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Featured Article

The Vascular Impairment of Cognition Classification Consensus Study

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Abstract

Introduction: Numerous diagnostic criteria have tried to tackle the variability in clinical manifestations and problematic diagnosis of vascular cognitive impairment (VCI) but none have been universally accepted. These criteria have not been readily comparable, impacting on clinical diagnosis rates and in turn prevalence estimates, research, and treatment.

Methods: The Vascular Impairment of Cognition Classification Consensus Study (VICCCS) involved participants (81% academic researchers) from 27 countries in an online Delphi consensus study. Participants reviewed previously proposed concepts to develop new guidelines.

Results: VICCCS had a mean of 122 (98–153) respondents across the study and a 67% threshold to represent consensus. VICCCS redefined VCI including classification of mild and major forms of VCI and subtypes. It proposes new standardized VCI-associated terminology and future research priorities to address gaps in current knowledge.

Discussion: VICCCS proposes a consensus-based updated conceptualization of VCI intended to facilitate standardization in research.

Keywords: Vascular cognitive impairment; Vascular dementia; Guidelines; Criteria; Consensus; Delphi

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1. Introduction

Cerebrovascular pathology, including microinfarcts, lacunar infarcts, larger infarcts (of embolic or thrombotic origin), and white matter lesions, is moderately to strongly associated with cognitive decline [1–4]. Risk factors include hypertension, diabetes mellitus, smoking, atrial fibrillation, positive family history, age, and hypercholesterolemia [5–7], with some risk from *APOE* (ε4 allele) and *MTHFR* variants [8]. From the time Hachinski et al. [9] proposed the term multi-infarct dementia, numerous subsequent proposals have tried to capture the clinical and etiologic complexity of cognitive impairment caused by heterogeneous cerebrovascular disease (CVD) and pathologies [10–21]. These include vascular dementia (VaD), vascular cognitive impairment (VCI), subcortical (ischemic) VaD, and vascular cognitive disorder (VCD), which have given rise to multiple criteria and research guidelines [13,17,19,21] that are not readily interchangeable [22,23]. These factors contribute to variable prevalence estimates in the literature, as do descriptions of clinical manifestations. However, VaD, used to describe a severe form in the continuum of VCI, is probably the second commonest cause of dementia after Alzheimer's disease (AD), although as populations age this is likely to increase [13,17,21,24]. Yet, incidence of dementia is now decreasing in high-income countries, which may partly relate to better CVD management [25]. CVD commonly contributes to many forms of dementia, including AD [26–28], and may be targeted with some success [29], although further research into possible associations and causal relationships is needed. Studies into causes and treatments of AD have greatly outnumbered those for VaD, partly by the availability of widely used diagnostic criteria that continue to evolve [30] and partly because of relatively more funding opportunities.

The lack of consensus criteria for diagnosis of VaD and VCI has impeded sharing and comparison of data on a larger scale, together with different specialties conducting narrow focused research [31]. Greater harmony of approach within the research community is needed [23,32]. A work group convened by the NINDS-CSN made some progress [33], producing detailed research recommendations for VCI. However, their subsequent implementation and adoption remains unclear.

The Vascular Impairment of Cognition Classification Consensus Study (VICCCS) was designed to achieve a broader consensus on the conceptualization of impairment in cognition contributed by vascular pathology, for clinical diagnosis and research. The aim was to provide criteria that could be widely adopted within the field, to underpin future research. VICCCS elaborated previous work to inform the way forward, with input from a broad spectrum of participants from the international research community.

2. Methodology

2.1. Participant selection

Previous attempts to develop consensus criteria were largely based on comparatively smaller pools of opinion leaders as part of organized meetings, conferences, or symposia [33]. The intention for VICCCS was to draw on the expertise of as many participants from as wide an array of disciplines as possible. Participants for VICCCS were identified through unbiased review of published articles relating to the concept or diagnosis of VaD/VCI in Pubmed, up to August 2010. Several relevant research networks, including the British Association for Stroke Physicians, Alzheimer's Disease Neuroimaging Initiative, and the European Alzheimer's Disease Consortium were also invited.

Nine hundred five individuals were initially identified, although it was not possible to find the contact details of all these most likely because of the fact that some of the source studies were published more than 20 years ago. Further efforts to source these missing contact details were made by inviting all potential participants who were contacted to nominate and provide contact details for potentially interested colleagues. This lead to 789 invitations initially sent that generated a potentially 367 (46%) initially interested pool of international participants. Unlike previous endeavors, VICCCS used periodic internet-based surveys to facilitate greater involvement and promote contributions through providing sufficient time for reflection and responses that were given with anonymity and parity. The study required considerable relevant clinical and research knowledge and time commitment to complete multiple surveys. Nonetheless, on average 122 participants contributed to each round (range 98–153). Of these, a mean of 72% (range 66%–76%) were clinicians with direct involvement in clinical decision-making. The remainder were nonclinical researchers. Average continental distributions were as follows: Europe 63%, North America 19%, South America 6%, Asia 9%, Africa 2%, and Australia 1%. Representation in each round is detailed in Supplementary Table 1. Bar graphs summarizing the professions and affiliations of the authors are also provided in Supplementary Fig. 1. The most common profession was Neurologist (46%) and the most common affiliation was academic researcher (68%).

2.2. VICCCS Delphi process

We used a Delphi approach, an iterative structured process involving a series of questionnaires with progressive refinement of questions to achieve consensus among respondents [34]. Only the independent moderator (O.A.S., who did not herself participate in the survey) had access to identification details of the respondents. The anonymity of responses facilitated free expression of opinion throughout the study. Structured feedback of responses after each round informed the nature of subsequent questions, allowing unbiased evolution of group judgments that may be difficult face

to face. A threshold of two-thirds agreement was chosen to represent consensus [35] for issues refined through multiple iterative rounds. Overall, six rounds of web-based surveys were administered, approximately one every 2 months, to maintain engagement. In the first two rounds, opinion was canvassed on published criteria, their utility, and weaknesses. The remaining 4 rounds focused on addressing weaknesses and standardization of terminology. A summary of the topics addressed in each round is provided as Supplementary data.

3. Results

3.1. VICCCS rounds 1 and 2: Critical appraisal of existing proposals

In the first round, views were sought on the most important issues to be resolved. The extent of use of existing criteria and guidance, identified through literature review, were assessed. We separated questions on "concept" articles, such as those concerning the scope and definitions ($n = 12$), from those proposing diagnostic criteria ($n = 15$). Four articles covered both aspects and were included in both sections. Round 1 gathered participants' views on these articles, but also invited additional suggestions for relevant articles that should be considered. Participants were asked to indicate their familiarity with the articles and score their usefulness, from "*no longer relevant*" to "*useful in all cases*," and to select three concepts that could form the basis for wider acceptance. To reduce bias in selection that might have been caused by definitions that were older and perhaps more familiar, those selected that scored "*useful in most*" *or useful in all cases* were ranked to represent what was a "considered useful vote." The ranking showed that more recently published concepts, even if not widely known, were better regarded as a foundation for future use. The collated scores were fed back to participants in round 2. Participants were then asked to reconsider all articles, including those that might be less familiar, before again ranking the criteria, after which low-ranking criteria would be eliminated from further consideration.

Almost 60% of respondents ranked the VCI construct of O'Brien et al. [13], representing a broad continuum from mild impairment to dementia, as the preferred conceptual basis. The second and third ranked definitions, which obtained 11% and 7% first-preference votes, also encompassed VCI and associated concepts (Supplementary Fig. 2).

In addition, 78% of respondents felt that the definition of VCI needed to be broader in scope. Therefore, the remaining VICCCS rounds focused on obtaining consensus on a revised conceptual model for VCI. The content of the subsequent rounds was based on responses to early round questions on definition, scope, sensitivity to subtypes of VCI, and clinical utility.

3.2. Rounds 3–6: Formulation of a revised VCI concept

In round 3, participants were asked to state their agreement or disagreement with proposed guiding principles for refinement of the concept of VCI. These had more than 94% agreement; amendments proposed by some participants were reported for comment in round 4. Consensus guiding principles are listed in Box 1.

Round 3 addressed *three areas* identified in round 2 as meriting clarification or modification. Although 29% of respondents thought the O'Brien construct did not need any major improvement, a percentage of respondents felt changes were desirable to its *scope* (13%), *sensitivity to subtypes* (31%), and *descriptiveness* (39%). The subsequent rounds worked toward improving these perceived limitations. Forty-two percent of respondents thought the O'Brien construct was not well aligned with clinical operational criteria. These limitations were subsequently addressed in a focused follow-on Delphi (VICCCS *diagnosis*) to develop operational criteria (in preparation; however see Box 2 and Supplementary data for some reported findings).

3.2.1. Scope

Approximately one-third (34%) of round 3 participants suggested that other potential mechanisms of VCI should be included in the revised concept. In round 4, participants were asked to vote on inclusion of the suggested mechanisms. There was consensus that the additional mechanisms listed in Table 1 should be included within the revised

Box 1
VICCCS consensus guiding principles of the refinement of the concept of VCI.

1. Be broad and capture forms of vascular- or cerebrovascular-related damage that are likely to contribute to cognitive impairment or dementia.
2. Address shortcomings in both mild and severe forms of VCI and means to assess the transition of patients from one stage to another.
3. Recognize the importance of people who are at risk of VCI; however, their consideration under this construct should be contingent on some level of impairment.
4. Acknowledge that the classification of a patient with a mild form of VCI (i.e., non-dementia) is not necessarily predictive of progression of the impairment to a more severe form of VCI (i.e., dementia).
5. Acknowledge that the classification of a patient with a mild form of VCI (i.e., non-dementia) is not necessarily predictive of an eventual subtype of dementia.

Box 2
VICCCS proposed definitions of major VCI (VaD) subtypes.

Post-stroke dementia: A patient described as having PSD may or may not have presented evidence of mild cognitive impairment before stroke. The patient may exhibit immediate and/or delayed cognitive decline that begins after, but within 6 months, of stroke, that does not recover. PSD results from different vascular causes and changes in brain. It includes cases with multiple corticosubcortical infarcts, strategic infarcts, subcortical ischemic vascular dementia, and various forms of neurodegenerative pathology, including AD, which develop within 6 months of stroke*. This temporal basis for cognitive decline after stroke differentiates PSD from other forms of major VCI (VaD).

Mixed dementias: A standalone umbrella subgroup termed mixed dementias includes all the phenotypes specified for each combination, that is VCI-AD, VCI-DLB, so forth. It is recommended that a patient is referred to as having "VCI-AD", according to the phenotypes present, rather than less specific mixed dementia, for example. Where discrimination is possible, the order of terms should reflect the relative contribution of the underlying pathology, that is AD-VCI or VCI-AD.

Subcortical ischemic vascular dementia (SIVaD):† Small-vessel disease is the main vascular cause of SIVaD. Lacunar infarct and ischemic white matter lesions are the main type of brain lesions, which are primarily located subcortically. It incorporates the overlapping clinical entities of Binswanger's disease and the lacunar state.‡

Multi-infarct dementia (MID): "MID relates to the involvement, and likely contribution, of multiple large cortical infarcts in the development of dementia."§ The previously mentioned VICCCS definition of PSD is built on the definition of O'Brien et al. [13].

*Because a key facet of the definition of PSD is a time component of the appearance of decline within 6 months of having a stroke that does not recover, then irrespective of the presence or absence or comorbid neurodegenerative pathology, the aspect of time should be the primary variable for delineating between PSD (with or without neurodegenerative pathology which if present should be described) and mixed pathology (where the contributing components are described). In other words, PSD and mixed dementias could both have mixed pathology but PSD is recognized by its more acute presentation.

†As part of the efforts in VICCCS to standardize the nomenclature and abbreviations to be used in the future, VICCCS *diagnosis* participants were asked which abbreviation, from those most commonly used for SIVaD, should be taken forward. Initially, no consensus was reached (SIVaD, 36%; SIVD, 23%; SiVaD, 19%; SiVD, 4%, with 18% stating no preference) but in the subsequent round, where participants were asked to choose their preference from the two most favored abbreviations from round 4, most support was for SIVaD (65%) and therefore adopted.

‡Ninety-nine percent of respondents asked about this definition in the VICCCS *diagnosis* study supported this original definition [11] of SIVaD, whereas 92% supported it as a diagnostic category. Seventy-six percent of respondents stated that they would use this term clinically.

§Sixty-nine percent of VICCCS *diagnosis* respondents agreed that MID should be a diagnostic category; however, opinion was split on the use of this term in the clinical setting, with only 52% in favor of it. There was a consensus (72%) support for the original definition of MID by Hachinski et al. [9]. MID reflects the traditional view that multiple large cortical infarcts are required for dementia to develop; however, the most frequent objection was use of the word "required." Therefore, to give opportunity for this objection to be considered, a modified definition was also presented along with the original definition for participants to state their support in the subsequent round. The modified definition, as given above, proposed received a consensus support (72%).

concept of VCI. For rounds 4 to 6, there was also agreement as to what should constitute the arteriopathies subgroup (proposed in the O'Brien construct); however, in VICCCS, specific arteriopathies are a descriptive term of cause rather than a subgroup (Table 2).

3.2.2. Sensitivity to subtypes

The O'Brien construct was thought by 31% of respondents to be limited in capturing subtypes of VCI. Although it acknowledged rare hereditary disorders cause VCI, the construct focused mainly on sporadic forms of VCI. Seventy-eight percent of VICCCS respondents suggested that both hereditary (i.e., "type I" or "familial" VCI) and sporadic (i.e., "type II") should be encompassed within VCI. In round 4, most (85%) respondents preferred the terms *sporadic* and *familial* to be used as *descriptive information* for various forms of VCI rather than to define separate categories.

The proposed subtypes of the revised concept of VCI according to the VICCCS are depicted in Fig. 1.

3.2.2.1. Mild and major VCI (VaD)

In the O'Brien construct, VaD was used as an umbrella term for subgroups of severe forms of VCI. Round 3 participants were asked whether the term VaD was still useful. No clear consensus emerged, although a small majority (56%) favored its continued use. However, the timing of this VICCCS round coincided with the drafting of the fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5), widely used by clinicians worldwide. The draft DSM-5 proposal was that VaD or major VCDs [36] be shown in parentheses with the description "major neurocognitive impairment because of vascular disease" as a classification group for severe forms of impairment heretofore referred to as VaD [37]. We therefore sought VICCCS participants' views on the use of the terms "mild" and "major" in relation to VCI. Although only 39% of round 4 respondents were aware of the draft DSM-5, 71% agreed that the revised VCI concept should use the terms mild and major to align VICCCS recommendations with DSM-5. In round 5, a 71% majority supported the terminology "mild forms of VCI" and "major forms of VCI (VaD)."

3.2.2.2. Further subtyping of mild forms of VCI

Subtyping of mild forms of VCI was addressed in rounds 3 to 6. Most respondents (68%) were in favor of specifying subtypes. However, in response to a separate

Table 1
Clarification of the possible mechanisms of cause of either sporadic or hereditary VCI

Mechanisms of cause suggested by VICCCS participants	Percentage support
Cerebral amyloid angiopathy	*93*
Mixed forms, any neurodegenerative diseases with CVD (e.g., DLB with CVD)	*93*
White matter hyperintensities	*93*
Microbleeds/microhemorrhages	*89*
Microinfarcts	*89*
Arteritis/vasculitis, including both local and systemic inflammatory syndromes	*82*
Subdural or subarachnoid hemorrhage	*70*
Option "others" for future developments	*67*
Venous thromboses/infarcts	63
Infectious vasculitis	53
Hippocampal sclerosis	42
Angiomatous lesions/vascular tumors with local steal phenomenon	33
Chronic migraine	9

Abbreviations: CVD, cerebrovascular disease; DLB, dementia with Lewy bodies; VCI, vascular cognitive impairment; VICCCS, Vascular Impairment of Cognition Classification Consensus Study.

NOTE. Participants were given the opportunity to propose additional causative mechanisms to those previously listed in the *O'Brien concept* [13]. Percentage support from respondents in the final round is detailed. Those highlighted in italics reached consensus support of 67% and therefore are recommended.

question 63% thought that this separation lacked supporting evidence and was premature, and no subtype option could be agreed. Further detail of this is provided in the Supplementary Materials. VICCCS propose that mild VCI is not subtyped at this time until research provides better justification.

3.2.2.3. *Further subtyping of major forms of VCI (VaD)*

In round 3, respondents were asked to decide which subtypes of dementia proposed by O'Brien et al. should be recognized in VICCCS. Variable levels (81%–50%) of agreement were found. In round 4, most respondents (94%) agreed that this lack of consensus might be overcome if it were possible to avoid mixing site, severity, and mechanism. Ninety-six percent supported an effort to develop a more systematic stepwise approach toward subtyping based on VICCCS proposed categories of *L*ocation, *E*tiology, *D*omains (affected), and *S*everity, provisionally named "LEDS" criteria. With this in mind, participants were asked which of the O'Brien subtypes allowed for more mutually exclusive grouping of patients or might be considered better suited as *descriptive terms* for either the "mechanism" or "location" of damage. The subtypes "specific arteriopathies," "hemorrhagic" and "hypoperfusion" were not supported as standalone subtypes (13%–18%) and thus are recommended as descriptive terms of causal mechanisms in VCI. The remaining subtype terms received variable support between rounds. Round 6 collected a definitive decision, with terms that did not achieve majority (67%) support to be descriptors. "Subcortical ischemic" (83%) and "multi-infarct (cortical)" (74%) were supported as subtypes of major VCI (VaD). As in earlier rounds, poststroke dementia (PSD) was supported (73%) as a subgroup and 86% thought it also helpful for clinical diagnosis. In contrast, despite near threshold support (66%), for consistency "strategic infarct dementia" will also be proposed as a descriptive term for VCI. Additional suggestions for standalone subtypes of VCI were also invited. None of these were supported but "vasculitis"

Table 2
VICCCS-recommended subtypes and descriptive terms

Subtypes in the VICCCS	Descriptive terms in the VICCCS	*O'Brien concept classification and causes of sporadic VCI*
Poststroke dementia		Poststroke dementia
		VaD
Multi-infarct (cortical)		Multi-infarct dementia (cortical VaD)
Subcortical ischemic		Subcortical ischemic VaD
	Strategic infarct	Strategic-infarct dementia
	Hypoperfusion	Hypoperfusion dementia
	Hemorrhagic	Hemorrhagic dementia
	Specific arteriopathies*	Dementia caused by specific arteriopathies
Mixed dementias†		Mixed AD and VaD
Mild VCI		Vascular mild cognitive impairment
	Vasculitis‡	

Abbreviations: AD, Alzheimer's disease; VaD, vascular dementia; VCI, vascular cognitive impairment; VICCCS, Vascular Impairment of Cognition Classification Consensus Study.

NOTE. Mild VCI, poststroke dementia, multi-infarct (cortical), subcortical ischemic, and mixed dementias are agreed subtypes in the VICCCS. Those in italics fall under the umbrella term major VCI (VaD). Agreed revised definitions of subtypes are detailed in Box 2.

*Specific arteriopathies were agreed in a separate question for two rounds to include genetic, hereditary and developmental anomalies (e.g., Fabry's disease, sickle cell disease, cerebral autosomal-dominant arteriopathy with subcortical infarcts and leukoencephalopathy [CADASIL], and cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencephalopathy [CARASIL]), small-vessel disease from chronic hypertension and/or diabetes, inflammatory/immunological vasculitis, Moyamoya disease, and intracranial atherosclerosis.

†A revised holistic subtype of mixed dementias was developed and agreed over the course of number of rounds to replace "mixed AD and VaD." VICCCS agreed descriptive terms include strategic infarct, hypoperfusion, hemorrhagic, and specific arteriopathies.

‡Vasculitis, which was not originally part of the *O'Brien concept,* was also discussed in more detail as being an important descriptive term. The original *O'Brien concept classification and causes of sporadic VCI* [13] are listed for comparison.

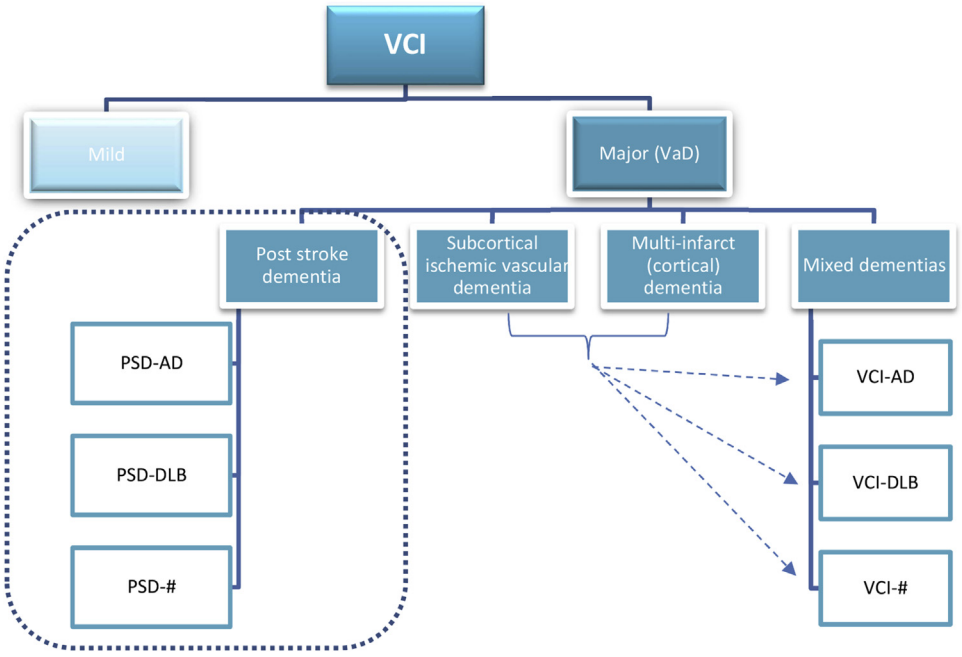

Fig. 1. Revised conceptualization of VCI in VICCCS. Subtypes of VCI are divided according to the level of VCI impairment into mild VCI and major VCI (VaD). Mild VCI is not further subdivided at this time. Major VCI (VaD) is classified into four main subtypes as depicted. The 6 month temporal basis (denoted by the hashed box) for cognitive decline after stroke differentiates poststroke dementia (PSD) from other forms of major VCI (VaD). PSD and mixed dementias are further delineated if a comorbid neuropathology is present (N.B. AD and dementia with Lewy bodies (DLB) are given as examples, with # denoting other possible combinations). Subcortical ischemic VaD or multi-infarct (cortical) dementia subtype cases with these specific types of dementia alone, however cases also presenting with any other neurodegenerative pathology would then be categorized as mixed dementias (dashed arrows) according to the comorbidities present. Abbreviations: AD, Alzheimer's disease; VaD, vascular dementia; VCI, vascular cognitive impairment; VICCCS, Vascular Impairment of Cognition Classification Consensus Study.

was agreed (69%) as a helpful descriptive term of cause (Supplementary Table 2). The resultant VICCCS-recommended subtypes and descriptive terms are presented in Table 2.

3.2.3. *Descriptiveness—clear definitions*

3.2.3.1. *Mixed dementias*

Mixed dementia and its definition in clinical practice and research were identified as needing elucidation from the earliest rounds, with 97% of respondents favoring change to the traditional imprecise usage. In the final Delphi round, 95% of respondents agreed with a proposed solution to the differences in opinion on the term (detailed in Supplementary Material). "Mixed dementias" proposed should serve only as an "umbrella" term for subtypes of major VCI (VaD) under which all phenotypes present would be specified. Patients would be referred to as having for example; VCI-AD, VCI–dementia with Lewy bodies, so forth according to whatever dementia comorbidities presented. A large number of respondents (81%) endorsed this approach for both research and clinical applications, and consensus (68%) was that the order of abbreviations should reflect the relative contributions of the comorbidities, as far as practicable.

3.2.3.2. *Poststroke dementia*

There was consensus for the term PSD to be used in research (73%) and clinical (86%) contexts, but no consensus (63%) around how PSD was previously described, which we had tried to address in later rounds and continued to do in VICCCS *diagnosis*. Related issues thought necessary to clarify PSD, including evidence of cognitive impairment before stroke and timeframes for the emergence of PSD, are detailed in Supplementary Material. VICCCS consensus (78%) views on delineation of PSD are detailed in Box 2 and Fig. 1. Of note is the temporal association between cognitive decline and stroke differentiates' PSD from other forms of major VCI (VaD), that is, cognitive impairment within 6 months of having a stroke would be the determining factor for a diagnosis of PSD.

Consensus proposed definitions for major VCI (VaD) subtypes (PSD, mixed dementias, subcortical ischemic VaD, and multi-infarct dementia) are presented in Box 2.

4. Discussion

VICCCS has provided revision and consensus-based elaboration of the construct of VCI in most areas addressed. Lack of consensus in some areas was mainly because of a

few research data available at the time, for example, the subcategorization of mild forms of VCI. VICCCS showed that although half of the respondents wanted to lessen the overemphasis on memory-impairment in the conceptualization of VCI, two-thirds acknowledged the benefit in the amnestic separation to facilitate alignment with current formats used for AD and mild cognitive impairment. Thus, subtypes of VCI require more research-based justification.

Definition of more homogeneous groups was supported for major VCI—also important for clinical trial design. Clinical diagnosis of coexisting pathologies remains a challenge. Previous definitions of mixed dementia were not greatly supported in VICCCS, partly because of dissatisfaction with the overemphasis of AD (see Supplementary Material). When the study concluded, a revised concept of the most favored definition (25% support) has been published for "mixed AD" [30] that does provide separate criteria for coexisting CVD and Lewy body pathology, however does not differentiate these by terminology. VICCCS proposes in mixed dementias and PSD that all phenotypes identified should be specified, depending on whatever dementia-related comorbidities are present, wherein the order of abbreviations reflects the perceived relative contributions. Improvements to the practicalities and accuracy of this would be important aspects of any future operational diagnostic protocols, whereas ongoing research in biomarkers may be helpful. Recent evidence lends weight to this approach, where subcortical VaD can be identified in an outpatient memory clinic setting according to the neuropsychological features and CSF-biochemical markers distinct from those of AD [38]. Box 3 summarizes this and other areas for future research either proposed or reflected in responses from VICCCS.

VICCCS was conducted between 2010 and 2013 that coincided with the development of *DSM-5* [39] and International Society for Vascular Behavioral and Cognitive Disorders (VASCOG) criteria for VCD [36]. VICCCS participants were given the opportunity to provide collective feedback on draft DSM-5 proposals that were made available before its finalization. This was enabled through a tailored survey developed (by O.A.S.) in consultation with P.S. acting on behalf of the DSM-5 Neurocognitive Disorders Work Group and was prompted by their online request for input from the clinical research community into the refinement process. Awareness among VICCCS participants of this request was relatively modest, demonstrating a need for wider advertisement of such consultations in future. VICCCS participants agreed that the *mild* and *major* terminologies proposed in DSM-5 were helpful and similarly should be adopted in VICCCS.

In relation to the subsequent published criteria (in 2014) for VCDs, VICCCS had previously explored but was not supportive of this concept and the use of this term VCD [11,17]. However, the VASCOG criteria are also reported to be aligned with DSM-5 [36].

4.1. Considerations of the Delphi process on VICCCS outcomes

A key principle of the Delphi method is that decisions from a structured specialist group of individuals are more accurate. The use of online surveys in VICCCS, to avoid scheduling constraints of a physical meeting, facilitated the inclusion of an unprecedented large number of international participants who have enriched discussions. The anonymity offered by Delphi reduced the potential for any individuals to dominate direction of discussions. Furthermore, in combination with the repeated group feedback, the anonymity allowed contemplation, review of initial judgments, and scope for participants to freely change opinions, all of which promoted the generation of consensus [34,40]. The use of specific published articles helped to focus the discussion points and in some cases, increased awareness of previous studies, aiding more-informed decision making. After the initial rounds, structured, mostly closed questions were mainly used to ensure continued focus when some feedback was possible, in the primary discussion of topics. This sometimes extended the duration of the study and

Box 3
Potential areas for future research as proposed directly or identified from responses from the VICCCS.

1. Evidence-based studies to support further subdivision of mild VCI.
2. Develop a more systematic stepwise approach toward subtyping of patients based on new VICCCS proposed categories of location, etiology, domains (affected), and severity.
3. Investigation of factors that determine immediate or delayed onset of VCI in PSD patients.
4. Investigation of factors (e.g., time to onset, biomarkers, cognitive parameters) that may better delineate comorbidity of PSD with other causes of VCI or nonvascular dementias.
5. Further elucidation to improve phenotyping of relative contribution of the co-occurring pathology, for example, AD-VCI or VCI-AD in mixed dementias, or other neurodegenerative diseases (e.g., Parkinson's disease) or psychiatric disorders that copresent with CVD.
6. Further exploration of the utility and validity of the traditional term multi-infarct dementia as either a specific-subtype of major VCI (VaD) or as a complementary descriptive term alongside the newly proposed subtypes of major VCI (VaD)

complexity of the arguments, such as the discussion of mixed dementias and PSD. Yet the extended debate was useful but increased risk of participant attrition, and variation in respondent numbers in each round did variably impact on the relative contribution of each respondent toward consensus. However, most topics were dealt with over multiple rounds giving many opportunities to confirm the consensus view. The maintenance of a high number of participants throughout the study provides assurance that a consensus concept of VCI has been realized, although by definition the consensus was based on a majority view.

5. Conclusions

VICCCS presents a new consensus-based set of guidelines supported by a large international pool of researchers. These guidelines have drawn on, expanded, and refined previous efforts to improve and clarify the conceptualization of VCI. It is anticipated that VICCCS guidelines will be widely adopted in the community to increase the levels of consistency and standardization in undertaking VCI research. This should significantly enhance the interpretation and comparison of findings across studies and support the likelihood of more large-scale collaborative research that will be vital to help overcome historical limitations posed by the prevalence of VCI.

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Supplementary data

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RESEARCH IN CONTEXT

1. Systematic review: Capturing the complexity involved in vascular cognitive impairment (VCI) has given rise to various terms such as *multi-infarct dementia*, *vascular dementia*, *subcortical (ischemic) vascular dementia*, *VCI*, and *vascular cognitive disorders.* These terms were used as search-terms in Pubmed for relevant published reports (by August 2010). The authors list identified potential study participants and a Steering Group. Twelve concept articles and 15 articles proposing diagnostic criteria were used in the Delphi study.
2. Interpretation: This process resulted in the formation of new consensus-based guidelines for VCI that have drawn on and refined previous initiatives. High levels of participation by the research community should ensure these guidelines will be more widely endorsed.
3. Future directions: Key research priorities include evidence-based studies to (1) determine appropriate subdivision of mild VCI and (2) improve phenotyping of the co-occurring pathology in mixed dementias, and other neurodegenerative diseases or psychiatric disorders that copresent with cerebrovascular disease.

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