Systematic Review of Clinical Prediction Rules for Neuroimaging in the Evaluation of Dementia

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Background: Clinical practice guidelines for dementia do not recommend routine neuroimaging but vary in their recommended clinical prediction rules to identify patients who should undergo neuroimaging for potentially reversible causes of dementia.

Methods: Using a MEDLINE search supplemented by other strategies, we identified studies from January 1, 1983, through December 31, 1998, that evaluated the diagnostic performance of a clinical prediction rule. We calculated the sensitivity and specificity of each rule, then evaluated their diagnostic performance in a hypothetical cohort of 1000 patients with dementia, varying the prevalence of potentially reversible dementia from 1% to 15%.

Results: We identified 7 studies that evaluated at least 1 of 6 different clinical prediction rules. Only one rule consistently had high sensitivity (>85%) across all studies; none consistently had high specificity (>85%). Six of the 7 studies included less than 15 cases of potentially reversible dementia; thus the sensitivity and specificity for each rule had relatively wide confidence intervals. At a 5% prevalence of potentially reversible dementia, all rules had low positive predictive value (<15%) in our hypothetical cohort. Depending on the rule, our analysis predicts 6 to 44 of the 50 patients with potentially reversible dementia (5% prevalence in cohort of 1000 patients) would not undergo imaging.

Conclusions: There is considerable uncertainty in the evidence underlying clinical prediction rules to identify which patients with dementia should undergo neuroimaging. Application of these rules may miss patients with potentially reversible causes of dementia.

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DEMENTIA has profound effects on health outcomes and is associated with high medical care utilization and costs.[1] The identification of potentially reversible causes of dementia is critical, given the adverse consequences of delayed diagnosis. Neuroimaging of the brain, commonly computed tomography (CT) or magnetic resonance imaging (MRI), is a high-cost technology that can identify potentially reversible causes of dementia such as subdural hematomas, normal pressure hydrocephalus, and tumors.[2] These causes are estimated to account for less than 5% of all cases of dementia.[3]

To date, 9 clinical practice guidelines on the evaluation of dementia have been published and endorsed by 12 different organizations or groups.[4-12] Eight guidelines contain a recommendation about neuroimaging; of these, none recommend the routine use of neuroimaging as part of the diagnostic evaluation of every case of dementia (**Table 1**).[5-12] Seven of the 8 guidelines recommend the use of clinical criteria (ie, a clinical prediction rule) to identify patients for whom a neuroimaging study is recommended.[6-12] These prediction rules are aimed at selecting patients with a higher likelihood of having a potentially reversible cause of dementia that can be diagnosed by neuroimaging (hereafter referred to as potentially reversible cause of dementia).

Despite the uniform recommendation for selective neuroimaging, the recommended clinical prediction rules vary widely across these guidelines (Table 1). Because of the observed variation of the clinical prediction rules for selective neuroimaging in dementia, we undertook an analysis of the evidence underlying these rules. The objective was to review systematically primary research studies on clinical prediction rules for neuroimaging in the evaluation of dementia, and to assess the sensitivity, specificity, and diagnostic performance of the rules.

MATERIALS AND METHODS

SEARCH STRATEGY

We conducted a MEDLINE search of articles published from January 1, 1983, through December 31, 1998. Using the keyword *dementia* and medical subject headings *dementia diagnosis* or *dementia etiology* and *tomography, x-ray computed,* or *magnetic resonance imaging,* we identified 886 articles. After reviewing titles and abstracts of these articles, we selected for in-depth review 51 articles with possible information about a clinical prediction rule for neuroimaging in dementia. We identified an additional 6 articles for in-depth review from bibliographies of textbook chapters, review articles, and the guidelines about dementia.

CRITERIA FOR CONSIDERING STUDIES

We included articles that met the following criteria: (1) they reported a clinical prediction rule for the use of neuroimaging in dementia; (2) the clinical variables in the prediction rule were explicit and presented in sufficient detail to apply consistently in clinical practice; (3) every patient underwent a neuroimaging study (ie, CT or MRI); (4) all subjects were categorized based on the neuroimaging results as having or not having a potentially reversible cause of dementia; and (5) enough data were presented to calculate the sensitivity and specificity of the clinical prediction rule.

DATA ABSTRACTION

For each study meeting eligibility criteria, we abstracted information on the age, sex, dementia severity, and clinical setting of the sample. We also abstracted the clinical variables in each prediction rule, who performed the clinical evaluation, and whether the clinical variables were collected prospectively or retrospectively (ie, medical record review). We also recorded the type of neuroimaging study used and whether the physicians applying the prediction rule were aware of the neuroimaging findings.

For each study, we abstracted or calculated the number of patients (1) with and without a potentially reversible cause of dementia as defined by the neuroimaging results; (2) who had at least 1 of the clinical characteristics contained in the prediction rule (rule-positive findings); and (3) who did not have any of the clinical characteristics contained in the prediction rule (rule-negative findings).

DEFINING THE DIAGNOSTIC UTILITY AND TRADE-OFFS FOR EACH PREDICTION RULE

We calculated the sensitivity, specificity, and 95% confidence interval (CI) for each rule. Sensitivity was defined as the proportion of patients with a neuroimaging-defined potentially reversible disorder and rule-positive findings. Specificity was defined as the proportion of patients with no neuroimaging-defined potentially reversible disorder and with rule-negative findings. We tested for heterogeneity between studies that evaluated the same prediction rule by constructing a summary receiver operating characteristic curve comparing the 95% CIs for the sensitivity plotted against 1–specificity for each rule, and by comparing sensitivities and specificities for each rule using χ^2 or Fisher exact test.[25]

Using a hypothetical cohort of 1000 patients with dementia, we estimated the positive and negative predictive values for each clinical prediction rule at different prevalences of neuroimaging-defined potentially reversible disorders (ie, 1%, 5%, 10%, and 15%). Since physicians and patients are frequently concerned that clinical prediction rules may miss treatable conditions,[26,27] we also reported the proportion of neuroimaging-defined potentially reversible disorders in patients with rule-negative findings (ie, 1–negative predictive value) and the number of potentially reversible cases of dementia missed by applying each prediction rule to the hypothetical cohort.

RESULTS

Of the 57 articles obtained for in-depth review, 7 met eligibility criteria for inclusion in this analysis[13,14,16,17,20-23,28-31] (**Table 2**). One study evaluated 4 different prediction rules with the use of the same patient population,[13] whereas another study compared 2 prediction rules in the same patient population.[17] The other 5 studies evaluated 1 prediction rule each. From these 7 studies, we identified 6 different clinical prediction rules that we labeled as the Dietch, Larson high-risk, Larson low-risk, Bradshaw, American Academy of Neurology (AAN)–Chui, and Canadian Consensus Conference rules (**Table 3**). Four of the 6 rules were developed from clinical data collected through chart review or standardized examinations (Dietch, Larson high-risk, Larson low-risk, and Bradshaw), whereas the other 2 rules (AAN-Chui and Canadian Consensus Conference) were derived from existing consensus-based guidelines.

Two of the remaining 50 articles evaluated a prediction rule for neuroimaging in dementia, although they did not meet all of our inclusion criteria.[29,30] One study only included patients with potentially reversible causes of dementia; thus, the specificity could not be calculated.[29] The other study did not include a sufficiently explicit set of clinical variables to allow others to consistently apply the prediction rule in clinical practice.[14] The other 48 articles were excluded because they did not assess prediction rules.

STUDY CHARACTERISTICS

Each study examined a consecutive series of patients with dementia who were referred to a dementia clinic[13,16,17,22] or to a radiology unit[20,28]; the total number of patients undergoing evaluation per study ranged from 98 to 500 (Table 2). The overall frequency of potentially reversible causes of dementia detectable by neuroimaging was lower in patient populations drawn from dementia and geriatric clinics (0%-3.9%) compared with studies where patients were identified from radiology units (6.5%-10.4%). The average age of patients in the 7 studies ranged from 63 to 76 years. In 3 studies, the sex distribution was not specified. In the remaining 4 studies, the percentage of female subjects studied ranged from 53% to 71%. The severity of dementia, as measured by

Table 1. Published Guidelines About Use of Neuroimaging in Dementia

Organization (Year)	Guideline Title	Neuroimaging Recommendation	Prediction Rule for Neuroimaging	References Cited by Guideline to Support Recommendation
American Association for Geriatric Psychiatry, Alzheimer's Association, and American Geriatric Society (1997)	Diagnosis and treatment of Alzheimer disease and related disorders[5]	Optional	None provided	None
US Dept of Veterans Affairs and University HealthSystem Consortium (1997)	*Dementia Identification and Assessment: Guidelines for Primary Care Practitioners*[7]	Not needed routinely	Recent-onset dementia, focal signs, dementia with atypical features, headaches, or when cause of cognitive changes are not apparent after history, physical, and laboratory studies	Martin et al,[13] Engel and Gelber,[14] and Corey-Bloom et al[15]
American Academy of Neurology (1995)	Practice parameter for diagnosis and evaluation of dementia[6]	Not needed routinely*	Insidious onset of dementia after 60 y of age, focal signs or symptoms, seizures, or gait disturbances	None†
American College of Physicians (1994)	Magnetic resonance imaging of the brain and spine: a revised statement[8]	Not needed routinely	Rapid onset or progression of dementia, focal symptoms, and signs	Clarfield,[3] Larson et al,[16,17] Siu,[18] and Simon et al[19]
Canadian Consensus Conference on the Assessment of Dementia (1991)	Assessing dementia: the Canadian consensus[10]	Not needed routinely	Age <60 y, short duration of symptoms (eg, <48 mo), rapid unexplained decline in cognitive function (eg, 1-2 mo), new localizing signs, unexplained neurologic symptoms (eg, new onset headaches or seizures), recent head trauma, anticoagulation use or history of bleeding disorder, history of malignant neoplasm, gait disorder or ataxia, or urinary incontinence	None
New York State Department of Health (1990)	*Guidelines for the Diagnosis of Alzheimer's Disease and Other Dementias*[12]	Not needed routinely	History of symptoms <2 y, acute deterioration from baseline cognitive function, abnormal neurologic findings suggestive of focal process, (eg, headache, diplopia, seizures, paralysis, paresis), or history of head trauma	Larson et al[17]
Office of Geriatrics and Extended Care, Dept of Veterans Affairs (1989)	*Dementia: Guidelines for Diagnosis and Treatment (2nd ed)*[11]	Not needed routinely	Dementia of brief duration, focal neurologic signs, history of mass, or when standard assessment fails to reveal a treatable cause	National Institutes of Health Consensus Conference[9]
National Institutes of Health Consensus Conference (1987)	Differential diagnosis of dementing diseases[9]	Not needed routinely	Dementia of brief duration, focal neurologic signs, or history suggestive of mass	None

**The official position of the American Academy of Neurology (AAN) is that neuroimaging need not be obtained routinely, as defined in the official AAN practice parameter,[24] although the published background paper for the AAN guideline recommends that every patient with dementia undergo a neuroimaging procedure at least once.*

†The published background paper for the AAN guideline cited studies[13,20-22] and an editorial.[23]

the Mini-Mental Status Examination, varied from an average of 15.4 to 23.4, but was not reported in 3 studies. In 6 studies, every patient received a CT scan; only 1 study used MRI. The use of contrast was reported in only 2 studies. In 3 studies, the prediction rules were assessed by collection of data abstracted from patient medical records, and no information was given as to whether the person abstracting the information was aware of the results of the CT scan of the head. The specialty of the physicians examining the patients varied within and between each study.

PREDICTION RULE CHARACTERISTICS

The Bradshaw, Larson high-risk, and Canadian Consensus Conference rules identified patients who should undergo a CT scan, whereas the Dietch, Larson low-risk, and AAN-Chui rules identified patients who need not undergo a CT scan. To compare all 6 prediction rules, we reworded the clinical variables in each rule so that neuroimaging is recommended if any of the variables are present (Table 3).

The Canadian Consensus Conference and Dietch rules included the largest number of clinical variables, whereas both Larson rules contained the fewest (Table 3). Although none of the 6 prediction rules were identical, they included common variables. All included a variable on the duration of dementia symptoms or acuity of change in cognitive function; 4 criteria included focal signs and symptoms. Clinical variables that might increase the likelihood of finding a subdural hematoma (eg, head trauma) or normal pressure hydrocephalus (eg, gait apraxia or urinary incontinence) were specified in only 3 rules.[10,21,28] Only 2 of the 6 prediction rules included an age cutoff as a criterion variable.[10,21] However, 3 of the 4 rules were developed in patient populations that excluded patients who were younger than 50 years[21] or 60 years.[2,22]

Table 2. Characteristics of Primary Studies Evaluating Prediction Rules for Neuroimaging Use in Dementia Evaluation

	Dietch,[28] 1983	Larson et al,[17] 1984	Larson et al,[16] 1986	Bradshaw et al,[20] 1983	Martin et al,[13] 1987	Chui and Zhang,[21] 1997	Freter et al,[22] 1998
Age, y							
Mean	67.7	75.8	75.7	63.5	75.0	69.9	74.6
Cutoff	>50	>60	>60	All ages	Not specified	Not specified	All ages
Female, %	Not specified	71	Not specified	53	71	Not specified	56
Setting	Principally inpatient, VA hospital	Outpatient dementia clinic	Outpatient dementia clinic	Outpatient and inpatient	Outpatient geriatric clinic	Outpatient memory disorders clinic	Memory clinic
Final sample size	200	107	200	500	204	98	196
MMSE, mean ± SD	Not specified	15.4	19.1 ± 7.9	Not specified	15.6	Not specified	23.4
No. (%) of potentially reversible causes of dementia in sample	13 (6.5)	2 (1.9)	0 (0)	52 (10.4)	8 (3.9)	3 (3.1)	6 (3.1)
CT/MRI, %	100/0	100/0	100/0	100/0	100/0	49/66†	100/0
Scanner type	CT Atronics fourth-generation fan beam	Not specified	Not specified	EMI 1007 CT scanner	Third-generation (GE 9800) CT scanner for "most patients"	Not specified	Not specified
Contrast used	Variable	Not specified	Not specified	Variable	Not specified	Not specified	Not specified
Patient identification	From CT scan requests that were for an evaluation of dementia	From first 107 patients seen in clinic with suspected dementia and symptoms >3 mo; 90% referred by geriatric and family service program	From first 200 patients seen in clinic with suspected dementia and symptoms >3 mo; 90% referred by geriatric and family service program	From referrals by specialists to neuroradiology unit for evaluation of dementia	Consecutive series of 204 patients meeting *DSM-III* criteria for dementia	All patients referred to memory disorders clinic meeting *DSM-III-R* and CDR criteria for dementia	All patients referred with dementia who had CT scan and follow-up visit ≥4 mo later
Source of clinical data	Chart review	Standardized evaluation	Standardized evaluation	Referral letters and hospital records	Standardized evaluation	Standardized evaluation	Standardized evaluation
Data collected and rule applied masked to CT scan results	Not specified	Not specified	Not specified	Yes	Not specified	No	Not specified
Specialty of physicians performing clinical evaluation	Neurologist or resident in neurology or internal medicine	Internists	Internist and psychiatrist or psychologists	Psychiatrist, neurologist, geriatrician, or neurosurgeon	Multidisciplinary team: internist or geriatrician, psychiatrists, social worker, and nurse	Neurologist or experienced physician assistant	Multidisciplinary team: neurologists, geriatrician, clinical psychologist, and geriatric nurse
Prediction rules evaluated‡	Dietch	Larson high-risk, Larson low-risk	Larson high-risk	Bradshaw	Larson high-risk, Larson low-risk, Dietch, and Bradshaw	AAN-Chui	Canadian Consensus Conference

**VA indicates Department of Veterans Affairs; MMSE, Mini-Mental State Examination; CT, computed tomography; MRI, magnetic resonance imaging; CDR, Clinical Dementia; Rating* DSM-III, *Diagnostic and Statistical Manual of Mental Disorders, Third Edition*[32]; DSM-III-R, *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition;*[33] *and AAN, American Academy of Neurology.*

†*Fifteen percent had both.*

‡*Described in the "Results" section.*

DIAGNOSTIC UTILITY OF THE CLINICAL PREDICTION RULES

Table 4 presents the raw data from 7 studies and the sensitivity and specificity for each rule. Depending on the study, sensitivity varied widely, from 12.5% to 100.0%. In addition, for the Bradshaw and both Larson rules, sensitivity varied considerably (ie, differences ≥50%), depending on the sample to which the rule was applied. Similarly, specificity also ranged widely from 37.2% to 85.7%. Only 1 rule consistently had high sensitivity (>85%) across all studies evaluating the same rule; no rule consistently had high specificity (>85%) (Table 4).

Based on our analysis of heterogeneity across studies evaluating the same rule, these studies were too heterogenous to allow for pooling of results (data not shown). However, one of the studies applied 4 rules (Dietch, both Larson, and Bradshaw rules) to the same patient population.[13] Thus, to estimate additional aspects of the diagnostic performance of all 6 prediction rules in a hypo-

Table 3. Clinical Prediction Rules Evaluated in Primary Studies*

Clinical Characteristics†	Prediction Rules (Reference)					
	Dietch (Dietch[28])	Larson High-risk (Larson et al[17])	Larson Low-risk (Larson et al[17])	Bradshaw (Bradshaw et al[20])	AAN-Chui (Chui and Zhang[21])	Canadian Consensus Conference (Canadian Consensus Conference on the Assessment of Dementia[10])
Age, y	–	–	–	–	Onset <60	<60
Duration of symptoms, mo	<1	<12	<36	>1 but <12	Noninsidious course	<48
Dementia severity	–	MMSE >20	MMSE >15	–	–	–
Acute change in cognitive function	<48 h	+	+	–	–	<1-2 mo
Focal signs or symptoms	+	–	–	+	+	+
Ocular or vision abnormalities	Papilledema or visual field deficits	–	–	Papilledema	–	–
Headache	+	–	–	+	–	+
Trauma	+	–	–	–	–	+
History of malignant tumor	+	–	–	–	–	+
Speech disorder	–	–	–	+	–	–
Seizures	+	–	–	–	–‡	+
History of stroke	+	–	–	–	–	–
Urinary incontinence	+	–	–	–	–	+
Gait disturbance	Apraxia or ataxia	–	–	–	Change in walking not attributed to a peripheral musculoskeletal disorder	+

*AAN indicates American Academy of Neurology; MMSE, Mini-Mental Status Examination; plus sign, clinical characteristic is part of the prediction rule; and minus sign, clinical characteristic is not part of prediction rule. Prediction rules are described in the "Results" section.

†If any one of the clinical characteristics is present, then neuroimaging should be performed.

‡Rule includes seizures, but seizures not included in the study.

Table 4. Raw Data, Sensitivity, and Specificity of Studies Evaluating Prediction Rules for Neuroimaging of Dementia*

Rule, Reference, y (No. of Patients)	No. of Patients With PRC		No. of Patients Without PRC		Sensitivity (95% CI), %	Specificity (95% CI), %
	With Rule-Positive Results	With Rule-Negative Results	With Rule-Positive Results	With Rule-Negative Results		
Dietch						
Dietch,[28] 1983 (200)	13	0	88	99	100 (80.8-100.0)	52.9 (45.6-60.3)
Martin et al,[13] 1987 (704)	7	1	123	73	87.5 (53.1-100.0)	37.2 (30.4-44.4)
Larson high-risk						
Larson et al,[17] 1984 (107)	2	0	15	90	100 (27.6-100.0)	85.7 (77.9-89.8)
Larson et al,[16] 1986 (200)	0	0	34	166	NA	83.0 (77.2-86.1)
Martin et al,[13] 1987 (204)	2	6	70	126	25.0 (2.9-64.2)	64.2 (57.2-68.3)
Larson low-risk						
Larson et al,[17] 1984 (107)	2	0	33	72	100 (27.6-100.0)	68.6 (59.0-77.5)
Martin et al,[13] 1987 (204)	4	4	47	149	50.0 (17.1-85.9)	76.0 (69.6-81.9)
Bradshaw						
Bradshaw et al,[20] 1983 (500)	35	17	138	310	67.3 (53.4-80.1)	69.2 (64.7-73.5)
Martin et al,[13] 1987 (204)	1	7	41	155	12.5 (0.9-50.6)	79.1 (72.9-84.7)
AAN-Chui						
Chui and Zhang,[21] 1997 (98)	2	1	55	40	66.7 (13.9-100.0)	42.1 (32.0-52.6)
Canadian Consensus Conference						
Freter et al,[22] 1998 (196)	5	1	71	122	83.3 (42.3-100.0)	63.2 (56.1-70.1)

*PRC indicates potentially reversible causes of dementia diagnosed by neuroimaging (ie, subdural hematoma, normal pressure hydrocephalus, or tumor); CI, confidence interval; NA, not applicable; and AAN, American Academy of Neurology. Prediction rules are described in the "Results" section.

thetical cohort of patients, we selected the sensitivity and specificity for these 4 rules from this study. The sensitivity and specificity for each of the other 2 rules were drawn from the single study in which they were evaluated.

The Canadian Consensus Conference and Dietch rules performed the best, missing the fewest number of patients with potentially reversible causes of dementia across the range of prevalences evaluated (**Table 5**). However, this comes at the expense of subjecting more patients to imaging, compared with the other 5 rules. Application of the Dietch rule would result in 63% of all patients presenting with dementia undergoing imaging,

Table 5. Effectiveness of Applying Prediction Rules to a Hypothetical Cohort of 1000 Patients With Dementia*

Prediction Rule	Prevalence of PRC, No. (%)	No. of PRC Missed by Applying Rule†	Positive Predictive Value‡	% of Patients With Rule-Negative Results Who Have PRC§
Dietch	10 (1)	1	1.4	0.3
Larson low-risk	10 (1)	5	2.1	0.7
Larson high-risk	10 (1)	7	0.7	1.2
Bradshaw	10 (1)	8	0.6	1.1
AAN-Chui	10 (1)	3	1.1	0.8
Canadian Consensus Conference	10 (1)	2	2.2	0.3
Dietch	50 (5)	6	6.8	1.7
Larson low-risk	50 (5)	25	9.9	3.3
Larson high-risk	50 (5)	37	3.6	5.8
Bradshaw	50 (5)	44	3.0	5.5
AAN-Chui	50 (5)	17	5.7	4.0
Canadian Consensus Conference	50 (5)	8	10.7	1.4
Dietch	100 (10)	13	13.4	3.6
Larson low-risk	100 (10)	50	18.8	6.8
Larson high-risk	100 (10)	75	7.2	11.5
Bradshaw	100 (10)	88	6.2	10.9
AAN-Chui	100 (10)	33	11.3	8.1
Canadian Consensus Conference	100 (10)	17	20.1	2.8
Dietch	150 (15)	19	19.7	5.6
Larson low-risk	150 (15)	75	26.9	10.4
Larson high-risk	150 (15)	113	11.0	17.1
Bradshaw	150 (15)	131	9.5	16.3
AAN-Chui	150 (15)	50	16.9	12.3
Canadian Consensus Conference	150 (15)	25	28.6	4.4

**All values for Dietch, Bradshaw, and both Larson rules were calculated using the sensitivity and specificity reported by Martin et al[13] that were evaluated in the same patient population (Table 4). Values for American Academy of Neurology (AAN)–Chui and Canadian Consensus Conference rules are drawn from the single studies in which each rule was evaluated (Table 4). PRC indicates potentially reversible causes of dementia detected by neuroimaging (ie, tumor, subdural hematoma, or normal pressure hydrocephalus). Prediction rules are described in the "Results" section.*

†Number of patients who have a PRC of dementia but have rule-negative results and therefore would not undergo imaging.

‡Percentage of all patients with rule-positive results who have a PRC of dementia.

§Percentage of all patients with rule-negative findings but who have a PRC of dementia (ie, 1 – negative predictive value).

whereas for the other rules, smaller proportions of patients would undergo imaging (24% for Larson low-risk rule; 36% for Larson high-risk rule; 21% for Bradshaw rule; 58% for Canadian Consensus Conference rule; and 37% for the AAN-Chui rule). The positive predictive value of all 6 rules was low, regardless of the prevalence of potentially reversible causes of dementia (Table 5). Of patients with rule-negative findings, most would not have a potentially reversible cause of dementia; however, the Dietch and Canadian Consensus Conference rules had the lowest proportion of patients with rule-negative findings and a potentially reversible cause of dementia (Table 5).

COMMENT

A clinical prediction rule used to identify dementia patients with a potentially reversible disorder should possess a high sensitivity to minimize the proportion of false-negative findings.[26,27] Most clinicians and patients want to know how the application of a given rule affects the risk of missing a potentially reversible cause of dementia. Our review indicates that wide variation exists in the content and diagnostic performance of the 6 prediction rules reported in the literature. One rule (Dietch) had relatively high sensitivity (100.0% and 87.5% in both studies evaluating the Dietch rule); the other rules had lower sensitivities with larger variability between studies evaluating the same rule. Alexander and colleagues[29] also reported a high sensitivity for the Dietch criteria, but the study was excluded from our review because their study design did not enable calculation of specificity. They applied the Dietch criteria to 83 patients in a large health management organization population of elderly patients who had a brain tumor, subdural hematoma, or normal pressure hydrocephalus and who initially presented with some form of possible dementia. Of these 83 patients, 79 met the Dietch criteria for imaging (ie, 95.2% sensitivity [95% CI, 88.8%-99.2%]). The desired high sensitivity of the Dietch criteria comes at the expense of a low specificity and, hence, the least reduction in neuroimaging use, relative to a setting in which all patients with dementia undergo imaging. Therefore, at the population level, application of the Dietch rule vs the other study rules would have the smallest effect in decreasing utilization.

The current estimates of sensitivity and specificity are imprecise, having wide CIs. For example, most of the primary studies evaluating the performance of a prediction rule include fewer than 15 cases of potentially reversible causes of dementia (despite having total sample sizes ranging from 100-500). To obtain more precise estimates about a rule's performance, larger sample sizes will be required.[27] This imprecision in these estimates may explain in part the lack of consen-

sus in the literature about whether all patients with dementia should undergo neuroimaging.[23,30,31,34]

It is not clear, by applying even the high-sensitivity rules, if the number of missed cases is acceptable to physicians and patients. For example, if the prevalence of potentially reversible causes of dementia is as low as 1%, then applying the highest-sensitivity rule (Dietch) would miss only 1 patient of 10 in a cohort of 1000 patients with dementia. However, as the prevalence of potentially reversible cases increases, even at 10%, the number of missed cases is 13 of 50. Nevertheless, this represents a small proportion (3.6%) of all patients with rule-negative findings. Many clinicians may consider this rate as unacceptably high—particularly if current practice is that all new dementia patients undergo imaging—given concerns about quality of care and medicolegal ramifications. Adoption of less sensitive rules or even the Dietch rule may lead to underutilization of neuroimaging and underdetection of potentially reversible causes of dementia.

To apply these rules effectively, physicians must be proficient in eliciting a neurologic history and in performing a neurologic examination. However, some authorities believe that nonneurologists receive an insufficient amount of training in neurology.[35-37] This belief is further supported by a recent study that found that 76% of patients with moderate to severe cognitive impairment were not recognized as possibly having a dementia syndrome by their primary care physician.[38] Thus, patients with a potentially reversible cause of dementia who have clinical findings consistent with criteria for neuroimaging may be misclassified as not meeting the criteria by physicians who do not perform a detailed neurologic history and physical examination.[34]

None of the clinical prediction rules evaluated in the primary studies were completely identical to any of the rules recommended by existing published guidelines on the evaluation of dementia. Three of the guidelines[7,9,11] contained imprecise definitions of clinical variables about the indications for neuroimaging (eg, "etiology of cognitive changes are not apparent after history, physical, or laboratory testing"), which precluded comparison with the clinical prediction rules from the primary studies. Only 4 guidelines cited a source for their prediction rule,[7,8,11,12] 3 of which cited at least 1 of the 6 studies we identified.[7,8,12] However, none cited all 6 studies, although 5 of them were published before or during the year (1987) the oldest guideline[9] was issued. In addition, no guideline included a summary of the data on the diagnostic utility of the previously published clinical prediction rules or estimated the possible diagnostic performance of the clinical prediction rule that they recommend. This is not in keeping with the recently published literature that recommends that guideline recommendations should be based on a comprehensive literature review and should present the evidence and rationale supporting each recommendation.[39-42] None of the guidelines included a discussion about the implications of implementing their recommendations in clinical practice, information that most physicians say they want in practice guidelines.[43]

It is unclear what effect application of any of the rules recommended by the clinical practice guidelines would have because of differences in content between the guideline rules and the rules evaluated in the literature. However, only the AAN[6] and the New York Department of Health[12] guidelines contained a set of clinical variables similar to—but not as comprehensive as—the Canadian Consensus Conference or Dietch rule, the highest-sensitivity rules evaluated in the literature.

The principal reason for identifying a neuroimaging-defined potentially reversible cause of dementia is to improve patient outcomes. However, none of the guidelines reviewed contain a discussion about the benefits to patients of identifying potentially treatable causes of dementia. This may result in part from lack of data on the effectiveness that treating potentially reversible causes has on cognitive function, quality of life, or survival. In a comprehensive review that pooled data from 11 studies, 42% of patients with potentially reversible cause of dementia detectable by neuroimaging had some improvement after treatment, whereas only 8% exhibited complete resolution of their dementia.[3] Early detection of normal pressure hydrocephalus or subdural hematomas is more likely to improve outcomes after surgery compared with patients with tumors causing dementia.[3,20,29,44] Further studies evaluating the impact of neuroimaging on physicians' management decisions and on patient outcomes are needed to evaluate the role neuroimaging has in the evaluation of dementia.

Research studies are needed to evaluate the tradeoffs in costs and health outcomes associated with application of a prediction rule relative to subjecting all dementia patients to imaging. Research is also needed to better understand what false-negative rates and costs society, physicians, and patients would tolerate and the impact of malpractice concerns on clinical decision making and receptiveness to use of these rules by primary care physicians and by specialists. These studies should also compare the different kinds of neuroimaging technology currently available, eg, the use of MRI compared with CT scanning to detect potentially reversible causes of dementia. In addition, these technologies should be evaluated for their ability to rule in other forms of dementia (eg, Alzheimer disease or vascular dementia), and the impact neuroimaging results have on patient outcomes. Although MRI may be more sensitive than CT scanning, it is unclear if MRI is superior to CT scanning in the routine evaluation of dementia, and further studies are needed to determine the role of MRI in dementia.[2,5,7,45]

CONCLUSIONS

We found that the body of research evaluating the clinical prediction rules for neuroimaging in dementia was insufficient to understand the risk and benefits with certainty. The inadequacy of the existing literature may have contributed partially to the considerable variation in the clinical prediction rules recommended within current clinical practice guidelines. The evidence suggests that application of these rules might result in underdetection of potentially reversible causes of dementia. Given the rising prevalence of dementia, the cost of this technology, and the potential adverse consequences of underusing this technology, there is an urgent need for large,

well-designed studies evaluating the utility of neuroimaging in patients with dementia.

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