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La “terapia multifattoriale” nel deterioramento cognitivo dell’anziano: quali evidenze?

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Il deterioramento cognitivo e la pluralità delle sue determinanti.

La crisi del modello medico "semplice" di fronte alle malattie di origine incerta, di lunga durata, dall'evoluzione impredicibile, come sono quelle dell'anziano.

Genetica e stili di vita giocano un ruolo integrato, anche se ancora largamente inesplorato.
Il caso della riduzione dell'incidenza dell'Alzheimer.

A two-decade comparison of prevalence of dementia in individuals aged 65 years and older from three geographical areas of England: results of the Cognitive Function and Ageing Study I and II

Fiona E Matthews, Antony Arthur, Linda E Barnes, John Bond, Carol Jagger, Louise Robinson, Carol Brayne, on behalf of the Medical Research Council Cognitive Function and Ageing Collaboration

Summary

Background The prevalence of dementia is of interest worldwide. Contemporary estimates are needed to plan for future care provision, but much evidence is decades old. We aimed to investigate whether the prevalence of dementia had changed in the past two decades by repeating the same approach and diagnostic methods as used in the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS) in three of the original study areas in England.

Methods Between 1989 and 1994, MRC CFAS investigators did baseline interviews in populations aged 65 years and older in six geographically defined areas in England and Wales. A two stage process, with screening followed by diagnostic assessment, was used to obtain data for algorithmic diagnoses (geriatric mental state–automated geriatric examination for computer assisted taxonomy), which were then used to estimate dementia prevalence. Data from three of these areas—Cambridgeshire, Newcastle, and Nottingham—were selected for CFAS I. Between 2008 and 2011, new fieldwork was done in the same three areas for the CFAS II study. For both CFAS I and II, each area needed to include 2500 individuals aged 65 years and older to provide power for geographical and generational comparison. Sampling was stratified according to age group (65–74 years *vs* ≥75 years). CFAS II used identical sampling, approach, and diagnostic methods to CFAS I, except that screening and assessement were combined into one stage. Prevalence estimates were calculated using inverse probability weighting methods to adjust for sampling design and non-response. Full likelihood Bayesian models were used to investigate informative non-response.

Findings 7635 people aged 65 years or older were interviewed in CFAS I (9602 approached, 80% response) in Cambridgeshire, Newcastle, and Nottingham, with 1457 being diagnostically assessed. In the same geographical areas, the CFAS II investigators interviewed 7796 individuals (14 242 approached, 242 with limited frailty information, 56% response). Using CFAS I age and sex specific estimates of prevalence in individuals aged 65 years or older, standardised to the 2011 population, 8·3% (884 000) of this population would be expected to have dementia in 2011. However, CFAS II shows that the prevalence is lower (6·5%; 670 000), a decrease of 1·8% (odds ratio for CFAS II *vs* CFAS I 0·7, 95% CI 0·6–0·9, p=0·003). Sensitivity analyses suggest that these estimates are robust to the change in response.

Interpretation This study provides further evidence that a cohort effect exists in dementia prevalence. Later-born populations have a lower risk of prevalent dementia than those born earlier in the past century.

Funding UK Medical Research Council.

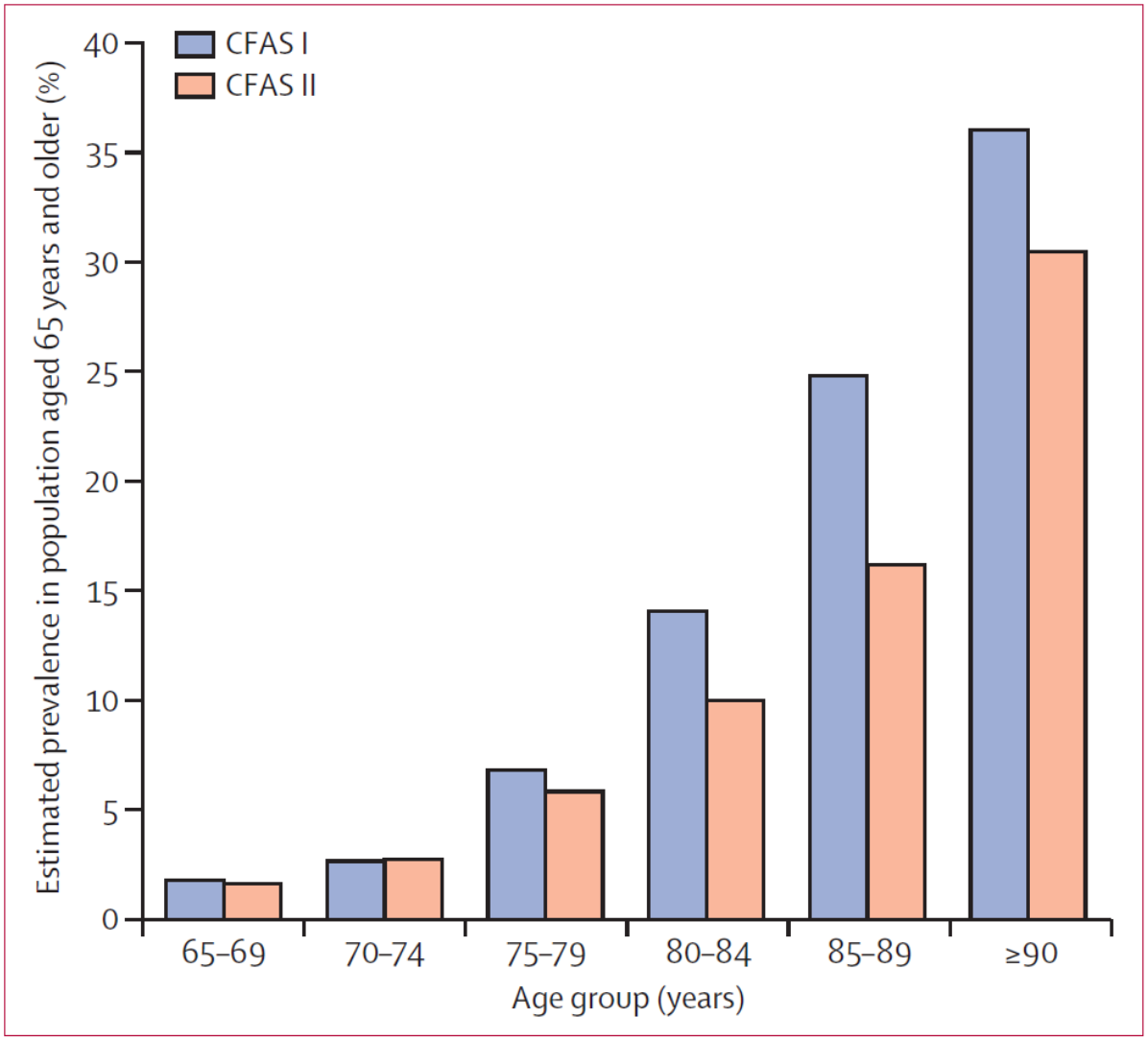

Figure 1: **CFAS I and CFAS II age-specific dementia prevalence**
CFAS=Cognitive Function and Ageing Study.

Fiona E Matthews, Antony Arthur, Linda E Barnes, John Bond, Carol Jagger, Louise Robinson, Carol Brayne, on behalf of the Medical Research Council Cognitive Function and Ageing Collaboration

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Physical and cognitive functioning of people older than 90 years: a comparison of two Danish cohorts born 10 years apart

Kaare Christensen, Mikael Thinggaard, Anna Oksuzyan, Troels Steenstrup, Karen Andersen-Ranberg, Bernard Jeune, Matt McGue, James W Vaupel

Summary

Background A rapidly increasing proportion of people in high-income countries are surviving into their tenth decade. Concern is widespread that the basis for this development is the survival of frail and disabled elderly people into very old age. To investigate this issue, we compared the cognitive and physical functioning of two cohorts of Danish nonagenarians, born 10 years apart.

Methods People in the first cohort were born in 1905 and assessed at age 93 years (n=2262); those in the second cohort were born in 1915 and assessed at age 95 years (n=1584). All cohort members were eligible irrespective of type of residence. Both cohorts were assessed by surveys that used the same design and assessment instrument, and had almost identical response rates (63%). Cognitive functioning was assessed by mini-mental state examination and a composite of five cognitive tests that are sensitive to age-related changes. Physical functioning was assessed by an activities of daily living score and by physical performance tests (grip strength, chair stand, and gait speed).

Findings The chance of surviving from birth to age 93 years was 28% higher in the 1915 cohort than in the 1905 cohort (6·50% *vs* 5·06%), and the chance of reaching 95 years was 32% higher in 1915 cohort (3·93% *vs* 2·98%). The 1915 cohort scored significantly better on the mini-mental state examination than did the 1905 cohort (22·8 [SD 5·6] *vs* 21·4 [6·0]; p<0·0001), with a substantially higher proportion of participants obtaining maximum scores (28–30 points; 277 [23%] *vs* 235 [13%]; p<0·0001). Similarly, the cognitive composite score was significantly better in the 1915 than in the 1905 cohort (0·49 [SD 3·6] *vs* 0·01 [SD 3·6]; p=0·0003). The cohorts did not differ consistently in the physical performance tests, but the 1915 cohort had significantly better activities of daily living scores than did the 1905 cohort (2·0 [SD 0·8] *vs* 1·8 [0·7]; p<0·0001).

Interpretation Despite being 2 years older at assessment, the 1915 cohort scored significantly better than the 1905 cohort on both the cognitive tests and the activities of daily living score, which suggests that more people are living to older ages with better overall functioning.

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	Both sexes			Men			Women		
	1905 cohort (n=1814)	1915 cohort (n=1247)	p value	1905 cohort (n=494)	1915 cohort (n=336)	p value	1905 cohort (n=1320)	1915 cohort (n=911)	p value
Cognitive composite score									
Mean (SD)	0·01 (3·6)	0·49 (3·6)	0·0003*	0·12 (3·6)	0·76 (3·6)	0·012*	−0·03 (3·6)	0·38 (3·6)	0·008*
Median (IQR)	0·05 (−2·25 to 2·26)	0·30 (−1·93 to 2·69)		0·09 (−2·23 to 2·30)	0·55 (−1·69 to 3·06)		0·05 (−2·25 to 2·24)	0·15 (−1·98 to 2·62)	..
Missing data, n (%)	30 (2%)	30 (2%)	0·146†	8 (2%)	6 (2%)	1·000†	22 (2%)	24 (3%)	0·130†
Mini-mental state examination results									
Mean (SD)	21·4 (6·0)	22·8 (5·6)	<0·0001‡	22·1 (6·0)	23·6 (5·8)	0·0003‡	21·2 (6·0)	22·5 (5·5)	<0·0001‡
Median (IQR)	23·0 (18·0–26·0)	24·0 (19·0–27·0)		24·0 (19·0–26·0)	25·0 (20·5–28·0)		23·0 (18·0–26·0)	24·0 (19·0–27·0)	
Missing data, n (%)	16 (1%)	24 (2%)	0·015†	2 (<1%)	4 (1%)	0·229†	14 (1%)	20 (2%)	0·035†
Grouped results, n (%)§			<0·0001†			<0·0001†			<0·0001†
0–17 (severe impairment)	400 (22%)	209 (17%)		86 (17%)	53 (16%)		314 (24%)	156 (18%)	
18–22 (mild impairment)	458 (25%)	281 (23%)		121 (25%)	60 (18%)		337 (26%)	221 (25%)	
23–27 (normal)	705 (39%)	456 (37%)		206 (42%)	112 (34%)		499 (38%)	344 (39%)	
28–30 (maximum)	235 (13%)	277 (23%)		79 (16%)	107 (32%)		156 (12%)	170 (19%)	
Depression symptomatology scores									
Mean (SD)	25·4 (6·3)	25·6 (6·3)	0·453*	24·8 (6·1)	24·9 (6·3)	0·928*	25·6 (6·3)	25·8 (6·4)	0·414*
Median (IQR)	24·0 (20·0–29·0)	24·0 (20·0–30·0)		24·0 (20·0–29·0)	24·0 (20·0–29·0)		24·0 (21·0–29·0)	25·0 (21·0–30·0)	
Missing data, n (%)	75 (4%)	22 (2%)	<0·0002†	23 (5%)	5 (1%)	0·017†	52 (4%)	17 (2%)	0·006†
Grouped results, n (%)§¶			0·173†			0·633†			0·281†
Score 17–20	438 (25%)	310 (25%)		135 (29%)	102 (31%)		303 (24%)	208 (23%)	
Score 21–24	504 (29%)	312 (25%)		133 (28%)	80 (24%)		371 (29%)	232 (26%)	
Score 25–29	389 (22%)	293 (24%)		103 (22%)	74 (22%)		286 (23%)	219 (24%)	
Score 30–50	408 (23%)	310 (25%)		100 (21%)	75 (23%)		308 (24%)	235 (26%)	

*Test of equal mean, with an assumption of equal variance (test of equal variance is not rejected). †Test of equal proportions (χ^2 test or Fisher's exact test). ‡Test of equal mean, without an assumption of equal variance (test of equal variance is rejected). §Missing data are excluded from the totals for percentage calculations. ¶Grouped by dividing the total distribution into quartiles.

Table 2: **Cognitive measures and depression symptomatology for the 1905 and 1915 cohorts (in-person participants only)**

ARTICLES

Is dementia incidence declining?

Trends in dementia incidence since 1990 in the Rotterdam Study

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ABSTRACT

Objective: To investigate whether dementia incidence has changed over the last 2 decades.

Methods: We compared dementia incidence in 2 independent subcohorts of persons aged 60–90 years from the Rotterdam Study, a population-based cohort study. The first subcohort started in 1990 (n = 5,727), the second in 2000 (n = 1,769). Participants were dementia-free at baseline and followed for at maximum 5 years. We calculated age-adjusted dementia incidence rates for the 2 subcohorts in total, in 10-year age strata, and for men and women separately. We also compared mortality rates, differences in prevalence of vascular risk factors, and medication use. Finally, we compared brain volumes and the extent of cerebral small vessel disease in participants who underwent brain imaging 5 years after the baseline examinations.

Results: In the 1990 subcohort (25,696 person-years), 286 persons developed dementia, and in the 2000 subcohort (8,384 person-years), 49 persons. Age-adjusted dementia incidence rates were consistently, yet nonsignificantly, lower in the 2000 subcohort in all strata, reaching borderline significance in the overall analysis (incidence rate ratio 0.75, 95% confidence interval [CI] 0.56–1.02). Mortality rates were also lower in the 2000 subcohort (rate ratio 0.63, 95% CI 0.52–0.77). The prevalence of hypertension and obesity significantly increased between 1990 and 2000. This was paralleled by a strong increase in use of antithrombotics and lipid-lowering drugs. Participants in 2005–2006 had larger total brain volumes ($p < 0.001$) and less cerebral small vessel disease (although nonsignificant in men) than participants in 1995–1996.

Conclusions: Although the differences in dementia incidence were nonsignificant, our study suggests that dementia incidence has decreased between 1990 and 2005. *Neurology*® 2012;78:1456–1463

Sube Banerjee

Dementia is a powerful example of the complexity and long-term nature of the disorders that are now the major outstanding challenges for health-care systems. Those with dementia are generally an old and frail population with multimorbidity; data from the Scottish School of Primary Care suggest that only 17% of people with dementia have no other long-term disorder. If we can get services right for dementia, then we will be a long way towards getting them right for all individuals with complex and long-term disorders. The CFAS results suggest that prevention is possible and that we can have agency in this most complex of disorders. These findings should spur us on, to go further and faster in secondary and tertiary prevention as well as primary prevention in dementia, for the benefit of all. This study shows that we can all make a difference.

Le modificazioni dell'incidenza sono attribuibili almeno in parte allo stile di vita migliorato e alla prevenzione delle malattie (in particolare quelle cardiovascolari e metaboliche).

21° Giornata Mondiale Alzheimer 2014

Un approccio terapeutico mirato deve tener conto delle molte variabili in gioco.
Il ruolo dei farmaci, dell'alimentazione, dell'attività motoria, di relazioni significanti ... nessuno in grado da solo di modificare la storia naturale, ma certamente capace di contribuire all'evoluzione della malattia.

La valutazione multidimensionale come premessa indispensabile per qualsiasi intervento.
Un bisogno complesso che richiede risposte integrate.

BMJ 2014;349:g4433 doi: 10.1136/bmj.g4433 (Published 8 July 2014)

FEATURE

ALZHEIMER'S DISEASE

Alzheimer's disease: still a perplexing problem

Funding for dementia research is being greatly increased in the UK. **Krishna Chinthapalli** examines the challenges after a century of frustratingly slow progress

Krishna Chinthapalli *associate editor, The BMJ and neurology specialty registrar, Royal Surrey County Hospital, UK*

We would like a cure to be available by 2025.
It's a big, big ambition to have.
If we don't aim for the stars we won't land on the moon.

To truly be a global response to the threat posed by dementia worldwide, future discussions and action plans must look beyond drugs, and include patients, carers, and developing countries.

(Editorial, Lancet 383(9936):2185, 2014)

“A larger vision and set of actions are needed to improve the lives of people with dementia and their carers worldwide” *(Editorial, Lancet 383(9936):2185, 2014).*

Il fallimento della prospettiva farmacocentrica ha spostato l'attenzione anche su altri obiettivi delle cure, con lo sviluppo di studi e ricerche significativi.

La centralità della relazione con l'ammalato di demenza per dare senso agli interventi di cura.

1. How to better support people with dementia to maintain their sense of uniqueness and personal identity (Respecting identity: 'It's not one size fits all')
2. Achieving the right balance between memory-based activities and enjoying the here and now (Embracing now: 'It's a moment-living life')
3. Ensuring people with dementia are able to experience meaningful human connections (Sustaining relationships: 'You don't always need words')
4. Ensuring people with dementia are able to experience a full range of emotions (Valuing contrast: 'Good days and bad days')
5. Taking risks - what are we protecting people with dementia from? (Supporting agency: 'What's there to worry about?')
6. Promoting good overall health for those who are living with dementia including physical and emotional wellbeing (Maintaining health: 'My priority in life').

(UK Alzheimer's Society, March 19, 2014)

The report of the UK Alzheimer Society, entitled "A good life with dementia", outlines a six-part framework for enabling a 'good life' with dementia – one rooted in universal notions of identity, happiness and fulfillment.

Come definire un percorso di cure che porti ad una "good life"?

La ricerca diretta a definire gli spazi per gli "small gains", che assumono un ruolo importante nell'interpretazione soggettiva del paziente e della sua famiglia:

- farmaci sintomatici
- alimentazione
- riduzione della disabilità e riabilitazione
- supporto alla famiglia
- controllo della patologia somatica