RSNA Press Release

Lower Bone Density Linked to Cognitive Decline

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OAK BROOK, Ill. – Researchers at Johns Hopkins University found that lower bone mineral density in the spine was associated with faster cognitive decline and accelerated age-related white matter injury, according to a new study published today in *Radiology*, a journal of the Radiological Society of North America (RSNA).

Bone mineral density measures the amount of minerals, such as calcium, within a certain volume of bone. When bone mineral density is low, bones become weaker and more likely to break. However, there is limited research analyzing the relationship low bone density may have with brain function.

A multidisciplinary research team led by Sara Momtazmanesh, M.D., postdoctoral research fellow in the Department of Radiology and Radiological Sciences at Johns Hopkins University in Baltimore, Maryland, conducted a secondary analysis of data from the Multi-Ethnic Study of Atherosclerosis (MESA). Participants underwent non-contrast chest CT, multimodal brain MRI and cognitive testing.

The researchers used a deep learning algorithm developed in the Johns Hopkins University lab of Shadpour Demehri, M.D., professor of radiology, to calculate baseline thoracic vertebral volumetric bone mineral density (vBMD) derived from the non-contrast chest CT scans of 2,086 MESA participants. The final study cohort included 715 participants with an established vBMD who underwent both MRI and cognitive testing.

MRI exams were analyzed for white matter hyperintensities and reduced fractional anisotropy, microstructural brain changes that are associated with cognitive decline and increased dementia risk. Longitudinal data for white matter hyperintensities and fractional anisotropy were available for 408 and 405 participants, respectively.

The results showed that lower baseline vBMD was associated with faster decline in global cognition.

The researchers observed associations in specific brain regions: lower vBMD was associated with white matter hyperintensities accumulation in the corpus callosum, which supports executive functioning, working memory and attention. Lower vBMD was also associated with a steeper decline in total white matter fractional anisotropy in the anterior limb of the internal capsule, which is also involved in executive function.

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"This study is the first longitudinal secondary analysis linking baseline vertebral bone mineral density to changes in white matter structure, white matter hyperintensity progression and cognition," Dr. Demehri said. "This comprehensive study using both imaging and clinical assessments sends a clear signal that bone density at baseline is associated with both functional and imaging measures of age-related brain degeneration."

The researchers cautioned that the findings do not suggest that osteoporosis causes dementia.

"This study is not about cause and effect, but rather the observation of a metabolic syndrome that may cause both bone and brain degeneration," Dr. Demehri said. "The co-occurrence observed in the study may reflect shared metabolic drivers of aging, including insulin resistance, dyslipidemia, and menopausal change, rather than a direct bone-to-brain effect."

The researchers said identifying individuals with low vBMD may help flag those at risk for parallel skeletal and neurologic decline, allowing earlier screening and shared risk-factor management.

"Chest CT is done for lung cancer screening, calcium scoring, nodule follow-up, and many other indications, Dr. Momtazmanesh said. "These scans could provide an opportunistic measurement of bone density from the thoracic spine that is associated with a loss of cognitive function."

Dr. Demehri concurred: "Diagnostic images contain an immense amount of data that AI can now synthesize at scale across multiple organ systems. This creates a robust, newly feasible opportunity to interconnect co-existing age-related pathologies that have traditionally been studied in isolation and to identify shared biological pathways and potential common causal mechanisms."

"Deep Learning-derived Bone Mineral Density and Longitudinal White Matter Microstructure and Cognitive Decline: Multi-Ethnic Study of Atherosclerosis." Collaborating with Drs. Demehri and Momtazmanesh were Quincy A. Hathaway, M.D., Ph.D., Michael P. Bancks, Ph.D., M.P.H., David A. Bluemke, M.D., M.S.B., Ph.D., R. Graham Barr, M.D., Dr.P.H., Wendy S. Post, M.D., M.S., Mohamad Habes, Ph.D., Ilya Nasrallah, M.D., Ph.D., Susan R. Heckbert, M.D., Ph.D., R. Nick Bryan, M.D., Ph.D., Jose A. Luchsinger, M.D., M.P.H., Mei Wan, Ph.D., Matthew Budoff, M.D., João A. C. Lima, M.D., M.B.A., Timothy M. Hughes, Ph.D., M.P.H., and Christos Davatzikos, Ph.D.

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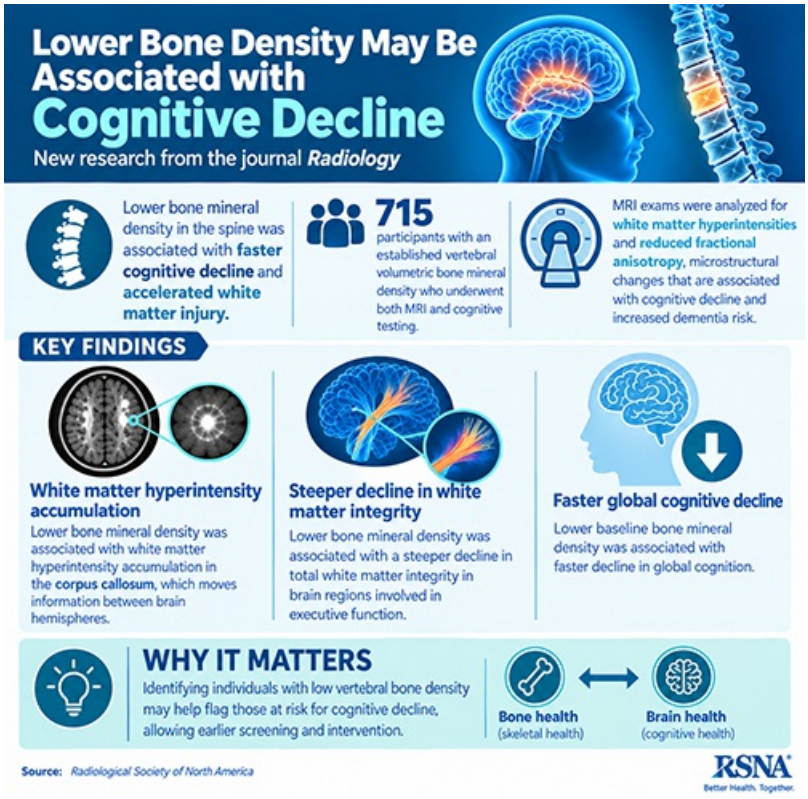

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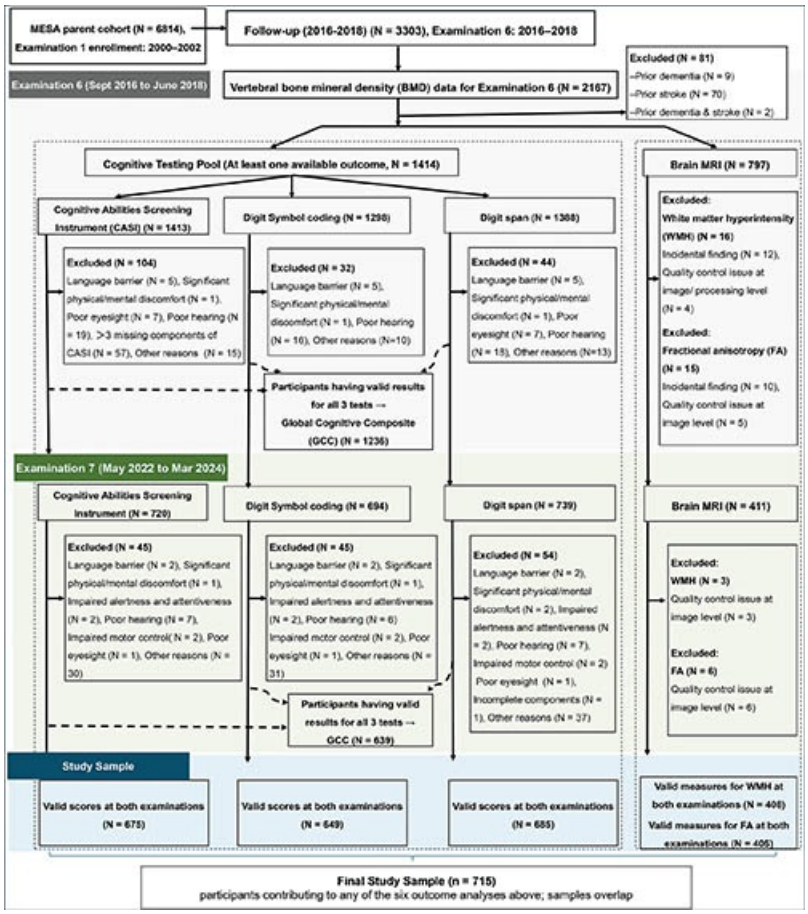

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Figure 1. Flow diagram of participant selection. Flowchart showing participant selection from 6,814 baseline participants (examination 1: 2000–2002) to the final study sample. Of 3,303 participants with follow-up data, 2,167 had vertebral bone mineral density measurements at examination 6. MESA = Multi-Ethnic Study of Atherosclerosis.

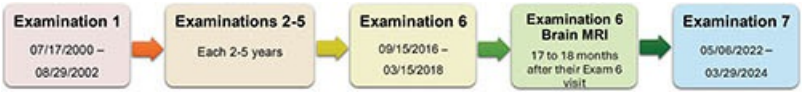

Figure 2. Study timeline and design in the Multi-Ethnic Study of Atherosclerosis (MESA). Timeline of MESA examinations. Baseline vertebral bone mineral density was measured at examination 6 (2016–2018); brain outcomes were assessed 17–18 months later and again at examination 7 (2022–2024), with approximately 5 years follow-up.

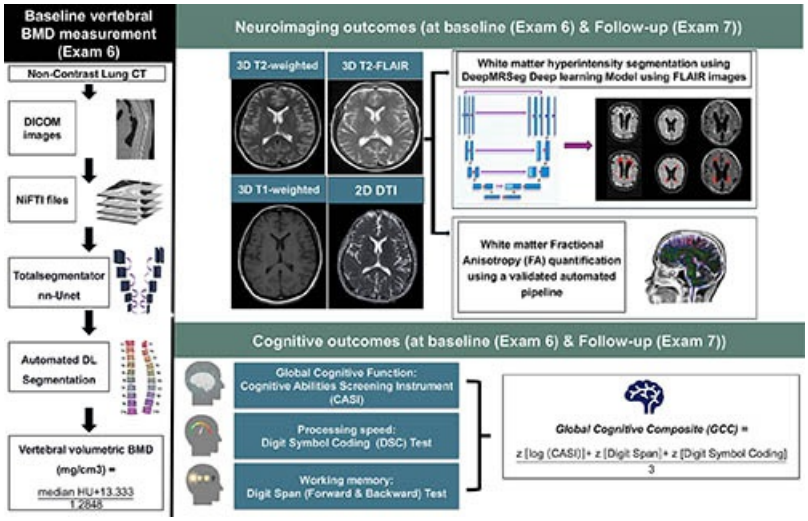

Figure 3. Study overview: assessment of vertebral volumetric bone mineral density (BMD) and neuroimaging and cognitive outcomes. Study overview is shown. Left panel: vertebral BMD was derived from noncontrast lung CT scans using TotalSegmentator for automated vertebral segmentation. Top right panel: neuroimaging outcomes included white matter hyperintensity burden. Bottom right panel: cognitive outcomes. Note the three head icons shown to the left of Cognitive Abilities Screening Instrument, digit symbol coding, and digit span were artificial intelligence–generated using Google Gemini and are included for illustrative purposes only. DICOM = Digital Imaging and Communications in Medicine, NIfTI = Neuroimaging Informatics Technology Initiative, 3D = three-dimensional.

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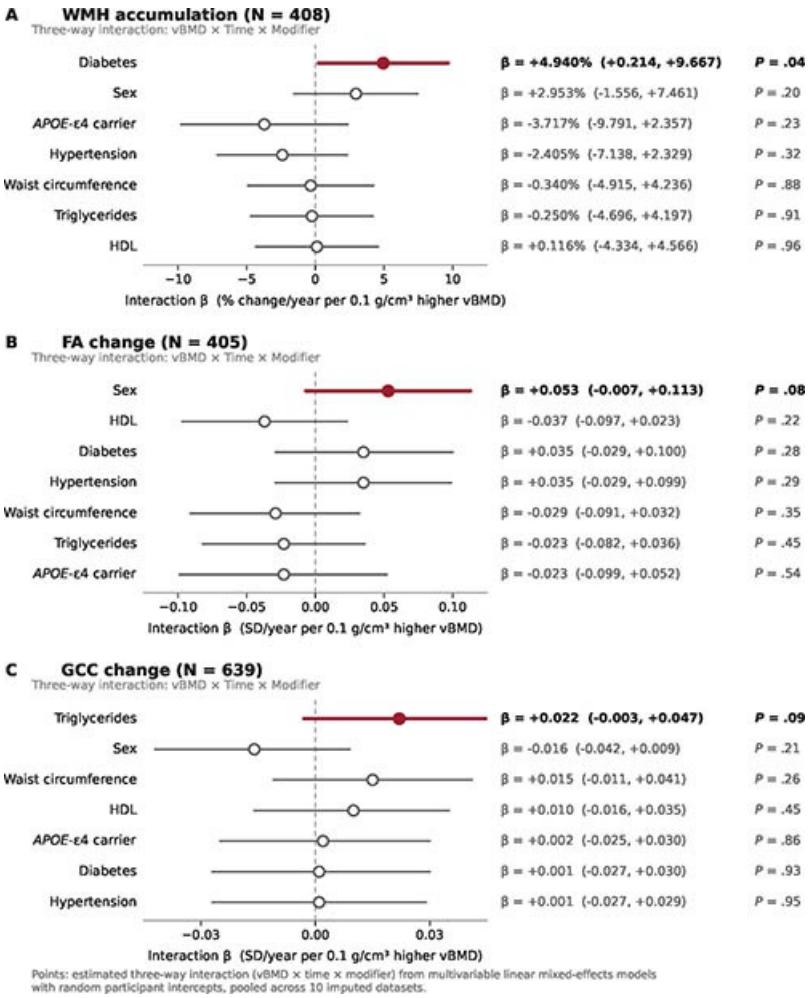

Figure 4. Effect modification of vertebral bone mineral density associations with longitudinal brain aging outcomes. **(A)** White matter hyperintensity (WMH) accumulation (n = 408) is shown, with percentage change per year in log-transformed WMH volume plotted on the x-axis. Diabetes status shows effect modification. **(B)** Fractional anisotropy (FA) change (n = 405) is shown. Sex shows suggestive effect modification. **(C)** Global cognitive composite (GCC) change (n = 639) is shown, with SD per year in z-standardized GCC plotted on the x-axis. *APOE* = apolipoprotein E.

Resources:

Abstract link

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