

Clinical implications

- The prevalence of asthma among children in Croydon has increased by 16% in the period 1978-91, a finding consistent with results of other studies in the United Kingdom
- This is likely to reflect changes in environmental factors which are, as yet, unknown
- In clear contrast there has been a substantial reduction by about half in the level of disability and of acute severe episodes
- This may be explained in part by more treatment and greater use of inhaled steroids in this population
- These findings indicate that the rising rates of hospital admissions for childhood asthma are unlikely to be explained by an increase in acute morbidity

decreased, perhaps because of the much higher level of treatment which now exists in this population. The occurrence of speech limiting attacks of asthma, an indicator of episodes which might be considered deserving of admission to hospital, has not increased substantially and may well have become much less common. These observations reinforce our earlier conclusion¹¹ that the recent rise in hospital admission rates for asthma in childhood has been influenced more by changes in medical care than by an increase in the prevalence or severity of asthma.

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Cardiovascular disease and distribution of cognitive function in elderly people: the Rotterdam study

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Abstract

Objective—To investigate the distribution of cognitive function in elderly people and to assess the impact of clinical manifestations of atherosclerotic disease on this distribution.

Design—Single centre population based cross sectional door to door study.

Setting—Ommoord, a suburb of Rotterdam, the Netherlands.

Subjects—4971 subjects aged 55 to 94 years.

Main outcome measure—Cognitive function as measured by the mini mental state examination.

Results—The overall participation rate in the study was 80%. Cognitive test data were available for 90% of the participants. Increasing age and lower educational level were associated with poorer cognitive function. Previous vascular events, presence of plaques in the carotid arteries, and presence of peripheral arterial atherosclerotic disease were associated with worse cognitive performance independent of the effects of age and education. On average the differences were moderate; however, they reflected the net result of a shift of the total population distribution of cognitive function towards lower values. Thereby, they resulted in a considerable increase in the proportion of subjects with scores indicative of dementia.

Conclusions—These findings are compatible with the view that atherosclerotic disease accounts for

considerable cognitive impairment in the general population.

Introduction

The incidence and severity of cognitive impairment and dementia strongly increase with age. Dementia is often labelled an age related disorder with the implicit suggestion that the decline in cognitive function may be intrinsic to aging itself. Many old people, however, show no mental decline at all.¹ In those instances when cognitive decline does occur, in general it develops insidiously and asymptotically before it reaches the clinical threshold at which it becomes manifest and is referred to as dementia. The division of populations into diseased versus normal tends to neglect this heterogeneity.^{2,3} It has therefore been suggested that research in degenerative disorders should focus not only on disease but also on the total distribution of health states.⁴ We present data on the distribution of cognitive function and on the impact of clinical manifestations of atherosclerotic disease on this distribution in a geographically defined sample of subjects aged 55 to 94 years.

Methods

STUDY POPULATION

The Rotterdam study is a single centre prospective follow up study for which the total population aged

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55 years or over, including institutionalised people, of the suburb of Ommoord in Rotterdam, the Netherlands, is studied. The study has been approved by the medical ethics committee of Erasmus University. Written informed consent is obtained from all participants. Rationale and design of the study have been described elsewhere.⁵ In short, the objective of the study is to investigate determinants of chronic and disabling cardiovascular, neurodegenerative, locomotor, and ophthalmological diseases. Independently living participants are extensively interviewed at home and are subsequently clinically examined during two visits to a research centre. For institutionalised people all examinations were performed in their institute. Enrolment in the study started in June 1990 and was based on random selection procedures. By 31 December 1992, 7120 residents of Ommoord had been invited and 5673 subjects had actually participated. The overall participation rate was 80%, similar for men and women. To guarantee adequate numbers for both sexes and all ages we confined our sample for this analysis to those aged 55 to 94 years, which left 5527 subjects. Of these, cognitive test data were available for 4971 (90%) and these data were included in the present analyses.

MEASUREMENTS

As part of the screening protocol for dementia, cognitive function of all participants was tested with the mini mental state examination during the first visit to the research centre.⁶ The examination contains 18 items that cover orientation, memory, attention, ability to follow commands, and copying a complex figure and yields a maximum score of 30 points.⁷ The test was administered by specially trained assistants.

Attained level of education was assessed by classifying formal schooling according to the standard classification of education used by the Netherlands Central Bureau of Statistics, which is comparable with the International Standard Classification of Education (UNESCO, Paris, 1976).⁸ For the present analyses subjects were grouped into those with at most primary education, those with junior vocational training, and those with senior vocational or academic training.

A history of stroke was assessed by direct questioning. For a diagnosis of stroke symptoms should have been present for at least 24 hours, and confirmation of the diagnosis by a treating physician was required. Presence of abnormalities that would suggest previous myocardial infarction were assessed on a 12 lead electrocardiogram by study physicians according to preset criteria with any suspected abnormality reviewed by a cardiologist. Atherosclerosis of the arteries of the lower legs and of the carotid arteries was non-invasively assessed with the use of Doppler and ultrasound. The ratio of the ankle to brachial systolic blood pressure (ankle-brachial index) is thought to reflect the presence of atherosclerotic abnormalities of the arterial walls in the lower extremities and has been shown to be a good indicator of generalised atherosclerosis.⁹ Ankle systolic blood pressure was determined with the subject in supine position at both right and left posterior tibial arteries with a Doppler ultrasound transducer by using a random zero sphygmomanometer (cuff size 38×14 cm). Arterial disease was considered present when the left or right ankle-brachial index was less than 0.90.^{10 11} Ultrasonography of both carotid arteries was performed with a 7.5 MHz linear array transducer and a duplex scanner (ATL UltraMark IV, Advanced Technology Laboratories, Bethel, Western Australia). Presence of atherosclerotic lesions, defined as a focal widening relative to adjacent segments with protrusion into the lumen, was assessed in the internal carotid arteries.

With respect to smoking behaviour subjects were categorised in groups of current smokers, former smokers, and those who had never smoked.

ANALYSIS

The total distribution of cognitive function in the population is presented graphically according to age, level of education, gender, vascular events, and indicators of atherosclerosis. For each of these characteristics the distribution of the mini mental state examination score among subjects with the characteristic was obtained by direct standardisation to the distribution of results in a reference population.¹² The reference populations for the distributions according to age, gender, and education were subjects aged 55 to 64 years, men, and lowest educational level, respectively. The reference populations for the distributions according to vascular events and atherosclerosis were subjects without the characteristic of interest. Distributions were standardised for age and gender.

In addition, we presented the distributions numerically. For each characteristic the mean score on the examination was calculated for those with and without the characteristic of interest. Because the distributions of scores were highly skewed to the left we further characterised them by calculating centile scores (5th, 25th, 50th, 75th, 95th).

An important question is how differences in scores should be interpreted. On an individual level a difference of, for example, one point cannot be considered clinically relevant and could easily be explained by inpatient variability. An average difference of one point on a population level, however, may have important clinical consequences. We substantiated the clinical relevance of the differences between distributions by calculating for each distribution the proportion of people who scored below cutoffs that have been recommended as suspect for dementia (scores of 24⁷ and 26¹³). The statistical significance of the difference between proportions scoring below the cutoff was assessed by multivariate logistic regression. Possible confounding by smoking was evaluated by adding this as a covariate (ever versus never; current versus never) to the multiple logistic regression models.

Although the overall response was reasonably high, the effective response rate was lower among older than younger subjects. Response rates were also higher among older subjects who were institutionalised than among their independently living contemporaries. To assess whether these differences could have biased our overall results we conducted additional analyses. Firstly, we evaluated whether the relations differed between younger (age 55 to 74 years) and older (age 75 to 94 years) subjects. Secondly, we compared the results in the oldest age group for institutionalised people with those for non-institutionalised people.

Results

Table I presents the age and gender distribution of the study population and the age specific participation rate and proportions of participants for whom cognitive test data were available. Total non-response increased with age as did the number of subjects who completed the interview but did not come to the research centre. Of the 4971 subjects for whom mini mental state examination scores were available, 1939 (39%) had attended only primary school or less, 1690 (34%) had junior vocational training, and 1342 (27%) had senior vocational training or academic training. Of this group, 249 (5%) had had a stroke, 348 (7%) had had myocardial infarction according to electrocardiographic readings, 1044 (21%) had peripheral

arterial disease, and 1790 (36%) had plaques in the internal carotid arteries on either or both sides.

Figure 1 depicts the population distribution of scores according to age, gender, and education. The upper panel shows that with increasing age the

TABLE I—Age specific participation rates and age and gender of participants

Age (years)	Participation rate (%)	No of subjects included in study			Availability of mini mental state examination scores (%)
		Men	Women	Total	
55-59	85	260	413	673	95
60-64	85	392	555	947	95
65-69	83	440	582	1022	93
70-74	83	378	591	969	91
75-79	76	296	494	790	89
80-84	72	175	406	581	86
85-89	70	84	292	376	74
90-94	76	25	144	169	69
Total	80	2050	3477	5527	90

TABLE II—Characteristics of distribution of cognitive function among subjects aged 55 to 94 years according to age, gender, and education

Variable	Mean mini mental score	Centiles of distribution of mini state examination scores					Proportion below cutoff (%)			
		5th	25th	50th	75th	95th	<24	P value*	<26	P value*
Age (years):										
55-64	28.1	25	27	28	29	30	1.8		5.2	
65-74†	27.8	25	27	28	29	30	3.0		8.1	
75-84†	26.6	22	26	28	29	30	7.8		17.1	
85-94†	23.1	16	22	26	28	30	31.1	0.0001‡	43.4	0.0001‡
Education:										
Primary school	26.3	20	25	27	28	30	12.5		25.4	
Junior vocational training§	27.6	23	26	28	29	30	5.2		13.6	
Senior vocational training/university§	28.0	24	27	28	29	30	3.7	0.0001‡	9.2	0.0001‡
Men	27.5	23	27	28	29	30	5.2		11.0	
Women	27.3	22	27	28	29	30	7.9	0.44	14.5	0.11

*Based on multiple logistic regression analysis.

†Standardised for gender and education to distribution among subjects aged 55 to 64 years.

‡Test for trend.

§Standardised for age and gender to distribution among subjects with at most primary school.

||Standardised for age and education to distribution among men.

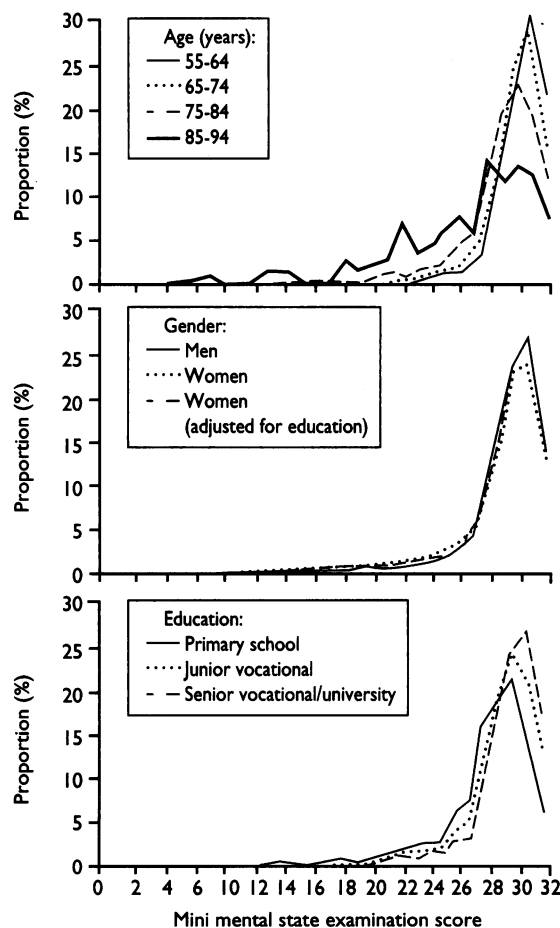


FIG 1—Distribution of cognitive function as measured by mini mental state examination among subjects aged 55 to 94 years according to age, gender, and education. Distributions for subjects aged 65 to 94 years standardised for gender and education to that for subjects aged 55 to 64 years; distributions for higher education standardised for age and gender to that for subjects with at most primary school; distribution for women standardised for age and education to that for men

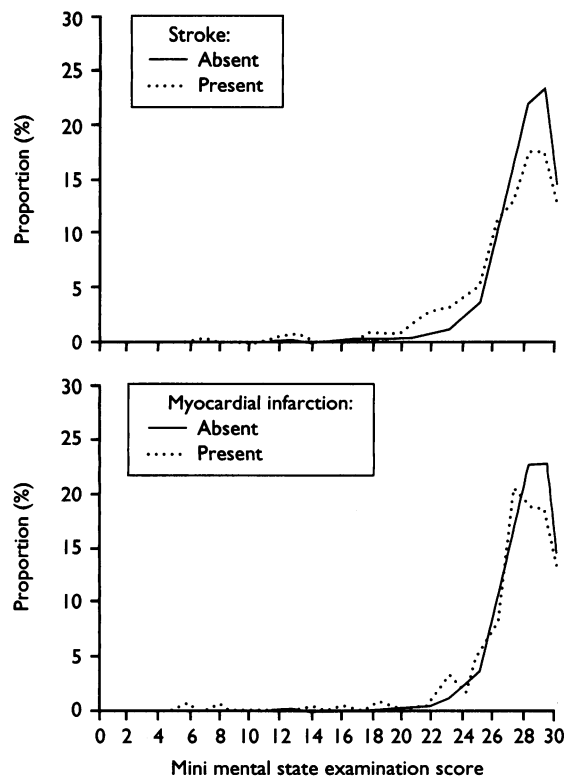


FIG 2—Distribution of cognitive function as measured by mini mental state examination among subjects aged 55 to 94 years according to previous vascular event (stroke or myocardial infarction). Distributions for subjects with previous vascular event standardised for age and gender to those for subjects without

distributions shifted toward lower values whereas their skew increased, reflecting increasing variability. The distributions for men and women overlapped almost completely, in particular when education was taken into account (fig 1, middle panel). The distributions by education are shown in the lower panel. Subjects with higher education performed better, as shown by a total shift of their distributions towards higher scores, and with less variability.

Table II further quantifies these distributions. The differences in mean scores across age and education and between men and women reflect the average shift of the distributions relative to that of their reference group. For subjects aged 85 to 94 years compared with subjects aged 55 to 64 years it was 5.0 points, for highly educated people compared with people with at most primary school education it was 1.7 points, and for women compared with men it was 0.2 points. The variability in the distributions is reflected in the range between the 5th and the 95th centile; the larger this range the more variation exists between people. In all instances a shift of the distribution towards lower values was accompanied by an increase in the variability, and the combined effect thereof was a considerable increase in the proportion of people scoring below the cutoffs.

Figure 2 compares the cognitive performance among subjects with and without a previous vascular event. Both a history of stroke and electrocardiographic evidence of a previous myocardial infarction were associated with a shift of the population distribution of scores toward lower values. A similar pattern was observed for presence versus absence of atherosclerotic disease, either localised in the carotid arteries or in the large vessels of the lower extremities (fig 3). Table III gives the quantitative data regarding these distributions. As can be seen from the range between the 5th and 95th centiles of the distributions shifts of the total distribution towards lower values were again accompanied by an increase in variability. Correspondingly, the proportion of subjects scoring below the

cutoffs of 24 or 26 on the mini mental state examination increased.

When we included current or ever smoking in the multiple logistic regression models with which we compared subjects below and above the cutoffs on the examination, the odds ratios for the various vascular determinants barely changed, suggesting that there was no confounding in our data due to smoking.

Subanalyses of the results among younger versus older subjects and among institutionalised versus non-institutionalised people did not show any substantial differences.

Discussion

We presented the distributions of cognitive function in a geographically defined population of subjects aged 55 to 94 years according to age, gender, and education and the influence of clinical manifestations of atherosclerotic disease on these distributions. We found that for subjects who were older, less well educated, and had vascular and atherosclerotic disease the distributions were shifted toward lower values and the variability was increased whereas gender had almost no effect on the localisation or shape of the distribution.

Before discussing our findings, we must consider whether non-response may have influenced our results.

The overall participation rate in our study was high (80%) and so was the overall availability of cognitive test results (90%). Furthermore, institutionalised people were included in our study and the participation rate among them was high (83%). Although high response rates diminish the possibility of serious distortion of the study results, among independently living people non-response increased with age, and part of this non-response was probably selective and related to physical or mental morbidity. The associations that we observed among older subjects, however, were similar to those among younger subjects for whom response rates were highest. Furthermore, the results were similar for institutionalised and independently living people. This suggests that the differences in effective response rates according to age did not introduce additional bias. We think the most plausible pattern of selective non-response is that it increased with increasing impairment particularly when there was a combination of physical and mental handicaps. Therefore, we consider it most likely that if selective non-response has biased our findings it resulted in an underestimation of the strength of the relations that we investigated.

The negative associations between age and cognitive performance and between education and cognitive test performance are well recognised.¹⁴⁻¹⁶ Most previous studies presented summary results. One study of 365 people presented information on the total distribution of cognitive function and concluded that with less education the distribution was shifted downwards but similarly shaped.^{17,18} Our results confirmed the previous reports but showed in addition that with a decrease in average performance the shape of the distributions changed owing to increasing variability among individual people. With regard to age an explanation for this finding could be that cognitive decline is not intrinsic to aging but rather that age is a proxy for accumulated lifetime exposures affecting cognitive function.

One putative risk factor for cognitive decline is vascular disease, in particular atherosclerosis.^{19,20} We found that previous vascular events and presence of atherosclerosis were associated with a shift of the total population distribution towards lower levels. The mean difference, however, was less than one point on the mini mental state examination, which raises the question of whether this is clinically relevant. The answer is not to be found on the individual level but rather on the population level. The mean difference reflects the aggregate experience of people with a large decline and of those with no decline at all. This study does not indicate which people suffered cognitive impairment as a result of vascular disease. These findings, however, are compatible with the view that on a population level atherosclerotic disease can account for considerable cognitive impairment as reflected by the shifts and change in shape of the distribution and the increasing proportion of subjects scoring below a specified cutoff. In most cases vascular events such as stroke and myocardial infarction reflect a near end stage of atherosclerotic disease. Therefore, it is not surprising that these were associated with a larger population shift in cognitive performance than mere presence of atherosclerosis. It should be noted that, whereas stroke and myocardial infarction were present in 5% and 7% of the population, respectively, one fifth to one third of the population had evidence for atherosclerosis in the peripheral or carotid arteries. This suggests that the total impact of atherosclerosis on the amount of cognitive impairment in the population at large may be much greater than that contributable to severe atherosclerosis resulting in clinically overt disease.

A question that remains to be answered is whether

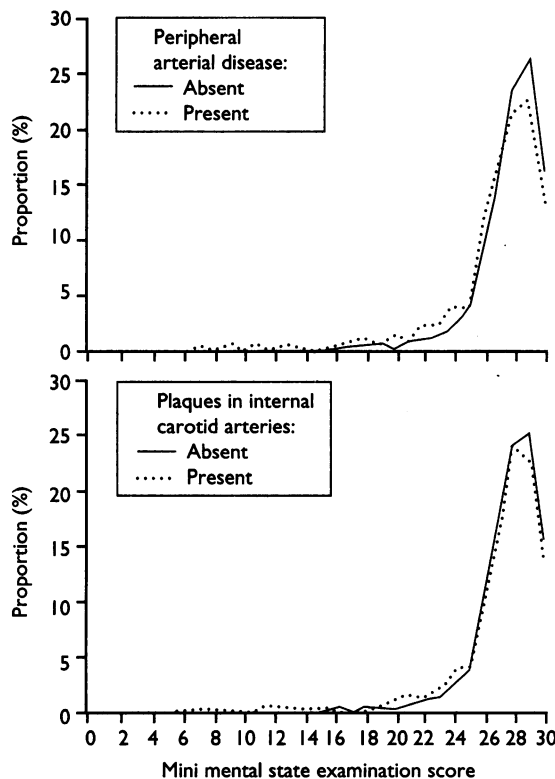


FIG 3—Distribution of cognitive function as measured by mini mental state examination among subjects aged 55 to 94 years according to presence or absence of atherosclerotic disease (peripheral arteries, carotid arteries). Distributions for subjects with atherosclerosis standardised for age and gender to those for subjects without

TABLE III—Characteristics of distribution of cognitive function among subjects aged 55 to 94 years according to presence or absence of vascular disease adjusted for age, gender, and education

Variable	Mean mini mental score	Centiles of distribution of mini mental state examination scores					Proportion below cutoff (%)			
		5th	25th	50th	75th	95th	<24	P value*	<26	P value*
History of stroke:										
No	27.4	23	27	28	29	30	6.5		13.5	
Yes	26.5	19	25	27	29	30	15.5	<0.0001	25.6	<0.0001
Electrocardiographic evidence of myocardial infarction:										
No	27.4	23	27	28	29	30	5.6		12.5	
Yes	26.7	20	26	28	29	30	11.3	0.0030	19.0	0.0078
Peripheral arterial disease:										
No	27.6	24	27	28	29	30	5.0		11.1	
Yes	26.8	20	26	28	29	30	10.4	0.0001	17.5	<0.0001
Plaques in internal carotid arteries:										
No	27.7	24	27	28	29	30	4.5		10.4	
Yes	27.3	22	26	28	29	30	7.3	0.0024	14.6	0.0010

*Based on multiple logistic regression analysis.

Clinical implications

- An increasing number of people are suffering from dementia or cognitive decline yet effective treatment is still lacking
- Intervention on vascular causes of dementia may be feasible
- This study suggests that cognitive decline is not synonymous with age but is associated with age related diseases
- Atherosclerosis results in a considerable increase in the proportion of cognitively impaired subjects in the population
- The most rational approach to prevent cognitive decline resulting from vascular causes is by mass intervention

the prevention of atherosclerosis would result in the otherwise affected subjects assuming the distribution of the now unaffected people. If so this could mean a major health benefit. Although the average gain per person would be small, the population gain might be substantial.⁴ It seems timely to conduct a study to investigate whether intervention on risk factors for atherosclerosis can prevent cognitive decline on a population level.

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Use of sinus x ray films by general practitioners

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Recent guidelines published by the Royal College of Radiologists suggest that plain sinus radiography is not indicated in the routine management of sinusitis and should be requested only by specialists.¹ This approach may be justified by the large radiation exposure (equivalent to five chest x ray procedures) and by the finding of abnormalities on x ray films of the sinus in up to half of the population.^{2,3} We assessed the prevailing use of sinus x ray films by general practitioners and surveyed current practice in sinus examination in radiology departments in the United Kingdom.

Methods and results

All 694 general practitioners in Greater Glasgow were sent a postal questionnaire asking about their use and interpretation of sinus x ray films. The routine sinus x ray views used in 50 hospitals throughout the United Kingdom (19 teaching, 29 district, two paediatric) were also surveyed.

Responses were received from 584 general practitioners (84%). Of these, only 136 (23%) never requested sinus x ray films. Most of the remainder requested an estimated one to three (286) or three to five (109) annually. The table gives the indications selected by the 448 regular users from those listed.

Most believed that sinus radiography was occasionally (269) or always (116) indicated when a patient was referred to an otorhinolaryngology specialist. Of the suggested findings, the four most likely to influence management were antral opacity (349), deviated nasal septum (345), frontal opacity (336), and nasal polyps (332). Sinus haziness, ethmoid mucosal thickening, and ethmoid disease were much less likely to influence management.

Half of the 50 radiology departments provided general practitioners with one occipitometrial view; the rest used this with occipitofrontal (13), lateral (three), or both (eight) views. One (children's) department did not accept direct requests from general practitioners. Eight departments provided a greater number of views (up to four) for otorhinolaryngologists than they did for general practitioners.

Comment

The excellent response to our survey indicates much interest in this subject among general practitioners, over three quarters of whom used sinus radiography. Is the investigation helpful? The commonest indication was persistent facial pain. If this is due to chronic rhinosinusitis, it is usually associated with other symptoms. Patients with recurrent attacks of acute sinusitis could have radiographs taken during remission of symptoms. In any case, the single view offered to general practitioners by half of the radiology departments surveyed shows adequately only one of the four main paranasal sinuses (the maxillary antra), whose x ray appearances differ from findings at antroscopy in over half of patients.⁴ The third most common

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