From Gustafson to Everyone: 12:31 PM

If time, can Dr. Mok comment on the role of the multisystem Renin Angiotensin System (RAS) and ACE2 receptor blockers in relation to treating both COVID-19 as well as central effects?

From Steven to Everyone: 12:31 PM

What is the role of the anti-phospholipid antibodies that have been reported in COVID

From Dr Subha Thiyagesh to Everyone: 12:39 PM

Thank you and a brief key take home messages would be very welcome given a number of us were not admitted into the session
Thank you so much.

From Philip Bath to Everyone: 12:39 PM

Primarily increase in large artery strokes but at non-athero sites and often in younger people. Probably decrease in lacunar stokes. Plus reduction in hospital attendance for TIA/minor stroke. SO overall less strokes but more severe ones and often in younger people.

From Gustafson to Everyone: 12:39 PM

Here is the paper authored by Dr. Mok.

From Dr Subha Thiyagesh to Everyone: 12:39 PM

Thanks Philip

From Pat Kehoe to Everyone: 12:44 PM

This is the link to paper in Vincent's first slide of the various COVID risk factors:
https://www.nature.com/articles/s41586-020-2521-4

From Chung Tong Vincent MOK to Everyone: 12:53 PM

Phil, same here in HK, we have less TIA presenting to hospitals, but more severe strokes who had preceding TIA, that is, patients less inclined to seek medical help with TIA during COVID

From CHRISTOPHER Chen to Everyone: 12:55 PM

there appears to quite wide variations - here in Singapore we had strokes associated with SARS but not with covid-19

From Steven to Everyone: 01:01 PM

Thoughts on treatment?

From hughmarkus to Everyone: 01:02 PM

Why do some mutation sonly contribute to heterozygous disease and not CARASIL- if they affect protease activity you'd expect them to cause more severe disease if homozygous

From Alessandra Granata to Everyone: 01:02 PM

Do you think all HTRA1 must are loss of function or het may play a dominant negative role? Also do you think is a SMC exclusive phenotype?

From CHRISTOPHER Chen to Everyone: 01:08 PM

apart from severe WMH and lacunes, do patients with CARASIL have microbleeds, microinfarcts and perivascular spaces on MRI?

From Raj Kalaria to Everyone: 01:23 PM

Apologies again to all over the first 100. Vincent also mentioned this paper at the beginning from Cos Iadecola in Cell: https://pubmed.ncbi.nlm.nih.gov/32882182/

From Marco Düring to Everyone: 01:29 PM

Thanks Donna for this nice overview. You mentioned the stratification kit, which includes NfL. Since elevated NfL levels are unspecific and also elevated in SVD (also e.g. in CADASIL), how will it be used in stratification?

From Gustafson to Everyone: 01:30 PM

How common is CSVD without vascular risk factors for dementia, i.e., a 'clean' CSVD as recommended early in your talk for recruitment to RCTs?

From Barry McColl to Everyone: 01:31 PM

Thanks for the interesting talk - can you comment on how much you think hypoxic signalling may drive the increase in the fluid markers given some are canonical HIF-1-regulated?

From Silvia Fossati to Everyone: 01:32 PM

Hello Donna!! Have you looked at possible differences in PlGF expression in brain and plasma in early stages versus late stages of WMD or differences in WMD versus pure AD?

From Philip Bath to Everyone: 01:32 PM

Does PLGF dimerise with VEGF-Aa and VEGF-Ab and if so is it pro and anti-angiogenic, and if so what is the balance between pro and anti?

From awn to Everyone: 01:32 PM

How do you define Clinical SVD in your intesting research? /A Wallin

From Chris Patrick Pflanz to Everyone: 01:34 PM

You've mentioned that the vascular risk factors were associated with reductions in WMH and FA. I was wondering to which extend diffusion MRI as compared with volumetric MRI adds information as an imaging biomarker. Is MRI likely to become a new standard in clinical trails?

From donnawilcock to Everyone: 01:38 PM

To answer Silvia’s question. We are working on the early vs late stage WMD in MarkVCID. We have looked at some of our “pure” AD and we do not see elevations in PlGF

From Silvia Fossati to Everyone: 01:39 PM

Thanks Donna! Great talk as usual!

From donnawilcock to Everyone: 01:42 PM

To answer Philip's question PlGF does dimerise with both VEGF-Aa and VEGF-Ab I believe. Primarily pro-angiogenic, but I do not believe this has been fully evaluated.
To answer awn's question, clinical SVD is defined as WMH on MRI and VCID as WMH with cognitive impairment
To answer Chris' question, I think for any SVD trial, MRI will be critical for recruitment and inclusion. DWI is much more useful for SVD as opposed to volumetrics, which can have utility in AD where you have significant atrophy

From Fergus Doubal to Everyone: 01:50 PM

Thank you very much Frank-Erik, were the incident DWI positive lesions in the Run DMC intense study associated with any symptoms and if so what were they?

From CHRISTOPHER Chen to Everyone: 01:53 PM

are there any patient factors which determine whether the acute DWI lesions are subcortical or cortical?

From Henk Mutsaerts to Everyone: 01:56 PM

The acute lesions are relatively small compared to the resolution, I would be interested if T2* or SWI in 7T (Hilde? ;) could actually show these lesions clearer

From Tessa to Everyone: 01:56 PM

Do you think the lesions which disappear are still contributing to clinical signs?

From Joel Ramirez to Everyone: 01:57 PM

thank-you Frank-Erik. Given the size of these lesions (very small) how do you ensure accurate co-registration from different time points using multiple imaging methods?

From Dr. Yoshiki Hase (UK) to Everyone: 01:58 PM

what is the advantage of R2* compare to T2*?

From Louise van der Weerd to Everyone: 01:59 PM

You contribute the presence of T2*/SWI lesions to conversion to microbleeds. Do you think that is always the case, or may these also be due to the presence of iron-positive activated microglia, as is e.g. seen in some MS lesions?

From Frank-Erik de Leeuw to Everyone: 02:06 PM

to Joel: very valid point; we tried to co-register as best as possible with great help of MArco Duering; he can provide you with more technical details.
to yoshiki: I think R2* offers the opportunity to quantify iron content in the brain and as such you may be able to monitor more closely what is going on in terms of pathophysiology. To my knowledge T2* is more of a yes/no phenomenon

From Marco Düring to Everyone: 02:09 PM

to Joel: Indeed, this level of registration quality is a challenge. After evaluating multiple methods, we chose ANTs for multimodal registration and did extensive QC checks. Also, we used cost functions and difference images to check registration quality and to facilitate the detection of incident lesions.

From ahainswo to Everyone: 02:31 PM

if a capillary dilates, do RBCs still pass through in single file?

From Erik Bakker to Everyone: 02:35 PM

Do (dilated) perivascular spaces interfere with neurovascular coupling?

From Louise van der Weerd to Everyone: 02:42 PM

To Yoshiki. The terms T2* and R2* are always a bit confusing. You can have T2*-weighted (T2*w) scans. These are GE scans with a single echo. The echo time determines the image contrast which you can assess qualitatively. T2* is the quantitative relaxation time, which you can calculate from multiple GE images with different echo times. R2* is simply 1/T2* , so T2* and R2* hold the same quantitative information.

From Sharmelee Selvaraji to Everyone: 02:44 PM

Thank you for the very interesting talk, Martin:) Given evidences that pial arteries respond earlier than penetrating arterioles, what mechanistic effect/influence do pial arteries have on the penetrating arterioles in regulating the CBF to meet the neural demands?

From Joel Ramirez to Everyone: 02:44 PM

Do you know if vascular re-modelling or very 'kinked' or 'curly' vessels modify the efficiency of these precapillary sphincters?

From marlau03 to Everyone: 02:47 PM

To Sharmale: First order capioillaries react fatser than pial arterioles, pial arterioles come in later.

From Stuart Allan to Everyone: 02:47 PM

thank you Martin for fantastic talk. do you know what the signal on to pericytes is after whisker stimulation and if this is solely from astrocytes?

From marlau03 to Everyone: 02:52 PM

to Stuart Allen: The signaling molecules from nerve cells, astrocytes and neurons, to pericytes and VSMCs together make up a complex set of mechanisms. Prostaglanding are involved, but the neurovascular coupling response also depends on K-ATP channels, NO, cGMP, and K+. There is no single factor that determines the bloodflow response.

From marlau03 to Everyone: 02:58 PM

Were vesselsm remodeled in the hypertensive mouse

From Joel Ramirez to Everyone: 03:06 PM

Thank you Hilde for a great talk, how do you determine if you are visualizing arteries/arterioles or veins/venules?

From Marialena Dounavi to Everyone: 03:06 PM

Are you planning to use any other techniques like ASL or PC-MRA ?

From Saskia Lesnik to Everyone: 03:07 PM

Very nice talk! Did you look for correlations with disease severity e.g. disability or cognition?

From CHRISTOPHER Chen to Everyone: 03:08 PM

thanks hilde, do these changes occur early and predict for later stage lesions?

From Hilde to Everyone: 03:12 PM

no worries masayo, maybe you can try to answer remaning questions through the chat

From Me to Everyone: 03:16 PM

The active life measure had a number of different components making it up, which do you think contributed to most to explaining the results?

From Raj Kalaria to Everyone: 03:17 PM

Thanks Anna! Have you mindetified any bllod markers?

From Olivia Hamilton to Everyone: 03:18 PM

Very interesting presentation Anna - did you examine socioeconomic status in this sample as this may be relevant to active vs. less active life score?

From Annebet Leeuwis to Everyone: 03:18 PM

Did you also have information on the type of dementia?

From CHRISTOPHER Chen to Everyone: 03:19 PM

are the mechanisms underlyfing activity and diabetes different?

From Joel Ramirez to Everyone: 03:25 PM

hi adrian, I think I missed this slide, were there group differences in medications (eg. were the intervention group on anti-hypertensives, other VRF controls etc.)?

From Una Clancy to Everyone: 03:25 PM

Great talk. Were these participants required to have neuroimaging done prior to recruitment to the study and if so, do we know why they had imaging done? How severe was this population's SVD?

From Donna Wilcock to Everyone: 03:26 PM

Fantastic talks by all of the early investigators, congratulations!

From Annebet Leeuwis to Everyone: 03:27 PM

Did participants have underlying Alzheimer's disease? Were results different in those participants? And my compliments on completing this RCT!

From Raj Kalaria to Everyone: 03:27 PM

To the preceding speakers, can you please check the chat and possibly answer any questions which might have been asked to you.

From Anna Marseglia to Everyone: 03:28 PM

As one of the major issue linked to intervention targeting behaviour change is to sustain the change in the longterm, and dance is an activity that could be easy to sustain over time, are you planning to have a long-term follow-up (like 1 or 2 years after the end of the trial)?

From Stuart Allan to Everyone: 03:29 PM

fantastic that ECI network being established

From Anna Marseglia to Everyone: 03:36 PM

@@Olivia thank you. The AL index already incorporated several measures that could reflect aspects of SES (i.e. education and work characteristics). We additionally explored the role of occupation-based social class (derived from the longest held occupation and categorized into white-collar vs. blue-collar workers). Results were substantially similar.

@Annabet In SNAC-K there is info on three subtypes (AD, Vascular and mixed) but unfortunately because of the different stratifications, we had power issues (there were only 33 cases of vascular dementia in the overall sample). But it would have been super interesting to look into the subtypes.

From Olivia Hamilton to Everyone: 03:40 PM

Thanks @Anna, great work!

From Anna Marseglia to Everyone: 03:41 PM

@christ chen. We could not test that, but info on possible blood/csf biomarkers would have helped to reply this question. I suspect the inflammation is a common mechanism underlying the physical component of AL and diabetes. But for the mental/social stimulating components, I believe that there could be neuroprotective and compensatory mechanisms that either restrict the development of primary neuropathologies or help compensating for the vascular damages (e.g. recriting alternative brain circuits). But this is really an hypothesis that need to be tested.

From Chung Tong Vincent MOK to Everyone: 03:46 PM

@Una Clancy, Thanks for your question, we invited mainly community older controls without stroke or dementia for a brief MRI screening (FLAIR), those with two or more lacunas and/or early confluent to confluent WMH were recruited, none had a clinical diagnosis of AD-MCI or AD dementia

From ahainswo to Everyone: 03:47 PM

Great idea to have Early career group. If you are an ISTAART member, we too have a dynamic ECR group in the Vascular PIA
https://action.alz.org/personifyebusiness/Membership/ISTAART/PIA/VascularCognitiveDisorders.aspx

From grosenberg to Everyone: 03:52 PM

Did you measure the albumin index (CSF/blood) to see if there was a relationship to these biomarkers?

From Dr Fatemeh Geranmayeh to Everyone: 03:55 PM

Can the moderator kindly ask speaker to go off presentation mode?
Thank you!

From Chris Patrick Pflanz to Everyone: 04:11 PM

Can a ketogenic diet help with NO metabolism?

From CHRISTOPHER Chen to Everyone: 04:11 PM

dear phil, is there any observational evidence that cardiac patients on ISMN have less cognitive decline?

From Philip Bath to Everyone: 04:14 PM

Chris, thanks. There is a developing literature that organic nitrates may be a double-edged sword producing both NO and reactive molecules such as peroxyinitite. I am not aware of ISMN-cog data but it may be that it could be good or bad - a question of LACI-2 and successors.

From ahainswo to Everyone: 04:28 PM

what drug types used to intensively lower BP?

From CHRISTOPHER Chen to Everyone: 04:29 PM

were other measures of small vessel disease measured?

From Hélène Girouard to Everyone: 04:29 PM

Thanks, great presentation! Any data on potassium in these groups

From Me to Everyone: 04:30 PM

Was there any relationship between the type of drug used, or the degree of BP reduction, and the extent of the serial brain volume loss in the intensive arm?

From CHRISTOPHER Chen to Everyone: 04:35 PM

the volume of WMH appears to be small in most of the sprint mind MRI subjects - has an analysis been performed in those with more severe WMH?
and amazing to hear that the data will be made publically available - thank you NIH!

the must be some participnts with AD pathology - does the effect of intensive lowering change if these are excluded? apologies if I missed

From Hilde to Everyone: 04:41 PM

Advertorial ;-) Please find here the link to our LinkedIn EI group:
https://www.linkedin.com/groups/13901078/

From ahainswo to Everyone: 04:42 PM

great conference, thanks all

From Hélène Girouard to Everyone: 04:42 PM

Thanks all, it was great!

From Chung Tong Vincent MOK to Everyone: 04:43 PM

this is a really great meeting! thanks to Raj, John and Hugh!! Looking forward to New Castle next year

From Donna Wilcock to Everyone: 04:43 PM

Great conference! Kudos to Raj, John and Hugh for pulling it all together

From Joel Ramirez to Everyone: 04:45 PM

great meeting!

From Ileana Camerino to Everyone: 04:45 PM

Very interesting talks, thank you very much to all speakers and organisers of VasCog 2020!

From ahainswo to Everyone: 04:47 PM

is there a VasCog twitter group? would be worth doing

From Gustafson to Everyone: 04:47 PM

twitter group
good idea

From Ogunniyi to Everyone: 04:49 PM

Great presentations and nice talking about the journal. Pleased to have logged in.

well worth staying up late for!

From Rebecca Gottesman to Everyone: 04:50 PM

Thanks for a terrific conference!

From awn to Everyone: 04:51 PM

Agree with Gustavo, welcome to submit papers to CCCB. Great afternoon; thanks! /anders

From Gustafson to Everyone: 04:52 PM

Please contact me if any questions!!

From Silvia Fossati to Everyone: 04:52 PM

Amazing talks and discussion! Looking forward to next year!!