Comment. This study of a large nationwide cohort study found no significant association between exposure to atovaquone-proguanil in early pregnancy and the risk of any major birth defect. To our knowledge, these are the first safety data ever reported on early pregnancy exposure to atovaquone-proguanil.

Although based on a limited number of exposed pregnancies and cases, the findings provide some reassurance that atovaquone-proguanil is not a major teratogen. However, the analysis could only exclude more than a 3-times higher risk of birth defects associated with atovaquone-proguanil exposure.

Main strengths of this study include its registry-based design, providing the opportunity to investigate an uncommon drug exposure in pregnancy among women living in an industrialized country and allowing independent ascertainment of dispensed prescriptions and birth defect diagnoses. However, a main limitation is that after filling prescriptions for atovaquone-proguanil, some participants may have found out that they were pregnant. Therefore, some of them may have cancelled their trip and never taken the drug. Any noncompliance to the dispensed drugs would bias estimates toward the null.

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Author Contributions: Both authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Pasternak and Hviid. *Acquisition of data:* Hviid. *Analysis and interpretation of data:* Pasternak and Hviid. *Drafting of the manuscript:* Pasternak. *Critical revision of the manuscript for important intellectual content:* Pasternak and Hviid. *Statistical analysis:* Hviid. *Obtained funding:* Hviid. *Study supervision:* Hviid.
Financial Disclosure: None reported.
Funding/Support: This study was funded by research grants from the Danish Medical Research Council and the Lundbeck Foundation.
Role of the Sponsors: The funding agencies had no role in the design and conduct of the study; in the collection, management, analysis, and interpretation of the data; or in the preparation, review, and approval of the manuscript.

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Use of Neuroimaging in US Emergency Departments

Advanced diagnostic imaging use is increasing, raising concerns about patient safety and cost.[1] Recent estimates indicate that 4000 future cancers may result from the head computed tomographic (CT) examinations performed nationwide in 2007[2] and that costs of CT and magnetic resonance imaging (MRI) doubled between 1997 and 2006.[3] In US emergency departments (EDs), the greatest increase has been in neuroimaging (head CT and MRI).[4] Nevertheless, there are no national benchmarks against which health care providers and hospitals can measure their use of ED neuroimaging. We aimed to calculate head CT and MRI use in US EDs and to examine patient and hospital factors associated with use.

Methods. We performed a cross-sectional analysis of neuroimaging in US EDs by analyzing the 2007 National Hospital Ambulatory Medical Care Survey (NHAMCS) ED component with a primary outcome of head CT use and a secondary outcome of head MRI use. We coded patient and hospital covariates a priori to identify predictors of neuroimaging and calculated the percentage of visits (with 95% confidence intervals [CIs]) associated with neuroimaging. We conducted multivariate logistic regression to estimate the adjusted association of covariates on the primary outcome. The regression model had good fit, with a

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C statistic of 0.71. Among visits in which head CT was performed, we calculated the leading reasons for visit[5] and discharge diagnoses by grouping primary *International Classification of Diseases, Ninth Revision, Clinical Modification* discharge diagnoses into the 285 clinical categories of the Clinical Classification System.[6] We performed all statistical analyses using SAS 9.1.3 (SAS Institute Inc, Cary, North Carolina).

Results. There were approximately 117 million visits to 4891 US EDs in 2007, based on 35 490 ED visits in the NHAMCS sample. Head CT scans were performed during 6.7% (95% CI, 6.1%-7.3%) of visits, while head MRIs were performed during 0.26% (95% CI, 0.18%-0.35%) of visits. Patient and hospital characteristics associated with neuroimaging are presented in the **Table**. Patient characteristics independently associated with lower use of head CT use were decreasing age and non-Hispanic black race and ethnicity (vs non-Hispanic whites). Hospital characteristics associated with lower CT use included rural setting (vs urban) and hospitals owned by state or local governments (vs nonprofit hospitals).

The 3 leading reasons for visits among patients receiving head CTs in the ED were trauma (18.1%; 95% CI, 12.8%-23.5%), headache (13.0%; 95% CI, 10.8%-15.2%), and dizziness (6.1%, 95% CI, 4.6%-7.6%). The 3 leading discharge diagnosis categories were trauma (20.5%; 95% CI, 15.8%-25.3%), headache (9.2%; 95% CI, 7.4%-11.0%), and epilepsy/convulsions (5.2%; 95% CI, 3.8%-6.6%).

Table. Head CT Use During US ED Visits in 2007[a]

Variable	Total ED Visits in Thousands (95% CI)	ED Visits With Head CTs in Thousands (95% CI)	Proportion of ED Visits With Head CTs, % (95% CI)	Odds Ratio (95% CI)
Overall	116 802 (102 112-131 492)	7842 (6582-9102)	6.7 (6.1-7.3)	
Age group, y				
0-2	9100 (7180-11 019)	135 (75-195)	1.5 (0.9-2.1)	0.38 (0.24-0.59)
3-17	17 794 (11 571-24 018)	651 (439-862)	3.7 (2.7-4.6)	0.83 (0.63-1.19)
18-30	25 924 (22 332-29 516)	1358 (985-1730)	5.2 (4.3-6.2)	0.97 (0.75-1.25)
31-40	15 461 (13 467-17 455)	827 (634-1,020)	5.3 (4.4-6.3)	1 [Reference]
41-50	15 806 (13 755-17 857)	1095 (875-1315)	6.9 (5.7-8.2)	1.11 (0.83-1.48)
51-60	11 939 (10 496-13 381)	905 (717-1092)	7.6 (6.4-8.8)	1.23 (1.01-1.51)
61-70	7491 (5044-99 337)	756 (576-937)	10.1 (8.1-12.1)	1.55 (0.14-2.10)
71-80	6607 (5627-7587)	849 (664-1034)	12.9 (10.9-14.8)	1.80 (1.33-2.44)
>80	6682 (5755-7608)	1267 (827-1706)	19.0 (16.3-21.6)	2.57 (1.92-3.34)
Sex				
Female	63 193 (55 096-71 290)	4135 (3436-4834)	6.5 (5.8-7.2)	NS
Male	53 609 (46 880-60 338)	3707 (3081-4334)	6.9 (6.2-7.6)	NS
Race/ethnicity				
White (NH)	71 776 (61 453-82 099)	5340 (4403-6278)	7.4 (6.7-8.1)	1 [Reference]
Black (NH)	26 196 (21 146-31 245)	1400 (1055-1746)	5.3 (4.5-6.2)	0.85 (0.72-0.99)
Hispanic	15 804 (12 286-19 321)	899 (609-1188)	5.7 (4.4-7.0)	1.12 (0.82-1.54)
Other	3026 (2313-3740)	203 (127-279)	6.7 (4.8-8.6)	1.04 (0.76-1.43)
Payment source				
Medicare	16 648 (14 565-18 730)	2248 (1878-2617)	13.5 (11.9-15.1)	1 [Reference]
MA/SCHIP	29 403 (25 466-33 340)	1390 (1104-1677)	4.7 (4.0-5.5)	0.83 (0.64-1.06)
Private/WC	40 060 (34 045-46 076)	2260 (1784-2736)	5.6 (4.9-6.3)	0.91 (0.71-1.16)
Self-pay/NC	20 207 (17 592-22 822)	1335 (1065-1605)	6.6 (5.7-7.5)	1.21 (0.91-1.60)
Region				
Midwest	25 062 (19 363-30 761)	2053 (1448-2659)	8.2 (7.1-9.3)	1 [Reference]
Northeast	20 484 (16 416-24 552)	1356 (921-1791)	6.6 (4.9-8.3)	0.75 (0.54-1.03)
South	48 713 (40 386-57 040)	3040 (2378-3702)	6.2 (5.3-7.2)	0.85 (0.67-1.07)
West	22 543 (12 375-32 710)	1393 (594-2191)	6.2 (5.0-7.4)	0.73 (0.53-1.01)
Location				
Urban	99 074 (80 382-117 767)	6838 (5428-8249)	6.9 (6.2-7.6)	1 [Reference]
Rural	17 728 (9059-26 397)	1004 (463-1544)	5.7 (4.4-6.9)	0.75 (0.57-0.97)
Academic status				
Academic	59 887 (48 840-70 933)	4184 (3232-5137)	7.0 (6.1-7.9)	1 [Reference]
Nonacademic	56 915 (46 000-67 831)	3657 (2783-4533)	6.4 (5.6-7.2)	0.84 (0.70-1.00)
Ownership				
Nonprofit	88 598 (75 801-101 395)	6331 (5174-7488)	7.1 (6.4-7.9)	1 [Reference]
Government	13 661 (8949-18 372)	559 (335-784)	4.1 (3.0-5.2)	0.63 (0.46-0.87)
Proprietary	14 543 (7519-21 567)	952 (464-1440)	6.5 (5.3-7.8)	1.03 (0.79-1.53)

Abbreviations: CI, confidence interval; CT, computed tomography; ED, emergency department; MA, Medicaid; NC, no charge; NH, non-Hispanic; NS, not significant; SCHIP, State Children's Health Insurance Program; WC, worker's compensation.

[a] Percentages and 95% CIs account for National Hospital Ambulatory Medical Care Survey multistage sampling design. Categories may not sum to total due to missing data.

Comment. To our knowledge, this study provides the first nationally representative benchmarks of ED neuroimaging. In 2007, 1 in 14 ED patients received head CT, while 1 in 400 underwent head MRI. Increasing age was the strongest predictor of head CT use. While 1 in 34 children younger than 18 years received head CT, 1 in 7 patients 65 and older received one. Current guidelines addressing the use of ED head CT for trauma[7] and acute headache[8] exclude these older patients. Organizations interested in measuring and reducing neuroimaging will be challenged to define acceptable evidence-based appropriateness standards for older adults.

Use of head CT varied by race: 1 in 14 non-Hispanic white patients received head CT, compared with 1 in 19 non-Hispanic black patients. Yet it remains unclear whether this difference represents a quality disparity (ie, underuse) or an overuse disparity because the optimal rate of imaging is unknown and we could not assess appropriateness.

Large numbers of US ED patients are undergoing high-cost neuroimaging and receiving ionizing radiation with known cancer risks. Further research on appropriate indications for neuroimaging and implementation of performance improvement programs are needed to ensure that these valuable technologies are used in a safe and cost-effective manner.

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Financial Disclosure: None reported.

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INVITED COMMENTARY

Emergency Department Neuroimaging: Are We Using our Heads?

Patterns of neuroimaging use in emergency settings vary widely. A study of Canadian EDs found that neuroimaging rates for patients with minor head trauma with similar characteristics ranged from 16% to 70% between hospitals and 6% to 80% among individual physicians.[1] Understanding these variations is a key step to determine appropriate use.

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In this issue of the *Archives*, Raja and colleagues report head CT and MRI rates in US EDs from 2007. The national average rate for neuroimaging in the ED was 6.7%. Rates were higher in elderly patients, in urban settings, and in nonprofit hospitals. The 3 leading complaints associated with neuroimaging were trauma, headache, and dizziness, and the 3 leading discharge diagnoses were trauma, headache, and seizure. While previous studies have reported local imaging rates[2,3] and rates of imaging in subpopulations with specific complaints,[4,5] this report provides neuroimaging rates from a national sampling of undifferentiated patients.

There are some challenges with extrapolating data from this study. Because the data are at the visit level rather than patient level, it is possible that a single patient generated multiple visits (and multiple CT scans). Also, because individual EDs were sampled over 4-week periods, it is possible that frequent visitors could have attended surrounding EDs. Finally, the usual limitations of using an administrative data set are present, including potentially lower accuracy of *International Classification of Diseases, Ninth Revision, Clinical Modification* coding and procedure codes (from which these imaging rates are obtained) and self-reported data fields (eg, race/ethnicity, where there is approximately a 15% nonresponse rate and therefore includes imputed values).

Even with such limitations, this study provides a valuable benchmark for national neuroimaging rates. What this report cannot answer, however, is whether our current imaging rates are too low (resulting in significant amounts of inappropriately missed disease), just right, or too high (resulting in excessive risks from imaging without significant improvements in outcomes). One reason for concern that rates might be too high is that the use of medical imaging over the past 2 and a half decades has increased anywhere from 6-fold[6] to 20-fold.[7] Reasons for increased imaging, especially CT scanning, include increased availability, improved acquisition times, improved image accuracy and detail, and the desire for increased diagnostic certainty.[8]

Besides the increase in the shear numbers of scans, there is also reason to worry about the doses of radiation delivered with any one scan. A recent report in the *New York Times* described a group of patients who presented with complaints and findings consistent with radiation poisoning, including hair loss in a circumferential band. It was discovered that these patients had received toxic doses of radiation during CT scanning of the head to evaluate for suspected stroke.[9] Research suggests that such experiences may present a more systematic problem than previously recognized. In an evaluation of medical imaging at 4 hospitals, Smith-Bindman and colleagues[10] reported that effective doses varied significantly (13-fold mean variation). For routine head CT scans, the minimum and maximum effective doses recorded ranged from 0.3 to 6 mSv, and for stroke studies, the doses ranged from 4 to 56 mSv.

Our ultimate goal in ordering medical imaging is to gain knowledge that will lead to an effective intervention. Said another way: no one's condition ever improves solely by having an imaging test. We would like to avoid unnecessary exposure to radiation, its consequent risks, and also detection of incidental findings that can lead to patient concern, further medical evaluation (often including further imaging and radiation), and interventions of undetermined value.

The development of decision rules represents an important step toward this goal. Neurotrauma is the leading indication for neuroimaging in the ED with 1.42 million head CT scans ordered annually for this indication based on this report by Raja and colleagues. There has been a significant investment in research to assist clini-