

ORIGINAL ARTICLE

# Incidental Findings on Brain MRI in the General Population

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## ABSTRACT

### BACKGROUND

Magnetic resonance imaging (MRI) of the brain is increasingly used both in research and in clinical medicine, and scanner hardware and MRI sequences are continually being improved. These advances are likely to result in the detection of unexpected, asymptomatic brain abnormalities, such as brain tumors, aneurysms, and subclinical vascular pathologic changes. We conducted a study to determine the prevalence of such incidental brain findings in the general population.

### METHODS

The subjects were 2000 persons (mean age, 63.3 years; range, 45.7 to 96.7) from the population-based Rotterdam Study in whom high-resolution, structural brain MRI (1.5 T) was performed according to a standardized protocol. Two trained reviewers recorded all brain abnormalities, including asymptomatic brain infarcts. The volume of white-matter lesions was quantified in milliliters with the use of automated post-processing techniques. Two experienced neuroradiologists reviewed all incidental findings. All diagnoses were based on MRI findings, and additional histologic confirmation was not obtained.

### RESULTS

Asymptomatic brain infarcts were present in 145 persons (7.2%). Among findings other than infarcts, cerebral aneurysms (1.8%) and benign primary tumors (1.6%), mainly meningiomas, were the most frequent. The prevalence of asymptomatic brain infarcts and meningiomas increased with age, as did the volume of white-matter lesions, whereas aneurysms showed no age-related increase in prevalence.

### CONCLUSIONS

Incidental brain findings on MRI, including subclinical vascular pathologic changes, are common in the general population. The most frequent are brain infarcts, followed by cerebral aneurysms and benign primary tumors. Information on the natural course of these lesions is needed to inform clinical management.

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**M**AGNETIC RESONANCE IMAGING (MRI) of the brain is increasingly used both in research and in clinical medicine, and scanner hardware and MRI sequences are improving. Performing MRI at higher resolution and field strength and with more sensitive sequences may lead to the detection of subtle or small brain abnormalities that would not have been detected previously. In combination with the increasing number of brain MRI scans obtained each year, these advances in MRI technology will probably result in more persons being confronted with incidental brain findings. Incidental findings are previously undetected abnormalities of potential clinical relevance that are unexpectedly discovered and unrelated to the purpose of the examination.<sup>1</sup> The detection of incidental findings poses various practical and ethical issues, particularly when the participants in a research study are healthy volunteers.<sup>2</sup> The clinical relevance and natural course of these unexpected asymptomatic findings are largely unknown and may differ markedly from those of similar symptomatic abnormalities.

Previous studies investigated incidental findings, such as brain tumors and vascular abnormalities, in healthy research volunteers or in populations of patients who underwent MRI examinations for various reasons.<sup>3-8</sup> Katzman et al. reported a prevalence of 1.1% for clinically serious abnormalities, such as brain tumors, in a retrospective study of a heterogeneous population of volunteers, 3 to 83 years old, who were participating in a variety of research studies.<sup>9</sup> To date, only one population-based study has reported the occurrence of incidental brain findings; this study showed a prevalence of 1.7%.<sup>10,11</sup>

Not generally classified as incidental findings are subclinical vascular pathologic changes such as asymptomatic brain infarcts and white-matter lesions, the prevalence of which is known to be high in elderly persons and to increase with age.<sup>12-17</sup> These lesions are potentially clinically relevant because of the increased risk of adverse neurologic events associated with them.<sup>17-22</sup> We report on the prevalence of incidental brain findings, including subclinical vascular pathologic changes, detected by high-resolution, state-of-the-art brain MRI in 2000 persons who participated in a population-based study.

## METHODS

### SOURCE POPULATION

The subjects of this study were participants in the Rotterdam Study, a prospective, population-based cohort study initiated in 1990 among persons 55 years of age or older who were living in a suburb of Rotterdam, the Netherlands.<sup>23</sup> The original cohort of the Rotterdam Study (7983 participants) was expanded in 2000 and again in 2006 to include participants who were 45 years of age or older. Every 2 to 3 years, participants are invited to the research center for interviews and extensive physical examinations. Since August 2005, all participants without contraindications to MRI have been invited to undergo MRI examination as part of the Rotterdam Scan Study, a neuroimaging study embedded in the Rotterdam Study that aims to investigate the causes and consequences of age-related brain changes.

The institutional review board at Erasmus MC University Medical Center approved the study, and all participants gave written informed consent; the consent form included a paragraph on incidental findings and the option to refuse to be informed about any unexpected abnormality. All patients who had incidental findings that required follow-up evaluation or treatment had previously agreed to be informed of such findings and were referred to appropriate specialists.

Between August 1, 2005, and February 1, 2007, 2027 of 2227 eligible subjects (91.0%) agreed to participate in the imaging study. In 27 subjects, imaging could not be performed because of physical constraints (in 21 subjects) or technical problems (in 6 subjects). Brain imaging results were thus available for 2000 participants.

### BRAIN MRI ACQUISITION

All scans were obtained with a 1.5-T scanner with an eight-channel head coil (GE Healthcare). Two trained technicians performed all examinations in a standardized way. The MRI protocol was identical for all participants and included four high-resolution axial sequences: a three-dimensional, T<sub>1</sub>-weighted sequence; a two-dimensional, proton-density-weighted sequence; a two-dimensional, fluid-attenuated inversion recovery (FLAIR) sequence; and a three-dimensional, T<sub>2\*</sub>-weighted

gradient-recalled echo (GRE) sequence. The slice thickness was 1.6 mm for the T<sub>1</sub>-weighted, proton-density-weighted, and T<sub>2</sub>\*-weighted GRE sequences (0 padded to 0.8 mm for the T<sub>1</sub>-weighted and T<sub>2</sub>\*-weighted GRE sequences) and 2.5 mm for the FLAIR sequence; all slices were contiguous. No contrast material was administered.

#### ASSESSMENT OF INCIDENTAL FINDINGS

All scans were read for incidental findings by one of two trained reviewers. The readings were usually performed within 1 day (over 90% of all scans) and at the latest 1 week after acquisition. One reviewer was a resident in radiology, and the other a resident in neurology, with 4.5 and 2.0 years of experience in reading brain MRIs, respectively. Both reviewers were unaware of any clinical information on the subjects. The readings were performed with a digital picture archiving and communication system (PACS). Incidental findings of potential clinical relevance were defined as those requiring urgent or immediate referral, as previously described by others<sup>9,10,24</sup>; examples include brain tumors, aneurysms, subdural fluid collections, and arachnoid cysts. The diagnoses were made on the basis of MRI findings characteristic of each lesion and were not confirmed by histologic studies. Case definitions for each incidental MRI finding are detailed in the Supplementary Appendix, available with the full text of this article at [www.nejm.org](http://www.nejm.org).

In addition, the presence of brain infarcts (both lacunar and cortical) was recorded. The distinction between symptomatic and asymptomatic infarcts was verified as follows. A history of stroke is obtained from each subject on entry into the Rotterdam Study.<sup>25</sup> Subsequently, participants are continuously monitored for incident stroke through automated linkage of the study database with files from general practitioners and hospital discharge information. All reported events are validated by an experienced neurologist.<sup>26</sup> White-matter lesion volumes (in milliliters) were quantified with a validated automated voxel classification technique, as described elsewhere.<sup>27</sup> Brain findings that were not considered clinically relevant and were not recorded as incidental findings included simple sinus disease and variations from the norm, such as pineal cysts, ventricular asymmetry, and enlarged Virchow–Robin spaces.

Two experienced neuroradiologists reviewed and reached a consensus on all initially reported abnormalities. To maximize sensitivity, the threshold for reporting abnormalities on initial review was kept low. To verify the sensitivity of the initial review for detecting incidental findings, an additional 230 scans (11.5% of the total of 2000) were also read by the neuroradiologists. No brain abnormalities were detected in addition to those already recorded by the initial reviewers. This result indicates that the initial review had a very high sensitivity for detection of brain abnormalities.

The management of incidental findings was defined in a protocol that was agreed on before the start of the study. Depending on the detected abnormality and after consultation with clinicians, persons with incidental findings requiring additional clinical workup or medical treatment were referred to a relevant medical specialist (a neurosurgeon, neurologist, or internist).

#### STATISTICAL ANALYSIS

We calculated the prevalence of each incidental brain finding in the study population. Multiple similar findings within one participant (e.g., more than one aneurysm or multiple asymptomatic brain infarcts) were counted as a single finding. Next, we calculated the age-specific prevalence rates of the most frequent incidental findings. For white-matter lesions, we calculated the age-specific median and interquartile range.

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## RESULTS

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The mean age of the study population was 63.3 years (range, 45.7 to 96.7), and 1049 of the subjects (52.4%) were women. Table 1 shows the prevalence of each incidental finding that was recorded. Asymptomatic brain infarcts were present in 145 persons (7.2%). Among findings other than brain infarcts, aneurysms (1.8%) were the most frequent. All aneurysms except two were located in the anterior circulation, and all except three were less than 7 mm in diameter (the smallest was 2 mm). Four aneurysms had an intracavernous location. Benign tumors were also frequent (1.6%), with meningiomas being recorded most often (0.9%). The meningiomas ranged from 5 to 60 mm in diameter, and their prevalence was 1.1% in women and 0.7% in men. Pituitary macroadenoma was

**Table 1. Incidental Findings on 2000 MRI Scans.\***

Finding	No. (%)
Asymptomatic brain infarct†	145 (7.2)
Lacunar infarct	112 (5.6)
Cortical infarct	41 (2.0)
Primary tumors, benign	31 (1.6)
Meningioma	18 (0.9)
Vestibular schwannoma	4 (0.2)
Intracranial lipoma‡	2 (0.1)
Trigeminal schwannoma	1 (<0.1)
Pituitary adenoma	6 (0.3)
Primary tumors, malignant§	1 (<0.1)
Other findings	
Aneurysm	35 (1.8)
Cavernous angioma	7 (0.4)
Metastases	1 (<0.1)
Subdural hematoma	1 (<0.1)
Arachnoid cyst¶	22 (1.1)
Type I Chiari malformation	18 (0.9)
Major-vessel stenosis**	9 (0.5)
Dermoid cyst of lateral orbital rim	1 (<0.1)
Fibrous dysplasia	1 (<0.1)

\* The diagnoses were based on imaging only, without histologic confirmation.

† Some subjects had both lacunar and cortical infarcts.

‡ One person had quadrigeminal cistern lipoma, and one had intravestibular lipoma.

§ This finding was a possible low-grade glioma.

¶ There were 16 temporal cysts (left-to-right ratio, 3:1) and 6 infratentorial cysts.

|| Type I Chiari malformation is defined as tonsillar herniation extending more than 5 mm below the foramen magnum.<sup>28</sup> The mean degree of herniation was 6.4 mm (range, 5.2 to 10.3).

\*\* Major-vessel stenosis is defined as lack of flow void in the cavernous internal carotid artery (in seven subjects) or the vertebral artery (in two subjects).

present in six persons (0.3%). Vestibular schwannomas had a prevalence of 0.2%. We found one possibly malignant primary brain tumor (a low-grade glioma that was not histologically confirmed) and one case of multiple cerebral metastases in a person who in retrospect was found to have been treated for lung cancer. The finding that was medically most urgent was a large, chronic subdural hematoma in an otherwise asymptomatic person, who in retrospect was found to have had minor head trauma 4 weeks before the MRI scan. Fig-

ure 1 shows a selection of the abnormalities that were incidentally detected in this study.

None of the persons with incidental brain findings reported any symptoms, with the exception of two subjects. One person with vestibular schwannoma reported hearing loss that had been investigated 3 years earlier by computed tomography, which had not revealed any abnormalities. The other person, who had a right-sided intravestibular lipoma, had longstanding ipsilateral hearing loss that had never been evaluated.

None of the incidental findings in Table 1 were histologically or surgically confirmed, except for those in two persons for whom operative treatment was indicated. One had subdural hematoma, and the other had a 12-mm aneurysm of the medial cerebral artery.

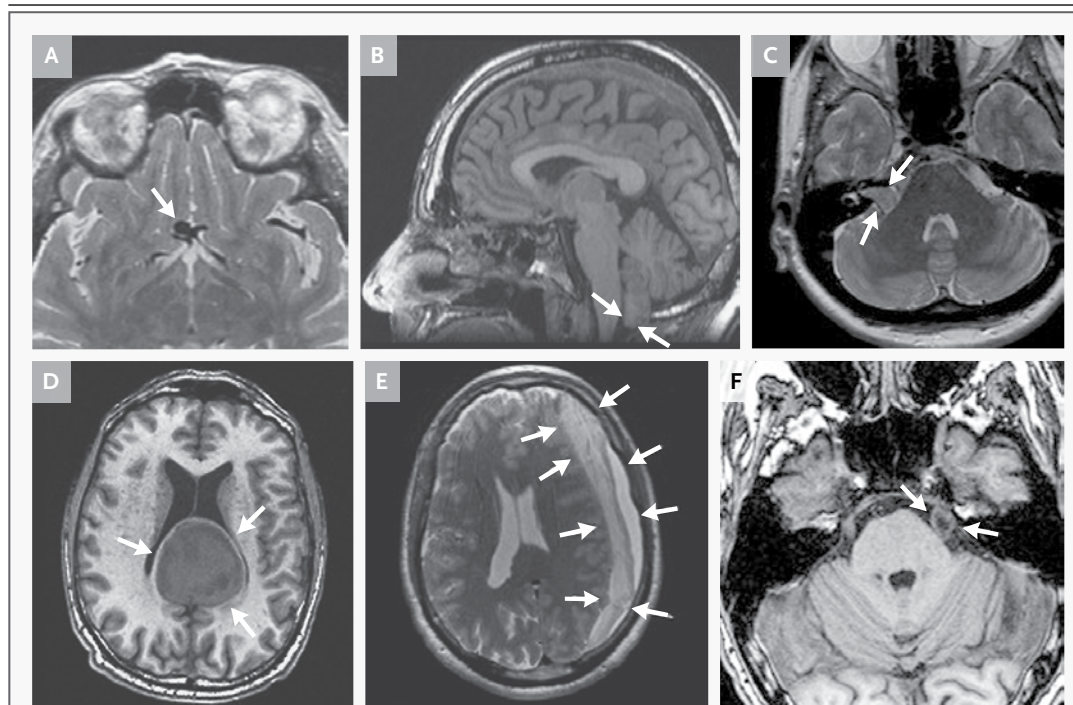
Table 2 shows the age-specific distribution of the most frequent incidental findings. The prevalence of asymptomatic brain infarcts increased with age. The prevalence of meningiomas increased from 0.5% in 45- to 59-year-olds to 1.6% in persons 75 years of age or older. Aneurysms showed no change in prevalence with age.

The median volume of white-matter lesions increased with increased age (Table 2). The distribution of white-matter lesion volumes according to age category is shown in Figure 2. The proportion of persons without any white-matter lesions decreased from 5.4% in 45- to 59-year-olds to 2.0% in persons 75 years of age and older. Furthermore, with increasing age, there was a greater spread in the distribution of white-matter lesion volumes (Fig. 2).

## DISCUSSION

In the general population of persons 45 to 97 years old, we found a high prevalence of potentially clinically relevant incidental brain abnormalities, including subclinical vascular pathologic changes. The prevalence of asymptomatic brain infarcts and meningiomas increased with age, as did the volume of white-matter lesions, whereas aneurysms showed no age-related increase in prevalence.

A major strength of our study is the large sample of persons 45 years of age or older. The MRI protocol was uniform for all subjects, and the reviewers were unaware of characteristics of the subjects, making detection bias unlikely. We used high-resolution, state-of-the-art imaging sequenc-



**Figure 1. Incidental Findings on Brain MRI.**

Arrows indicate the abnormalities in each image. An aneurysm of the anterior communicating artery (diameter, 6 mm) is shown on the proton-density-weighted axial image in Panel A. Panel B shows a tonsillar herniation (type I Chiari malformation) more than 5 mm below the level of the foramen magnum on a T<sub>1</sub>-weighted sagittal image. A typical vestibular schwannoma with extension into the right internal auditory canal is visible on the proton-density-weighted axial image in Panel C. A large meningioma is shown on the T<sub>1</sub>-weighted axial image in Panel D. Panel E shows a large, chronic subdural hematoma on a proton-density-weighted axial image. A trigeminal schwannoma of the left fifth cranial nerve, with cystic degeneration, is shown on the T<sub>1</sub>-weighted axial image in Panel F.

es representing the advanced imaging techniques that are increasingly used in brain research.

A potential limitation with respect to the generalizability of our study results is the fairly homogeneous composition of our geographically defined study population, which consisted mainly of white, middle-class persons.<sup>29</sup> Our results may not be generalizable to populations that include other ethnic or socioeconomic groups.

Another potential limitation of our study is that not all scans were read by neuroradiologists. However, all scans with abnormalities detected on initial review were reviewed again by two neuroradiologists. In addition, a randomly chosen subgroup of all scans was reviewed by two neuroradiologists, who did not detect any incidental findings missed on initial review. Therefore, our initial review by physicians who were not neuroradiologists had a very high sensitivity for the

detection of brain abnormalities, and we do not think the results would have been different if the scans had been read primarily by neuroradiologists. The sensitivity may be lower when scans are read by professionals who are not medically qualified, as is reportedly the case in many research centers in the United States.<sup>30</sup>

The incidental brain findings in our study were all diagnosed on the basis of imaging. Pathological confirmation of presumed brain tumors was not obtained, since none of these tumors required surgery after referral of the subject. However, the imaging characteristics of all lesions listed in Table 1 were typical and are usually considered diagnostic (see the Supplementary Appendix).

We did not use contrast-enhanced MRI. Because our study population consisted of volunteers without neurologic symptoms who were participating in a research study, the risks associated

**Table 2. Distribution of Incidental Findings According to Age.**

Finding	45 to 59 Yr of Age (N = 750)	60 to 74 Yr of Age (N = 993)	75 to 97 Yr of Age (N = 257)
Asymptomatic brain infarct — no. (%)	30 (4.0)	68 (6.8)	47 (18.3)
Meningioma — no. (%)	4 (0.5)	10 (1.0)	4 (1.6)
Aneurysm — no. (%)	13 (1.7)	18 (1.8)	4 (1.6)
Volume of white-matter lesions — ml			
Median	1.80	3.05	7.74
Interquartile range	1.06–3.17	1.87–5.49	2.64–16.49

with the administration of contrast material were not considered warranted. However, the effect of the absence of contrast material, if any, would have been to leave some small lesions undetected, which would have resulted in an underestimate of the prevalence of incidental findings.

The prevalence of subclinical vascular pathologic changes in our population was high and increased with advancing age. This finding was not unexpected, since age-related changes, such as asymptomatic brain infarcts and white-matter lesions, have been reported to be very frequent in the general elderly population.<sup>12,13,15-17,31</sup> Although such changes have been shown to be associated with increased risks of stroke and cognitive decline,<sup>18,20,32</sup> preventive therapies for patients with these MRI findings have not been evaluated in randomized trials.

The prevalence of incidental brain findings other than subclinical vascular pathologic changes in our population was much higher than that reported in previous studies,<sup>8-10,24</sup> even when the subjects were of similar age to the patients in our study.<sup>10</sup> We found an especially high prevalence of small aneurysms.<sup>4,9,10,24</sup> This difference can partly be explained by differences among study populations, since aneurysms are very infrequent in children and young adults. However, the population-based study by Yue et al. showed aneurysms in only 0.11% of persons 65 years of age or older.<sup>10</sup> We feel that a more likely explanation for the difference is that our scanning protocol, especially the high-resolution, proton-density-weighted sequence (Fig. 1A), permitted very good visualization of the circle of Willis as compared with conventional T<sub>1</sub>-weighted and T<sub>2</sub>-weighted sequences. Of course, the use of even more sensitive sequences, such as magnetic resonance angiography, might have resulted in the detection of even smaller aneurysms. However, in a systematic re-

view of autopsy and angiographic studies, Rinkel et al. concluded that aneurysms can be found in approximately 2% of adults without risk factors for subarachnoid hemorrhage,<sup>33</sup> a proportion very close to the 1.8% detected by MRI in our study.

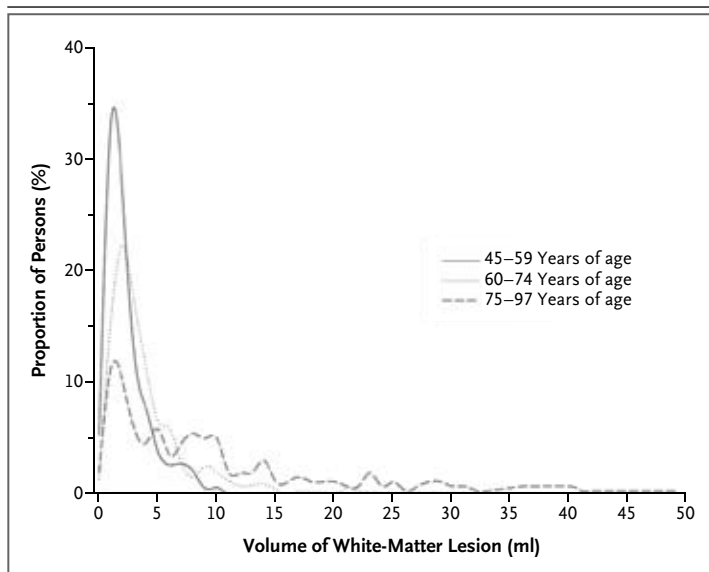
Meningiomas and small aneurysms were highly prevalent in our study population of persons 45 years of age or older. The rate of growth of meningiomas is typically slow,<sup>34,35</sup> and most meningiomas remain asymptomatic throughout life, which explains why 50% of all meningiomas are discovered at autopsy.<sup>36</sup> The prevalence of meningiomas found at autopsy in persons over 60 years of age is 3%, and the majority of the lesions are less than 1 cm in diameter.<sup>37</sup> Nevertheless, it is generally believed that asymptomatic meningiomas require close clinical and radiologic follow-up to rule out rapidly enlarging tumors.<sup>34,38</sup> The current practice of many clinicians is to perform MRI yearly for at least 2 to 3 years to ascertain that rapid tumor growth does not occur. If this were done for all persons incidentally found to have meningiomas, many MRI examinations would be performed in otherwise healthy asymptomatic persons. In view of the resulting medical costs, as well as the psychological burden for those undergoing examination, it would be of great interest to review these guidelines on the basis of the natural course of meningiomas incidentally found on brain MRI.

Guidelines for the management of small aneurysms might also be reviewed. More than 90% of unruptured, asymptomatic aneurysms found by means of autopsy or angiography are less than 10 mm in diameter.<sup>33,39</sup> In our study, all but three aneurysms were smaller than 7 mm, and all but two were located in the anterior circulation. The reported risk of rupture for aneurysms of this size in the anterior circulation over a period of 4 years is 0%.<sup>40</sup> This finding was based on follow-

up of a group of patients who had no history of subarachnoid hemorrhage. However, in this group there was an overrepresentation of persons with a family history of aneurysm and of persons with symptoms that had led to the detection of the unruptured aneurysm.<sup>40</sup> The risk of rupture associated with asymptomatic aneurysms in the general population would be expected to be even lower than the reported risk in the described patient population.<sup>33</sup> Preventive surgery or treatment of risk factors may thus not be indicated in the general population, and the benefit of longer follow-up has not yet been proven.<sup>41</sup> Therefore, persons in our study with aneurysms of the anterior circulation that were under 7 mm in diameter were not referred for follow-up or medical treatment.

Several large, population-based MRI studies in the elderly are ongoing,<sup>11,16,42-45</sup> and more will be conducted because of the increasing scientific interest in age-related brain diseases such as dementia. Moreover, imaging at higher MRI field strengths and with increased resolution, as well as the use of new MRI sequences that are more sensitive to subtle structural changes, will probably increase the number of small brain abnormalities detected. Incidental findings from brain MRI in middle-aged and elderly persons will therefore become an important issue that should be considered in designing studies. The present study, as well as some previous studies,<sup>9,10</sup> provides information on the prevalence of clinically asymptomatic brain abnormalities. This information is especially important in view of the ethical and practical issues involved in the management of incidental findings.<sup>1,2</sup>

In conclusion, incidental findings on brain MRI in the general population are common. The most frequent findings are brain infarcts, followed by cerebral aneurysms and benign primary tumors. Such findings should be anticipated in the design



**Figure 2. Age-Specific Distribution of White-Matter Lesion Volumes.**

Measured volumes of white-matter lesions were rounded to the nearest milliliter before plotting. The proportion of persons with a specific volume of white-matter lesions within each age category is shown on the y axis. Fourteen persons (<1%) had a white-matter lesion volume of more than 50 ml. Of these persons, one was under 59 years of age, four were 60 to 74 years of age, and nine were 75 years of age or older. The maximum white-matter lesion volume measured was 95 ml.

of research protocols and the use of neuroimaging in clinical practice. Information on the natural course and prognosis of these lesions is needed to inform clinical management.

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