UMC Utrecht

Future challenges in VCI

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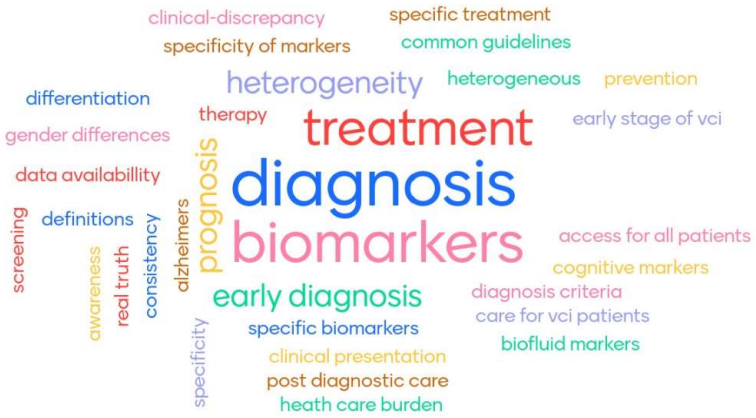
University Medical Center Utrecht

Challenges in VCI > what's your view?

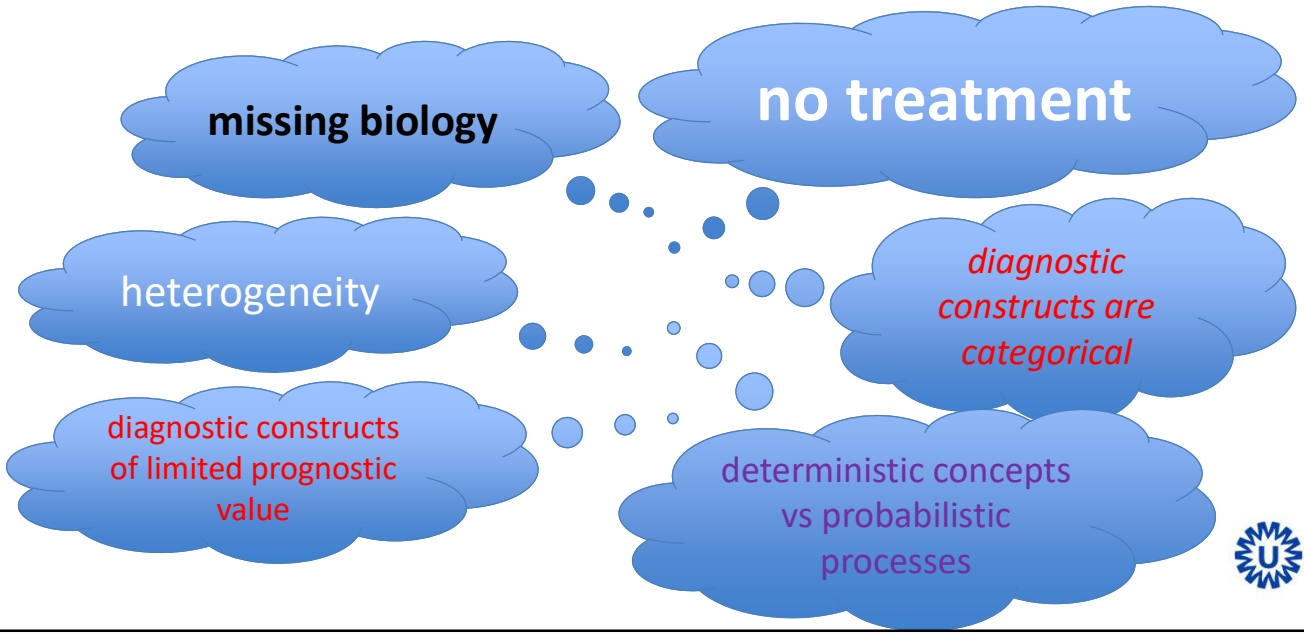
Mentimeter

What are the challenges in VCI
56 responses



43

Challenges in VCI > my "word cloud"



Diagnosing and studying VCI

- take a step back on current criteria and markers
- what we can do today
- future perspectives

Vascular dementia: diagnostic criteria

NINDS-AIREN criteria

I. Criteria for the clinical diagnosis of PROBABLE vascular dementia include all of the following:

+ • Dementia defined by cognitive decline from a of functioning and manifested by impairment or more cognitive domains (orientation, attent visuospatial functions, executive functions, m praxis), preferably established by clinical exar documented with neuropsychologic testing; de enough to interfere with activities of daily livi effects of stroke alone.

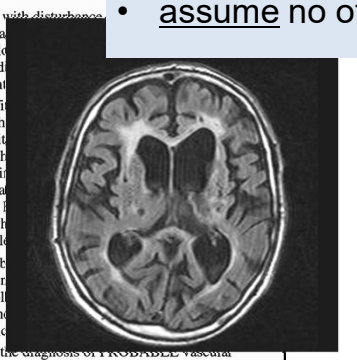
+ — Exclusion criteria: cases psychosis, severe aphasia precluding neuropsycholo disorders or other brain d themselves could account

- • Cerebrovascular disease, defi neurologic examination, such Babinski sign, sensory deficit with stroke (with or without h relevant CVD by brain imagi vessel infarcts or a single stra thalamus, basal forebrain, or l multiple basal ganglia and wh periventricular white matter l

• A relationship between the ab inferred by the presence of or dementia within 3 months foll deterioration in cognitive func progression of cognitive defic

II. Clinical features consistent with the diagnosis of PROBABLE vascular dementia include the following:

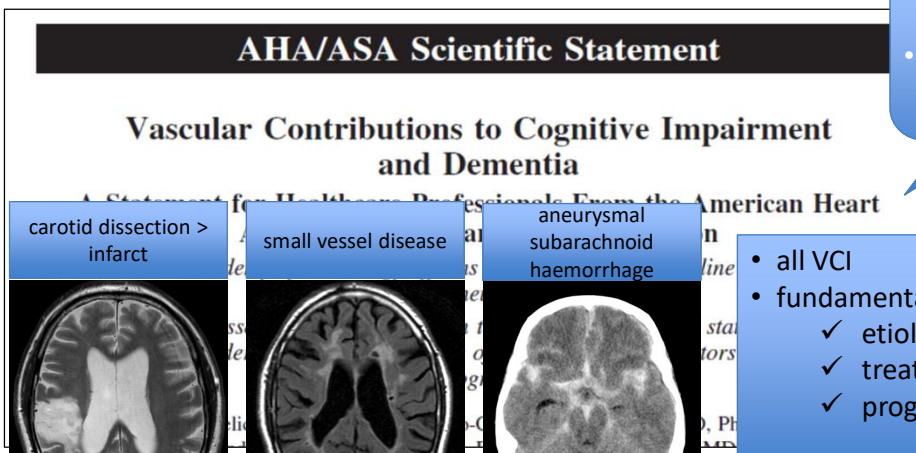
• Early presence of a gait disturbance (small-step gait or marche à petits



essence:
- establish clinical syndrome
- show vascular pathology
- assume no other causes

Vascular dementia: diagnostic criteria

more inclusive:



- acquired cognitive impairment
- vascular disease is a likely cause

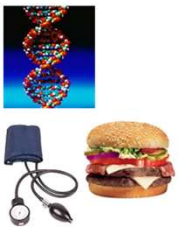
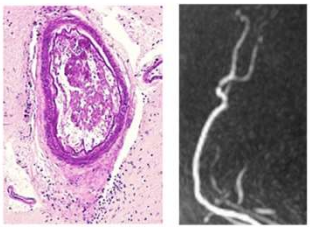
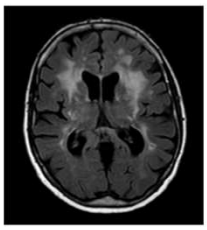
carotid dissection > infarct

small vessel disease

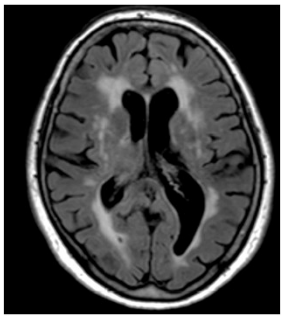
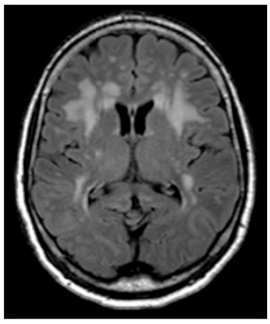
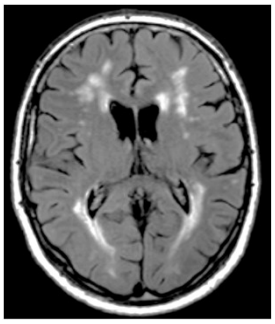
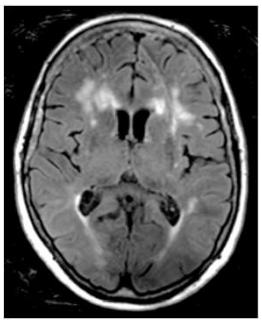
aneurysmal subarachnoid haemorrhage

- all VCI
- fundamental differences in
  - ✓ etiology/biology
  - ✓ treatment
  - ✓ prognosis

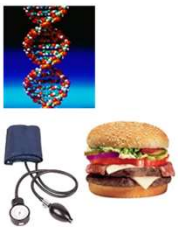
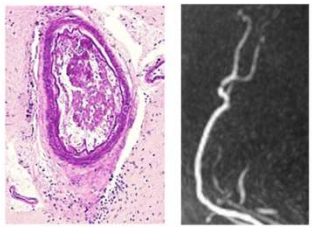
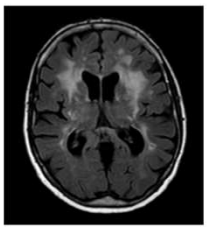
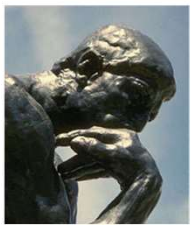
studying, diagnosing & treating VCI – current status

	risk factors	vascular disease processes	tissue injury	cognition
				
diagnostic info	✓		✓	✓

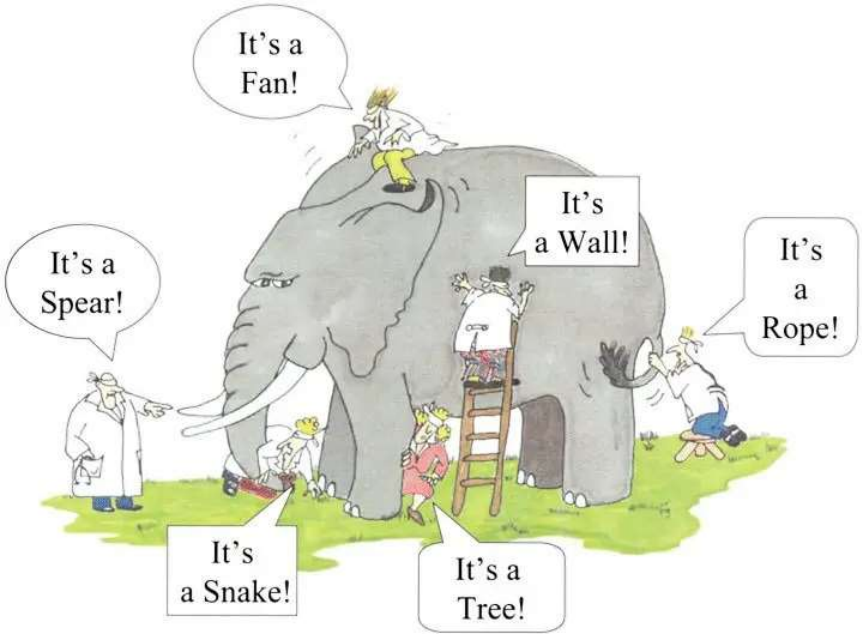
MRI & diagnosis VCI due to SVD

woman 83 MCI	woman 62 mild cognitive decrement	man 75 dementia	woman 73 cognitively intact
			
Dx: VCI due to SVD	Dx: cognitive decrement due to SVD	Dx: Alzheimer's disease with vascular component	Healthy volunteer research project

studying, diagnosing & treating VCI – current status

	risk factors	vascular disease processes	tissue injury	cognition
				
diagnostic info	✔		✔	✔
assumptions				

VCI – what's in a name....



VCI – what's in a name....

Fortunately no AD..
This doctor knows what she is talking about..
Can I be treated?
What will the future bring?
……..

I checked everything
I followed the guidelines
Patient meets the criteria
My colleagues will understand my diagnosis
……..

ELSEVIER

Alzheimer's & Dementia 14 (2018) 535-562

Alzheimer's & Dementia

2018 National Institute on Aging—Alzheimer's Association (NIA-AA) Research Framework

NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease

Clifford R. Jack, Jr.,[a,*]
Samantha Budd Ha

AT(N) biomarker groupi

A: Aggregated Aβ or asso
CSF $A\beta_{42}$, or $A\beta_{42}/A\beta_4$
Amyloid PET
T: Aggregated tau (neurofi
CSF phosphorylated tau
Tau PET
(N): Neurodegeneration or
Anatomic MRI
FDG PET
CSF total tau

ELSEVIER

Check for updates

Alzheimer's & Dementia 15 (2019) 158-167

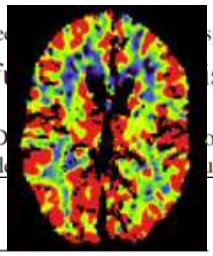
Alzheimer's & Dementia

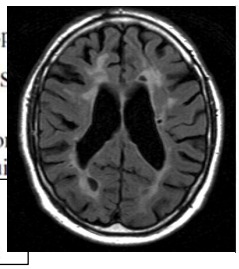
Spe

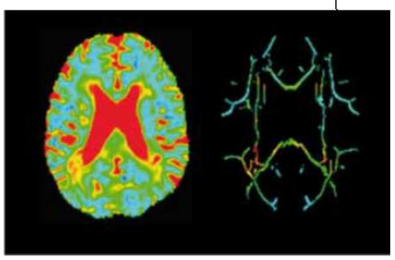
Vascular dysf

Melanie D
Lon S. Schneid

where is the "V"??







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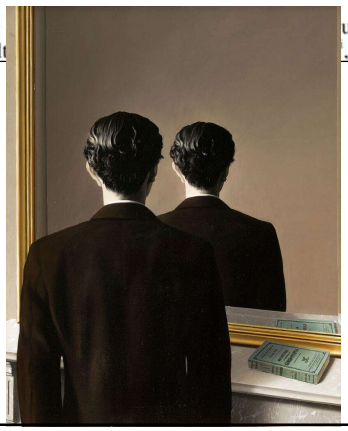
2018 National Institute on Aging—Alzheimer's Association (NIA-AA) Research Framework

NIA-AA Research Framework: Toward a biological definition of Alzheimer's disease

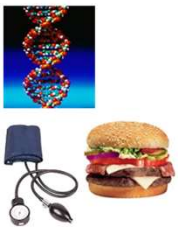
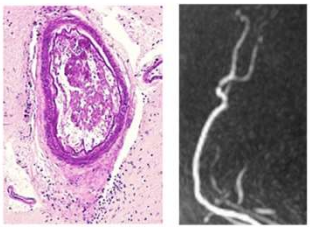
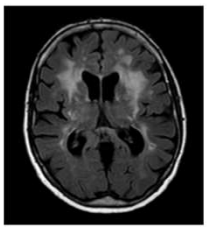
Clifford R. Jack, Jr.,[a,*], David A. Bennett[b], Kaj unn[e],
Samantha Budd Haeberlein[f], David M. Holt

toward biological definitions of VCI



VCI – developments

risk factors | vascular disease processes | tissue injury | cognition

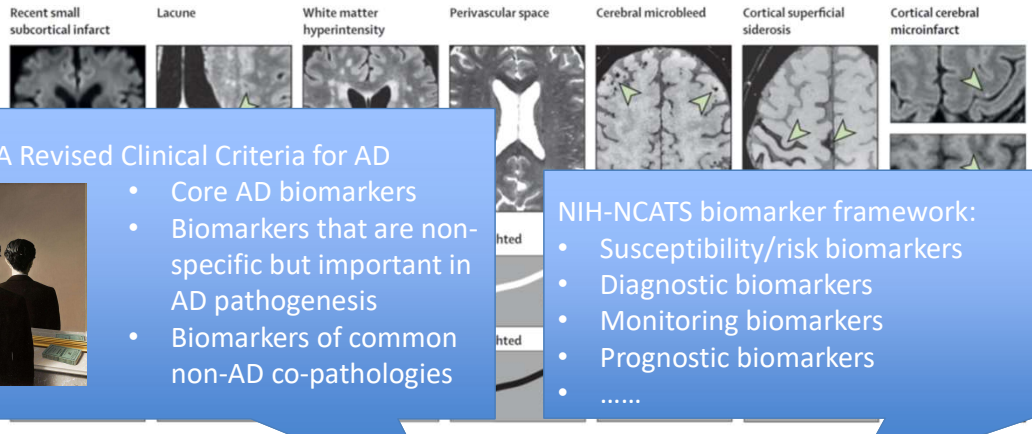

novel markers of disease processes

- genetics
- circulating biomarkers

- imaging markers

potential for novel imaging markers

updated STRIVE criteria



NIA-AA Revised Clinical Criteria for AD

- Core AD biomarkers
- Biomarkers that are non-specific but important in AD pathogenesis
- Biomarkers of common non-AD co-pathologies

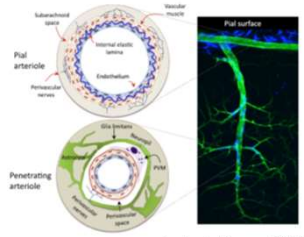
NIH-NCATS biomarker framework:

- Susceptibility/risk biomarkers
- Diagnostic biomarkers
- Monitoring biomarkers
- Prognostic biomarkers
- ……

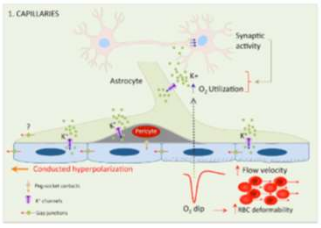
Duering et al Lan… …ogy 2023

(novel) VCI biomarker? consider biology, biomarker goal

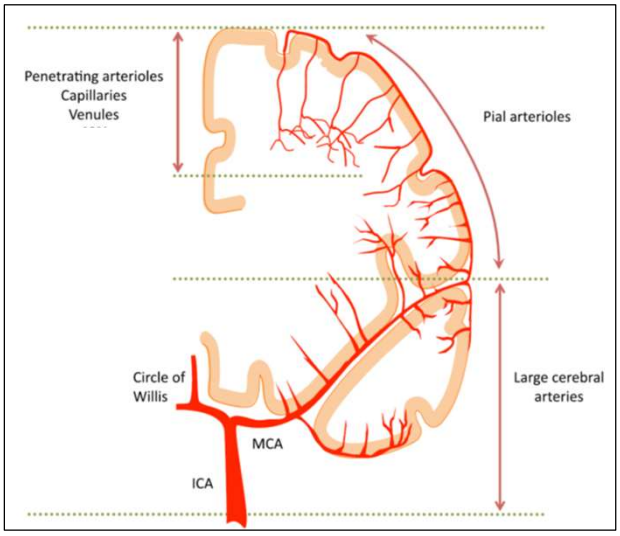
neuroscience & clinic of small vessel disease:
developments & translational gaps



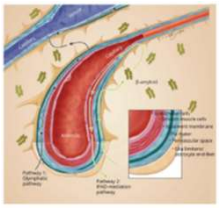
Iadecola Neuron 2017



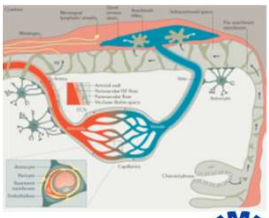
Neurovascular coupling



Iadecola Neuron 2017

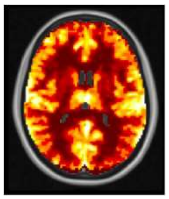


pervivascular spaces – brain clearance

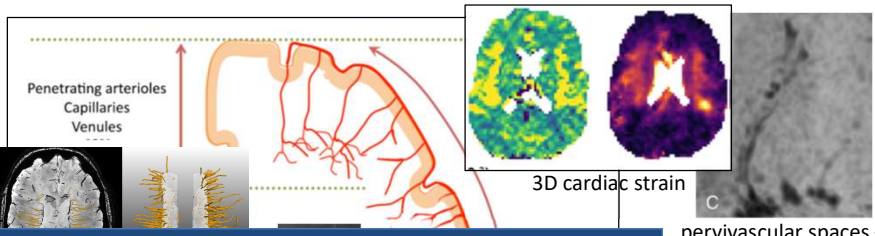


BBB

translational gap in small vessel disease:
opportunities for (7T) MRI

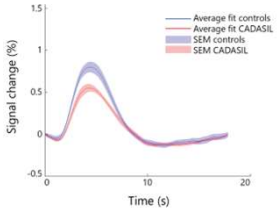


Cerebrovascular reactivity



3D cardiac strain

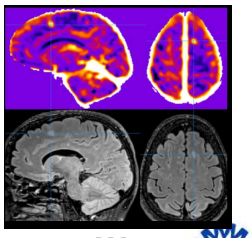
pervivascular spaces – brain clearance



Neurovascular coupling

application in SVD:

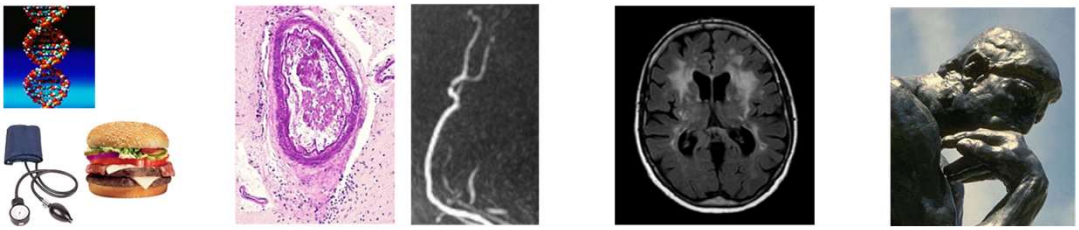
- early stages
- rapid development
- emerging patterns of differential vessel involvement – different diseases



BBB

VCI – developments

risk factors | vascular disease processes | tissue injury | cognition



novel markers of disease processes

- genetics
- circulating biomarkers
- imaging markers

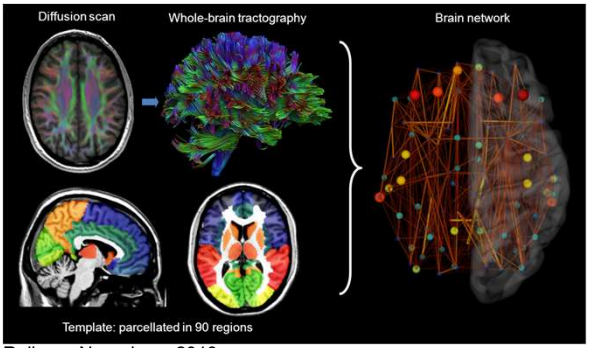
novel markers of functional impact

- connectomics
- lesion pattern analyses

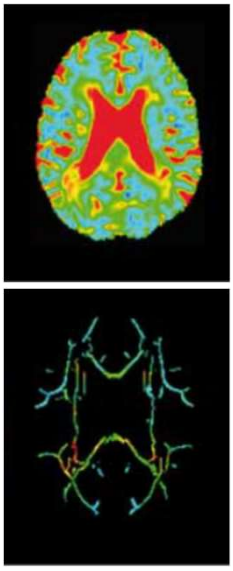
Markers of cognitive impact of vascular injury

diffusion MR

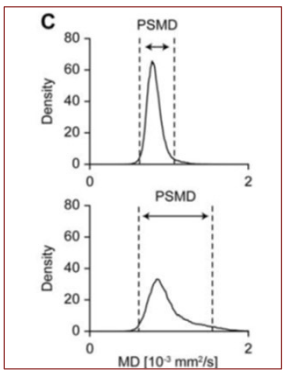
connectomics



Reijmer, Neurology, 2013



peak width of skeletonized mean diffusivity [PSMD]



Baykara, Annals Neurol 2016

Markers of cognitive impact of vascular injury

lesion patterns – strategic lesions

special article

Vascular dementia: Diagnostic criteria for research studies

Report of the NINDS-AIREN International Workshop*

G.C. Román, MD; T.K. Tatemichi, MD; T. Erkinjuntti, MD; J.L. Cummings, MD; J.C. Masdeu, MD; J.H. Garcia, MD; L. Amaducci, MD; J.-M. Orgogozo, MD; A. Brun, MD; A. Hofman, MD, PhD; D.M. Moody, MD; M.D. O'Brien, MD; T. Yamaguchi, MD; J. Grafman, PhD; B.P. Drayer, MD; D.A. Bennett, MD; M. Fisher, MD; J. Ogata, MD; E. Kokmen, MD; F. Bermejo, MD; P.A. Wolf, MD; P.B. Gorelick, MD; K.L. Bick, PhD; A.K. Pajeau, MD; M.A. Bell, DPhil; C. DeCarli, MD; A. Culebras, MD; A.D. Korczyn, MD; J. Bogousslavsky, MD; A. Hartmann, MD; and P. Scheinberg, MD

Neurology 1993

Table 1. Brain imaging lesions associated with vascular dementia

I. Topography

Radiologic lesions associated with dementia include ANY of the following or combinations thereof:

1. Large-vessel strokes in the following territories:
   - Bilateral anterior cerebral artery
   - Posterior cerebral artery, including paramedian thalamic infarctions, inferior medial temporal lobe lesions
   - Association areas: parietotemporal, temporo-occipital territories (including angular gyrus)
   - Watershed carotid territories: superior frontal, parietal regions

mostly from case studies
comprehensive map lacking

lesion symptom mapping

MetaVCI Map consortium - https://metavcimap.org/

aim: "to perform meta-analyses on strategic lesion locations for VCI using LSM."

Approach: "integration of data from different cohorts to increase sample sizes, to improve brain lesion coverage and support comprehensive LSM studies"

Weaver, Alz&Dem 2019

lesion symptom mapping – MetaVCIMap.org

Strategic infarct locations for post-stroke cognitive impairment: a pooled analysis of individual patient data from 12 acute ischaemic stroke cohorts

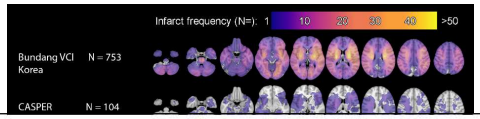
Nick A Weaver, Hugo J Kuijf, Hugo P Aben, Jill Abrigo, Hee-Joon Bae, Mélanie Barbay, Jonathan G Best, Régis Bordet, Francesca M Chappell, Christopher P L H Chen, Thibaut Dondaine, Ruben S van der Giessen, Olivier Godefroy, Bibek Gyanwali, Olivia K L Hamilton, Saima Hilal, Irene M C Huenges Wajer, Yeonwook Kang, L Jaap Kappelle, Beom Joon Kim, Sebastian Köhler, Paul L M de Kort, Peter J Koudstaal, Gregory Kuchcinski, Bonnie Y K Lam, Byung-Chul Lee, Keon-Joo Lee, Jae-Sung Lim, Renaud Lopes, Stephen D J Makin, Anne-Marie Mendyk, Vincent C T Mok, Mi Sun Oh, Robert J van Oostenbrugge, Martine Roussel, Lin Shi, Julie Staals, Maria del C Valdés-Hernández, Narayanaswamy Venketasubramanian, Frans R J Verhey, Joanna M Wardlaw, David J Werring, Xu Xin, Kyung-Ho Yu, Martine J E van Zandvoort, Lei Zhao, J Matthijs Biesbroek, Geert Jan Biessels

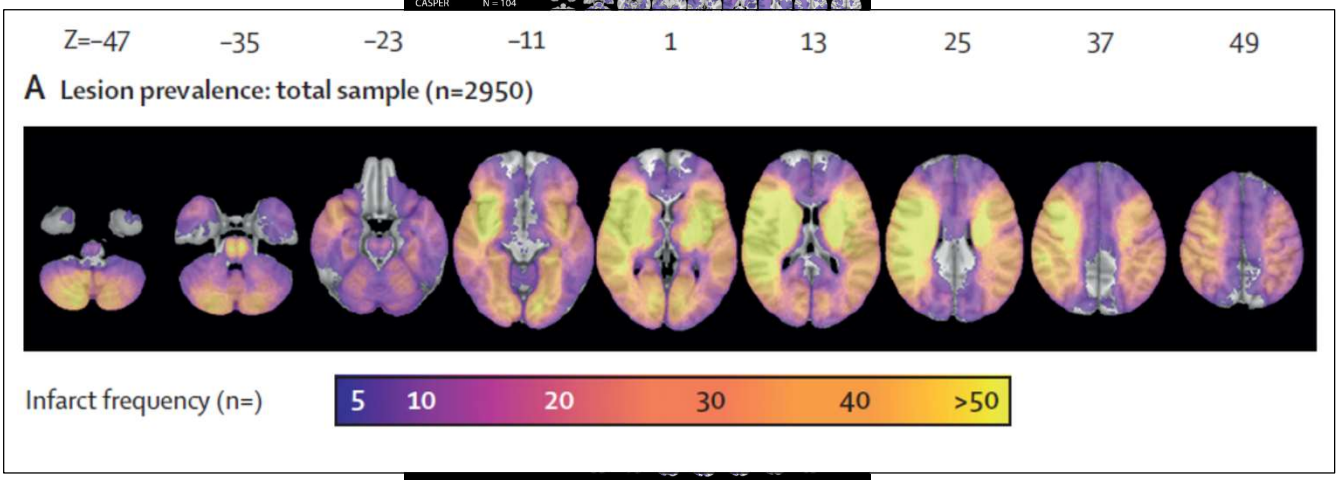
Summary

Background Post-stroke cognitive impairment (PSCI) occurs in approximately half of people in the first year after stroke. Infarct location is a potential determinant of PSCI, but a comprehensive map of strategic infarct locations

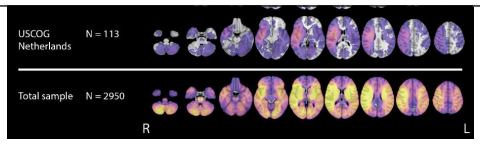
Lancet Neurol 2021
Published Online

results:



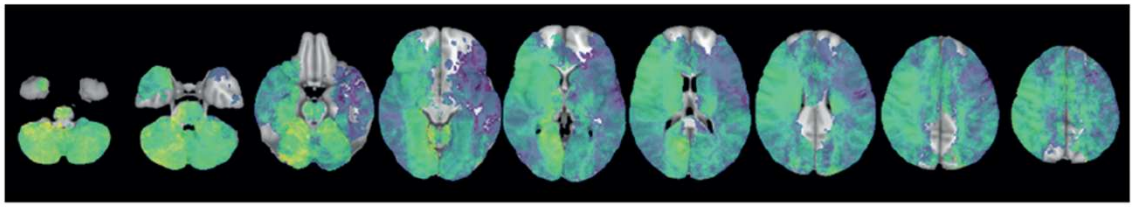


lesion coverage 86·9% of brain voxels

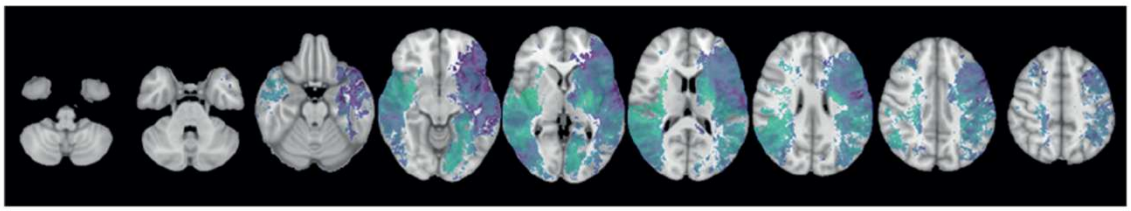


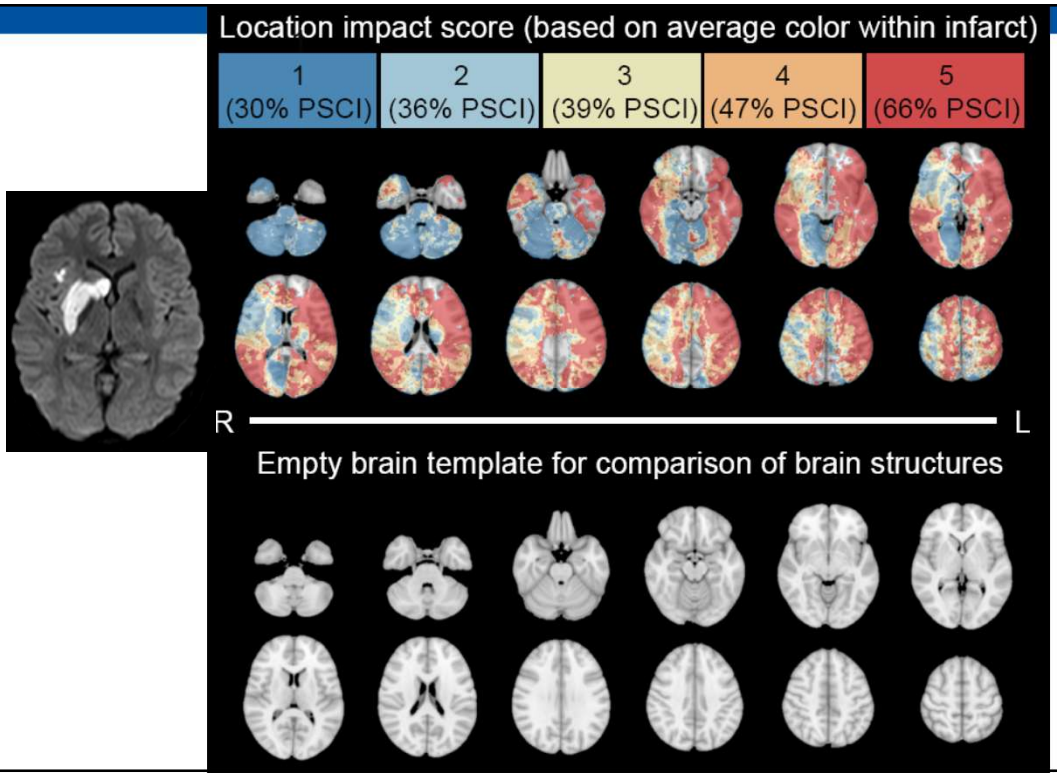
results:

B ORs for PSCI: total sample, all tested voxels (n=2950)

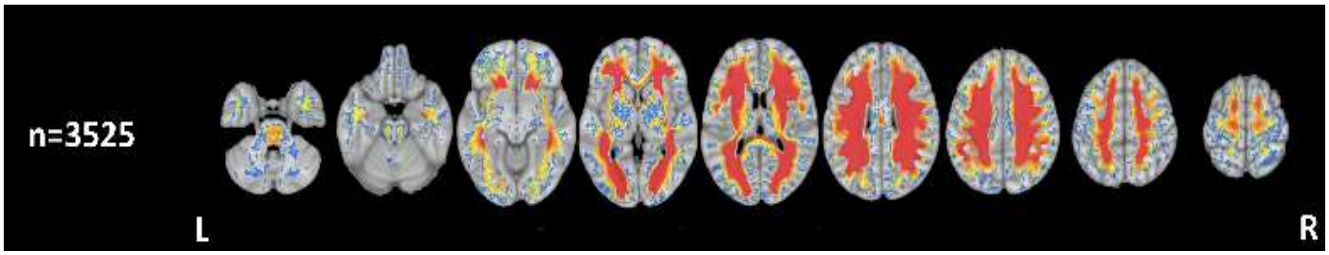


C ORs for PSCI: total sample, significant voxels (n=2950; FDR q<0·01)





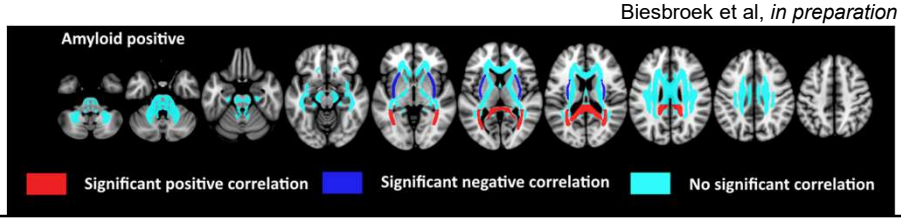
lesion symptom mapping – MetaVCIMap.org



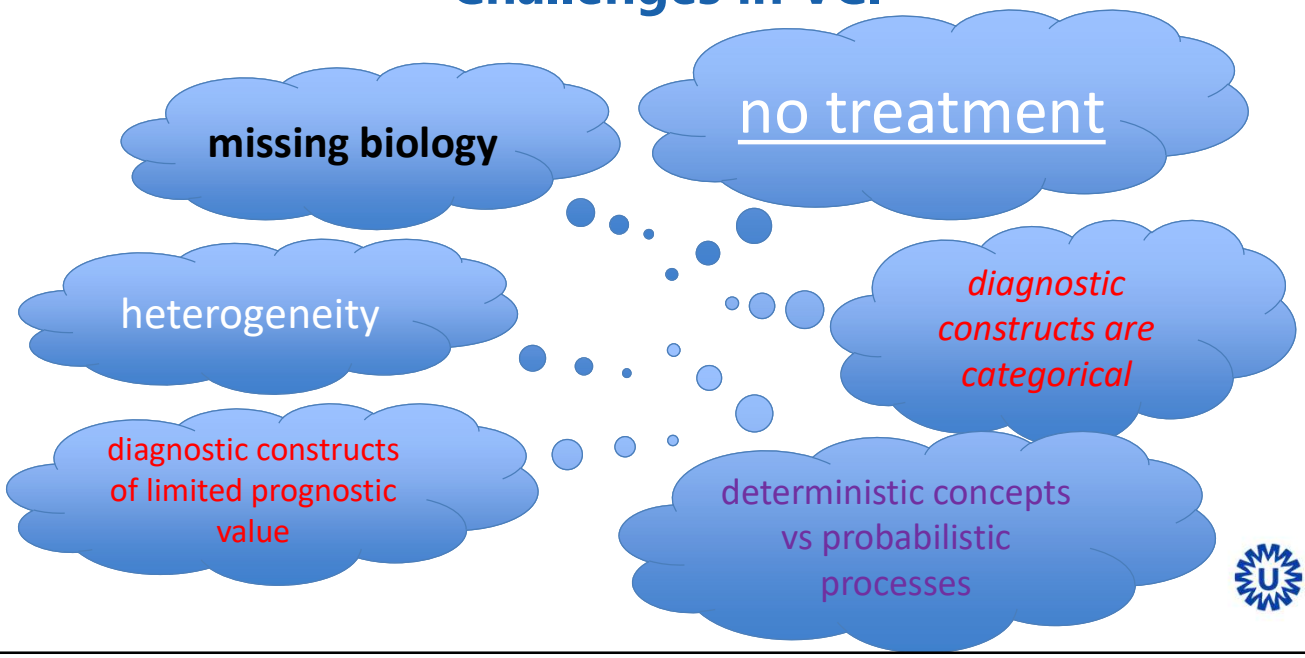
WMH: memory clinic (11 cohorts, 3525 patients) Coenen, Alz&Dem 2023

- strategic WMH score based on four key tracts inversely correlated with cognitive performance

Biesbroek et al, *in preparation*



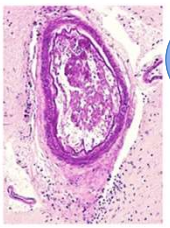
Challenges in VCI

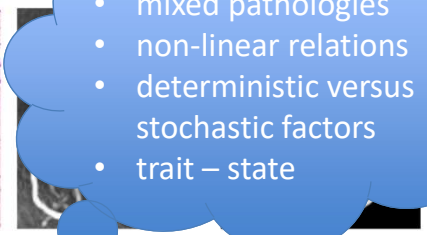


VCI – opportunities

risk factors

vascular disease pr





consider:
- mixed pathologies
- non-linear relations
- deterministic versus stochastic factors
- trait – state

ognition

novel markers of disease processes

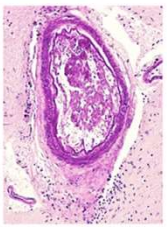
- genetics
- circulating biomarkers

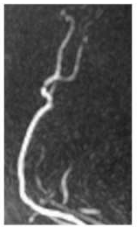
- imaging markers

VCI – opportunities

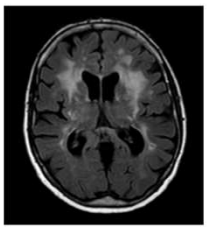
risk factors

vascular disease processes

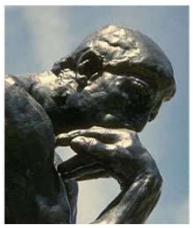




tissue injury



cognition



novel markers of disease processes

- genetics
- circulating biomarkers

- imaging markers

novel markers of functional impact

- connectomics
- lesion pattern analyses

thank you !

NWO Vidi, Vici

SVDs @target

HORIZON 2020

Dutch CardioVascular Alliance

Nederlandse Hartstichting

UMC Utrecht