

Bulletin Board

Cholesterol and blood pressure-lowering drugs should be available to everyone over the age of 55 years, a controversial study recommends

The results of a recently published *PLOS* study have led the authors to suggest that everyone over the age of 55 years should be offered preventative treatments for stroke and heart disease, with no further screening carried out.

The study compared the current screening methods, which consider gender, blood pressure, cholesterol level and whether or not the individual is a smoker, to a more blanket approach, where everyone over the age of 55 years was offered the drugs.

The results indicate that both approaches had an 84% detection rate and broadly similar false-positive rates. Screening by age alone would incorrectly diagnose 24% of people as being at risk of heart problems, whereas existing methods of screening identified 21% of false positives.

Lead author Nicholas Wald from the Wolfson Institute at Barts and the London Medical School, UK, advocates that, "this study shows that age screening for future cardiovascular disease is simpler than current assessments, with a similar screening performance and cost–effectiveness. It also avoids the need for blood tests and medical examinations".

He explains that, "the policy of selecting people above a certain age is, in effect, selecting people at high risk. It recognizes that age is by far the most important determinant of that risk, with other factors adding little extra prognostic information".

However, although the authors of the study recommend that this course of action would be more time- and cost-effective, it seems that there is widespread concern that many people will be unwilling to take drugs to prevent an illness that they are at no greater risk of developing than anyone else their age.

The UK Department of Health released a statement of caution; "This study looked at the risk of cardiovascular disease alone – a narrower focus than the NHS Health Check programme, which also identifies those at risk of diabetes and chronic kidney disease.

"We start risk assessment at age 40 years. Blood pressure, cholesterol, height, weight and whether people smoke are all considered. This group of simple measurements, along with age, sex and ethnicity, are used to assess risk.

"The NHS Health Check programme is based on evidence of how to measure and tackle risk – and underpinned by modeling that demonstrates it is clinically and cost effective".

The UK Department of Health state that "we agree that we must focus on prevention".

It is widely acknowledged that there is a need to improve prevention of diseases such as stroke and heart disease. "Identifying people at high risk of cardiovascular disease needs to be greatly simplified, enabling people to obtain easy access to preventive treatment from nurses and pharmacists as well as from doctors", Wald argues.

Source: Wald NJ, Simmonds M, Morris JK: Screening for future cardiovascular disease using age alone compared with multiple risk factors and age. *PLoS ONE* 6(5), e18742 (2011).

Aging HEALTH

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Comparison trial indicates bevacizumab may be as effective as ranibizumab for treating age-related macular degeneration

A more cost-effective drug has been found to give similar results as conventional treatment for age-related macular degeneration (AMD).

The *New England Journal of Medicine* published study, part of the Comparison of AMD Treatments Trials (CATT), compared ranibizumab (Lucentis®), an US FDA-approved therapy for AMD with bevacizumab (Avastin®), a common therapy for colorectal cancer which is used off-label to treat age-related macular degeneration, and showed both drugs to have equivalent effectiveness when administered in the same way.

The news is being greeted with much enthusiasm as, while the drugs demonstrate similar efficacy, they have very different prices. The cancer therapy bevacizumab costs around US$50 per dose, in comparison to Lucentis which comes in at roughly four-times the price.

Suresh Chandra, leader of the University of Wisconsin School of Medicine-Madison center of clinical trials comments, "this is wonderful, it could result in billions of savings for the Medicare program". He continues, highlighting how the reduction in financial burden of AMD treatment could help healthcare in the third world, "it also has important implications for patients in developing countries where they just can't afford Lucentis".

> "However, the study did highlight that bevacizumab treatment had a greater risk of severe adverse events than ranibizumab treatment."

The CATT was launched in 2008 by the National Eye Institute in order to compare the effectiveness of bevacizumab and ranibizumab. A total of 1208 patients with neovascular AMD were enrolled in the multicenter, single-blind, noninferiority trial and randomized to receive intravitreal injections of either ranibizumab or bevacizumab. Injections were on a monthly basis, or as needed following monthly evaluation. The primary end point was the average change in visual acuity after 1 year, measured by letters gained on an eye-chart test. The results so far show that improvements in visual acuity are virtually equivalent for either drug for monthly and as-needed doses, with the improvements being within one letter on the eye chart. However, the study did highlight that bevacizumab treatment had a greater risk of severe adverse events than ranibizumab treatment. These events were observed in disease categories that had not been highlighted as potential risk factors in previous studies.

The researchers will follow the participants for another year to elucidate long-term effects of both therapies as well as studying the difference in the rates of serious adverse events.

Sources: The CATT Research Group: Ranibizumab and bevacizumab for neovascular age-related macular degeneration. *N. Engl. J. Med.* 364(20), 1897–1908 (2011); Avastin works well against age-related macular degeneration: www.med.wisc.edu/news-events/news/avastin-works-well-against-age-related-macular-degeneration/31287

Alzheimer's diagnostic guidelines introduced for the first time in nearly 30 years

It has been 27 years since the last clinical diagnostic criteria for Alzheimer's disease dementia were published, so the recent revisions published online in *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* have been long awaited.

The National Institute on Aging/Alzheimer's Association Diagnostic Guidelines for Alzheimer's Disease reflect current knowledge in the field and outline more advanced guidance for clinicians and researchers on the diagnosis and treatment of Alzheimer's disease.

> "...topics now addressed include the use of imaging and biomarkers in blood and spinal fluid that are employed in the research setting to detect onset of the disease and to track progression."

The original criteria only addressed the later stages of the disease, once symptoms of dementia had already become evident, whereas the updated guidelines describe the full spectrum of the disease from the earliest preclinical stages of the disease, mild cognitive impairment, through to dementia due to Alzheimer's pathology. Other topics now addressed include the use of imaging and biomarkers in blood and spinal fluid that are employed in the

research setting to detect onset of the disease and to track progression.

The guidelines were put together by a team of experts from National Institute on Aging (NIA), part of the NIH, and the Alzheimer's Association in 2010 and were first announced at the Association's International Conference on Alzheimer's Disease in July 2010, but were officially released in April 2011.

"Alzheimer's research has greatly evolved over the past quarter of a century. Bringing the diagnostic guidelines up to speed with those advances is both a necessary and rewarding effort that will benefit patients and accelerate the pace of research", explained the NIA Director Richard J Hodes.

"We believe that the publication of these articles is a major milestone for the field", said William Thies, chief medical and scientific officer at the Alzheimer's Association. "Our vision is that this process will result in improved diagnosis and treatment of Alzheimer's, and will drive research that ultimately will enable us to detect and treat the disease earlier and more effectively. This would allow more people to live full, rich lives without or with a minimum of Alzheimer's symptoms".

Source: Clifford JR Jr, Albert M, Knopman DS *et al.*: Introduction to the recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *The Journal of the Alzheimer's Association* 7(3), 257–262 (2011).

Results from the Phase III ORAL Standard and ORAL Step studies demonstrate promise for tofacitinib as a treatment for rheumatoid arthritis

Pfizer have announced top-line results from two pivotal Phase III studies of its investigational, novel oral JAK inhibitor, tofacitinib. Both the ORAL Standard and ORAL Step studies met their primary end points and demonstrated no new safety concerns regarding the use of tofacitinib in patients with active rheumatoid arthritis (RA). ORAL Standard and ORAL Step are the final two pivotal trials in a program designed by Pfizer to study tofacitinib for RA. The program consists of five pivotal trials and a sixth long-term treatment study carried out at more than 350 locations in 35 countries worldwide.

The 12-month ORAL Standard trial enrolled 717 patients with moderate-to-severe active RA who had an inadequate response to methotrexate (MTX). Patients were randomized to receive tofacitinib 5 or 10 mg b.i.d., adalimumab 40 mg subcutaneously every other week or placebo, each of which was added to stable background MTX. All primary end points of the study were met, demonstrating statistically significant changes versus placebo in reducing the signs and symptoms of RA as measured by ACR20 response rates at 6 months, in improving physical function, as measured by mean change in HAQ DI at 3 months; and in reaching DAS28-4(ESR) <2.6 at 6 months.

> "Both the ORAL Standard and ORAL Step studies met their primary end points and demonstrated no new safety concerns regarding the use of tofacitinib in patients with active rheumatoid arthritis."

The ORAL Step study was conducted over a 6-month period and enrolled 399 patients with moderate-to-severe active RA who had an inadequate response to a TNF-inhibitor. Patients were randomized to receive tofacitinib 5 or 10 mg b.i.d. or placebo, which were added to stable background MTX. As with the ORAL Standard study, all primary end points of the ORAL Step were met, at both the 5 and 10 mg b.i.d. doses. Tofacitinib demonstrated statistically significant changes versus placebo in reducing signs and symptoms of RA, as measured by ACR20 response rates; in improving physical function, as measured by mean change in HAQ DI; and in reaching DAS28-4(ESR) <2.6, all assessed at 3 months.

A more detailed analysis of the ORAL Standard and ORAL Step efficacy and safety data is likely to be presented at a scientific meeting in the near future.

Source: Pfizer newsroom: www.pfizer.com/news/press_releases/pfizer_press_releases.jsp#guid=20110428005895en&source=RSS_2011&page=1

About the Bulletin Board

The Bulletin Board highlights some of the most important events and research in the field of aging health. If you have newsworthy information, please contact:

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Potential for an α-synuclein antibody-based diagnostic test for Parkinson's disease

A group of scientists from Umeå University, Sweden, have found antibodies against a key amyloid producing protein implicated in Parkinson's disease. It is hoped that detecting levels of these antibodies in patients sera could be used as a diagnostic marker for the condition prevalent in the elderly population.

Diagnostic markers of neurodegenerative diseases such as Parkinson's disease are crucial as it is important to diagnose the condition early so that any potential therapeutic intervention can help slow down further nerve damage.

The group measured autoantibodies against α-synuclein a major amyloidogenic protein involved in Parkinson's disease in the blood of patients with early and late Parkinson's disease and in healthy controls. The antibodies were measured using ELISA, western blot and Biacore surface plasmon resonance. The group found significantly higher antibody levels against α-synuclein in Parkinson's disease patients as compared with the healthy controls although levels did decrease with increasing severity of disease. The authors, led by Ludmilla Morozova-Roche (Umeå University), note that "α-synuclein can be of value in the development of treatment and diagnostic strategies, especially during the early disease stages".

A diagnostic test assessing α-synuclein antibody levels would only require a blood sample and as such would be clinically very useful.

Source: Yanamandra K, Gruden MA, Casaite V, Meskys R, Forsgren L, Morozova-Roche LA: α-synuclein reactive antibodies as diagnostic biomarkers in blood sera of parkinson's disease patients. *PLoS ONE* 6(4), e18513 (2011).