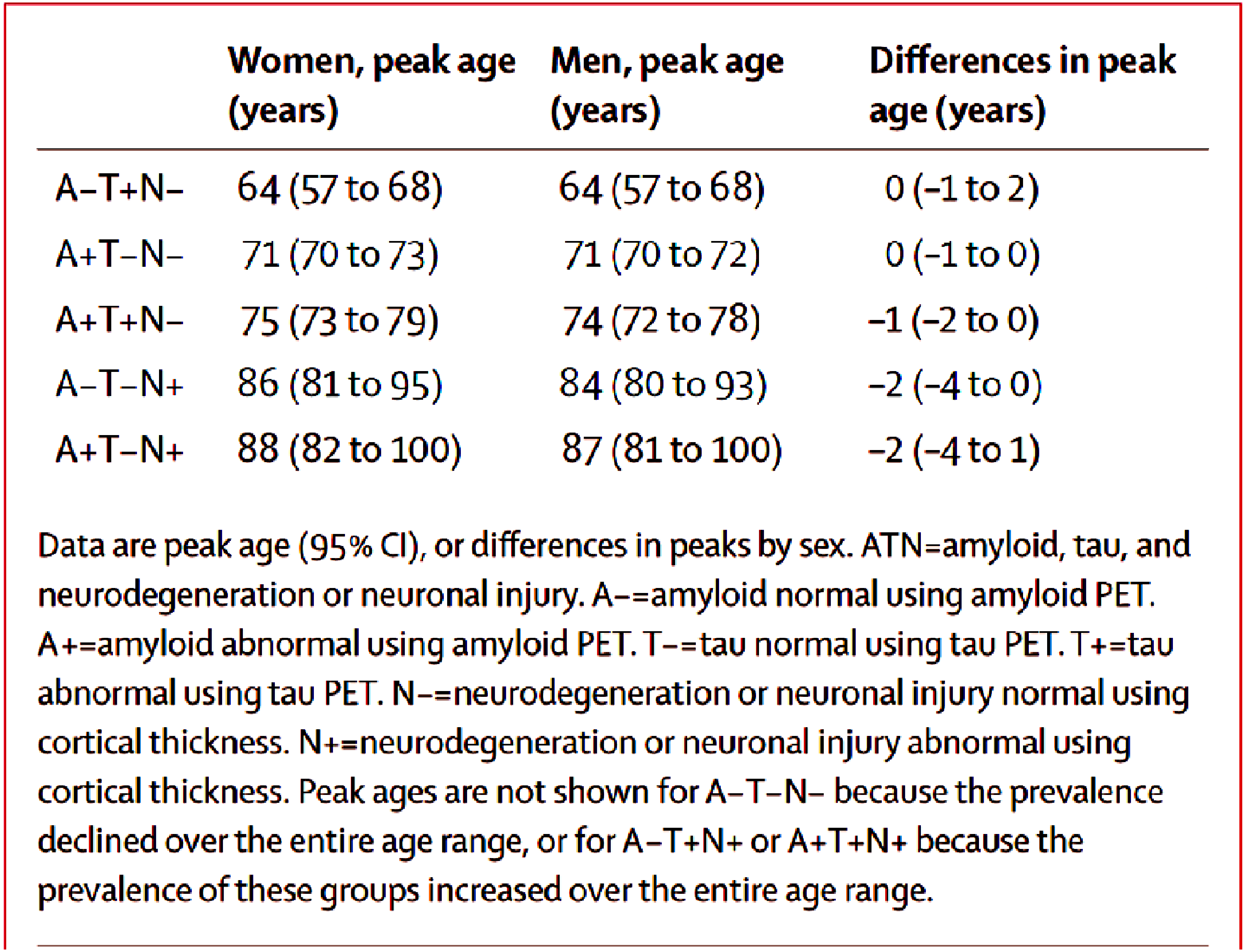
Methods All participants were in the Mayo Clinic Study of Aging, a population-based study that uses a medical records linkage system to enumerate all individuals aged 50–89 years in Olmsted County, MN, USA. Potential participants are randomly selected, stratified by age and sex, and invited to participate in cognitive assessments; individuals without medical contraindications are invited to participate in brain imaging studies. Participants who were judged clinically as having no cognitive impairment and underwent multimodality imaging between Oct 11, 2006, and Oct 5, 2016, were included in the current study. Participants were classified as having normal (A–) or abnormal (A+) amyloid using amyloid PET, normal (T–) or abnormal (T+) tau using tau PET, and normal (N–) or abnormal (N+) neurodegeneration or neuronal injury using cortical thickness assessed by MRI. We used the cutoff points of standard uptake value ratio (SUVR) 1·42 (centiloid 19) for amyloid PET, 1·23 SUVR for tau PET, and 2·67 mm for MRI cortical thickness. Age-specific and sex-specific prevalences of the eight groups were determined using multinomial models combining data from 435 individuals with amyloid PET, tau PET, and MRI assessments, and 1113 individuals who underwent amyloid PET and MRI, but not tau PET imaging.

Findings The numbers of participants in each profile group were 165 A–T–N–, 35 A–T+N–, 63 A–T–N+, 19 A–T+N+, 44 A+T–N–, 25 A+T+N–, 35 A+T–N+, and 49 A+T+N+. Age differed by ATN group (p<0·0001), ranging from a median 58 years (IQR 55–64) in A–T–N– and 57 years (54–64) in A–T+N– to a median 80 years (75–84) in A+T–N+ and 79 years (73–87) in A+T+N+. The number of *APOE* ε4 carriers differed by ATN group (p=0·04), with carriers roughly twice as frequent in each A+ group versus the corresponding A– group. White matter hyperintensity volume (p<0·0001) and cognitive performance (p<0·0001) also differed by ATN group. Tau PET and neurodegeneration biomarkers were discordant in most individuals who would be categorised as stage 2 or 3 preclinical Alzheimer's disease (A+T+N–, A+T–N+, and A+T+N+; 86% at age 65 years and 51% at age 80 years) or with suspected non-Alzheimer's pathophysiology (A–T+N–, A–T–N+, and A–T+N+; 92% at age 65 years and 78% at age 80 years). From age 50 years, A–T–N– prevalence declined and A+T+N+ and A–T+N+ prevalence increased. In both men and women, A–T–N– was the most prevalent until age late 70s. After about age 80 years, A+T+N+ was most prevalent. By age 85 years, more than 90% of men and women had one or more biomarker abnormalities.

Interpretation Biomarkers of fibrillar tau deposition can be included with those of β-amyloidosis and neurodegeneration or neuronal injury to more fully characterise the heterogeneous pathological profiles in the population. Both amyloid-dependent and amyloid-independent pathological profiles can be identified in the cognitively unimpaired population. The prevalence of each ATN group changed substantially with age, with progression towards more biomarker abnormalities among individuals who remained cognitively unimpaired.

Lancet Neurol 2017; 16: 435–44

Age at which the percentage of each ATN prevalence curve reaches its peak for women and men



	Women, peak age (years)	Men, peak age (years)	Differences in peak age (years)
A–T+N–	64 (57 to 68)	64 (57 to 68)	0 (–1 to 2)
A+T–N–	71 (70 to 73)	71 (70 to 72)	0 (–1 to 0)
A+T+N–	75 (73 to 79)	74 (72 to 78)	–1 (–2 to 0)
A–T–N+	86 (81 to 95)	84 (80 to 93)	–2 (–4 to 0)
A+T–N+	88 (82 to 100)	87 (81 to 100)	–2 (–4 to 1)

Data are peak age (95% CI), or differences in peaks by sex. ATN=amyloid, tau, and neurodegeneration or neuronal injury. A–=amyloid normal using amyloid PET. A+=amyloid abnormal using amyloid PET. T–=tau normal using tau PET. T+=tau abnormal using tau PET. N–=neurodegeneration or neuronal injury normal using cortical thickness. N+=neurodegeneration or neuronal injury abnormal using cortical thickness. Peak ages are not shown for A–T–N– because the prevalence declined over the entire age range, or for A–T+N+ or A+T+N+ because the prevalence of these groups increased over the entire age range.

(Clifford R Jack Jr. et al, Lancet Neurol 2017:16: 435-44)

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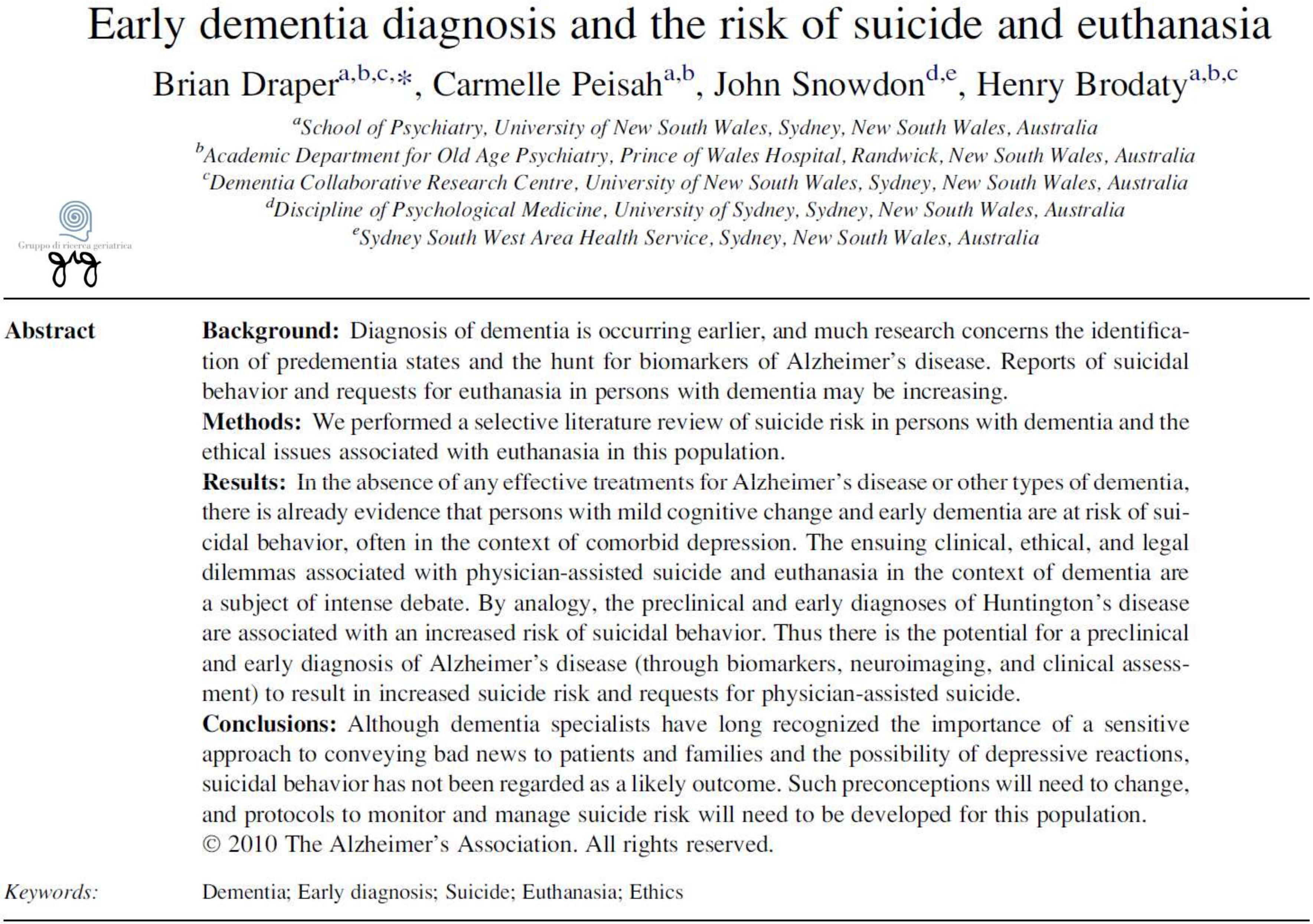
La complessità diagnostica e il suo significato clinico

The pros and cons of early diagnosis in dementia.

Chris Fox, Louise Lafortune, Malaz Boustani and
Carol Brayne

Br J Gen Pract 2013; 63 (612): e510-e512.



Early dementia diagnosis and the risk of suicide and euthanasia

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Abstract

Background: Diagnosis of dementia is occurring earlier, and much research concerns the identification of predementia states and the hunt for biomarkers of Alzheimer's disease. Reports of suicidal behavior and requests for euthanasia in persons with dementia may be increasing.

Methods: We performed a selective literature review of suicide risk in persons with dementia and the ethical issues associated with euthanasia in this population.

Results: In the absence of any effective treatments for Alzheimer's disease or other types of dementia, there is already evidence that persons with mild cognitive change and early dementia are at risk of suicidal behavior, often in the context of comorbid depression. The ensuing clinical, ethical, and legal dilemmas associated with physician-assisted suicide and euthanasia in the context of dementia are a subject of intense debate. By analogy, the preclinical and early diagnoses of Huntington's disease are associated with an increased risk of suicidal behavior. Thus there is the potential for a preclinical and early diagnosis of Alzheimer's disease (through biomarkers, neuroimaging, and clinical assessment) to result in increased suicide risk and requests for physician-assisted suicide.

Conclusions: Although dementia specialists have long recognized the importance of a sensitive approach to conveying bad news to patients and families and the possibility of depressive reactions, suicidal behavior has not been regarded as a likely outcome. Such preconceptions will need to change, and protocols to monitor and manage suicide risk will need to be developed for this population.

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Keywords: Dementia; Early diagnosis; Suicide; Euthanasia; Ethics

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Alzheimer's & Dementia 6 (2010) 75–82

La diagnosi precoce ed aspetti psicologici
(le paure preventive, la pressione per avere risposte anche privatamente, le ansie postdiagnosi,
la riorganizzazione del sistema famiglia, le incertezze sul futuro), lavorativi, assicurativi, sociali
(siamo tutti potenziali ammalati?)

LA PERSONA AFFETTA DA DEMENZA IN OSPEDALE

Marco Trabucchi

LE PROFESSIONI SANITARIE

Carocci Faber

2007

Ma gli ospedali italiani accolgono spesso pazienti senza diagnosi oppure senza che la diagnosi venga comunicata oppure senza che venga presa in considerazione dal personale.

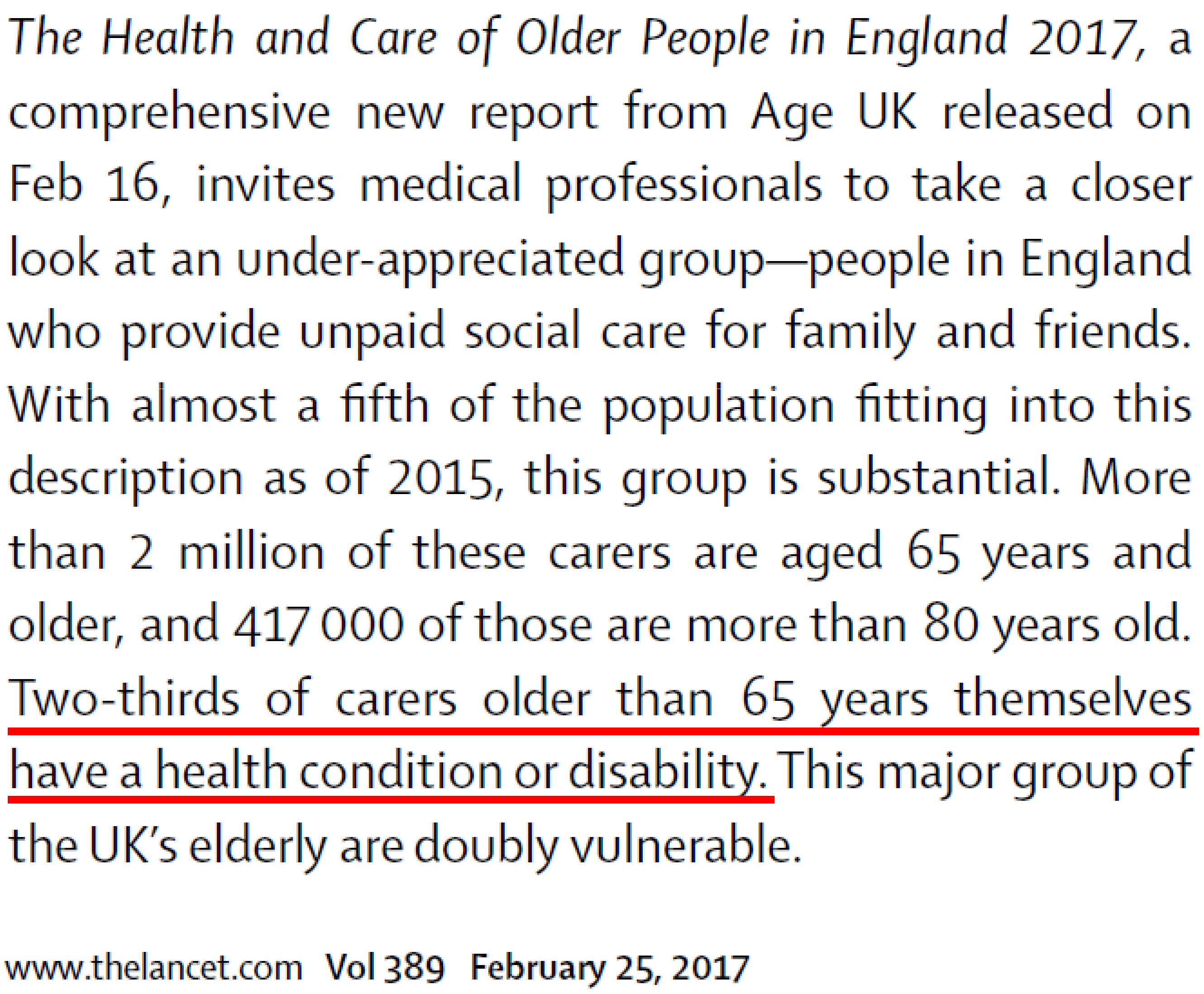
Codice blu:
Griglia di valutazione delle variabili associate alla fragilità dell’anziano

		No=0	Si=1
1.	Ha compiuto 75 anni?		
2.	Ha avuto un accesso in PS negli ultimi sei mesi?		
3.	E’ stato ricoverato in ospedale negli ultimi sei mesi?		
4.	Ha bisogno di qualcuno che gli prepari o somministri le medicine?		
5.	Ha bisogno di una persona che l’aiuti ad alzarsi dal letto o camminare?		
6.	E’ seguito dai servizi socio assistenziali (Centro diurno, casa protetta, RSA, SAD, ADI)?		
	Totale Codice blu se punteggio totale >3		☐ ☐

La diagnosi precoce è un evento che -seppure positivo, come dimostrato- comporta certamente una crisi nel vissuto dell’ammalato e della sua famiglia. E’ quindi opportuno che attorno a loro si sviluppi un’azione di “protezione”, sia sul piano psicologico sia su quello pratico.

L'esigenza di un sistema di counselling presente nei CDCD. L'intera equipe deve essere coinvolta.

Who cares for the carer?



The Health and Care of Older People in England 2017, a comprehensive new report from Age UK released on Feb 16, invites medical professionals to take a closer look at an under-appreciated group—people in England who provide unpaid social care for family and friends. With almost a fifth of the population fitting into this description as of 2015, this group is substantial. More than 2 million of these carers are aged 65 years and older, and 417 000 of those are more than 80 years old. Two-thirds of carers older than 65 years themselves have a health condition or disability. This major group of the UK's elderly are doubly vulnerable.

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Nel prossimo futuro sarà necessario affrontare i costi di diagnosi e terapie iniziate in età adulta e quindi di lunga durata, nonché molto costose.

L’appropriatezza diagnostica e terapeutica.

La Dementia Friendly Community potrebbe esercitare un'importante azione sinergica rispetto agli interventi clinici (riduzione dello stigma, facilitazione negli accessi ai servizi diagnostici, supporto nel mantenimento di uno stile di vita “normale”).