



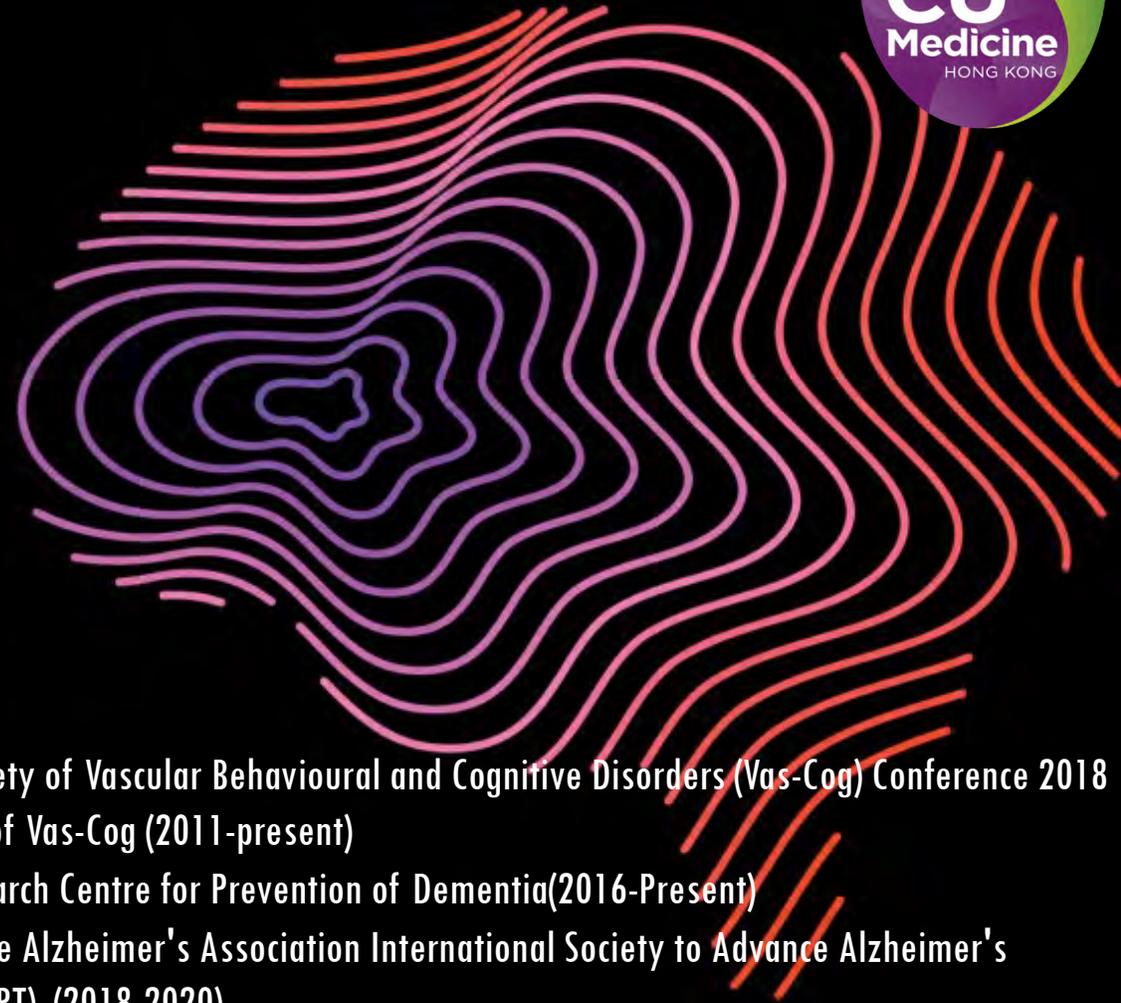
Health and Medical Research Fund (HMRF)
Journal Club Presentations, 28 January 2022



Amyloid in Poststroke Dementia

Project No.: 07080411

Review Insights into Dementia Prevention



Professor Vincent Mok

Awardee of Excellent Research Award 2017 and
10th HMRF Anniversary Award 2022
Endowed Mok Hing Yiu Professor of Medicine
Assistant Dean (Student Affairs)
Chief of Neurology (Academic Affairs)
Faculty of Medicine

Chairman of International Society of Vascular Behavioural and Cognitive Disorders (Vas-Cog) Conference 2018
Executive Committee Member of Vas-Cog (2011-present)
Director Therese PF Chow Research Centre for Prevention of Dementia(2016-Present)
Advisory Council Member of the Alzheimer's Association International Society to Advance Alzheimer's
Research and Treatment (ISTAART) (2018-2020)
Past President of Chinese Dementia Research Association (2015-2016)
Advisory Council Member of Charles K. Kao Foundation for Alzheimer's Disease (2021-present)

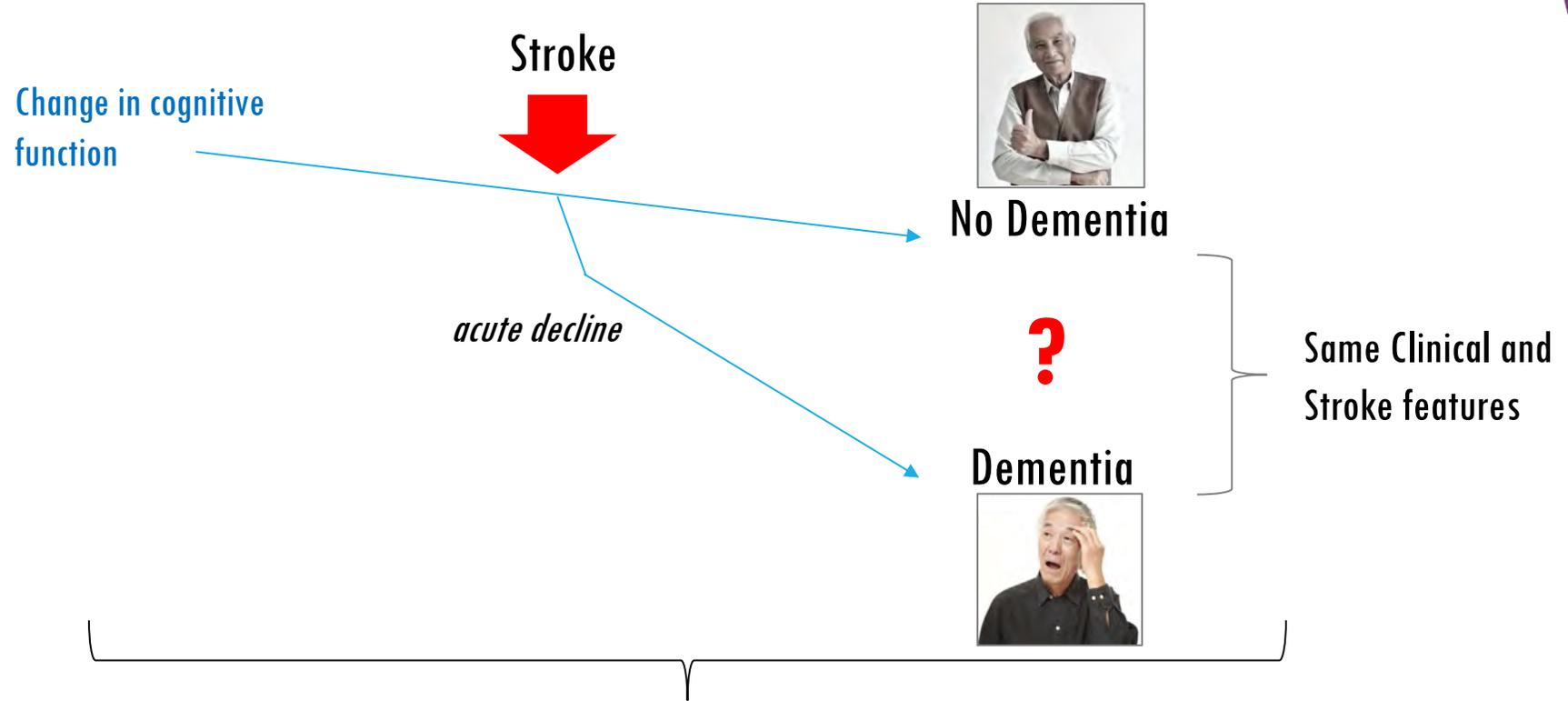


內科及藥物治療學系腦神經科
Division of Neurology
Department of Medicine & Therapeutics



#EndDementiaTogether

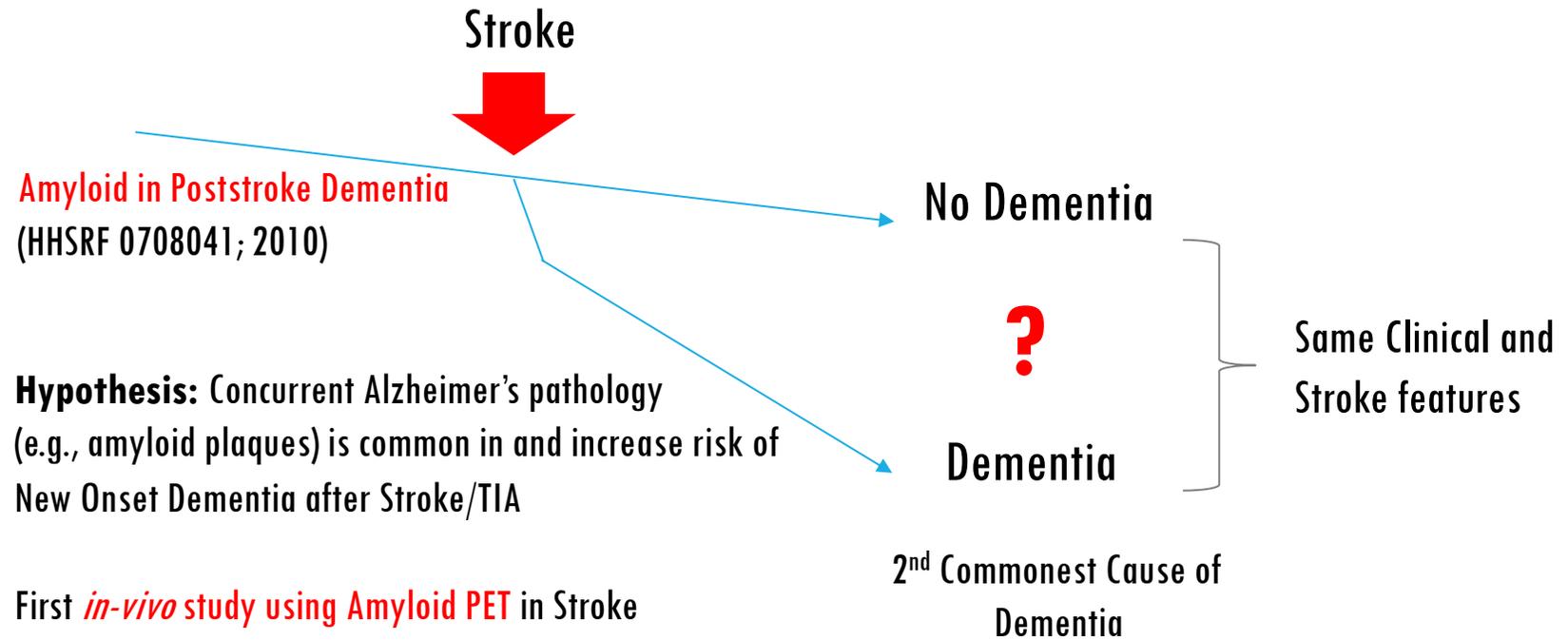
Strategies for Dementia Prevention depends on Underlying Mechanisms



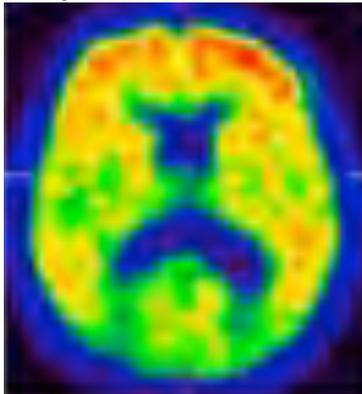
Vascular Dementia

2nd Commonest Cause

Strategies for Dementia Prevention depends on Underlying Mechanisms



Amyloid PET



First *in-vivo* study using Amyloid PET in Stroke
 n=72: 2/3 new onset dementia vs 1/3 without dementia



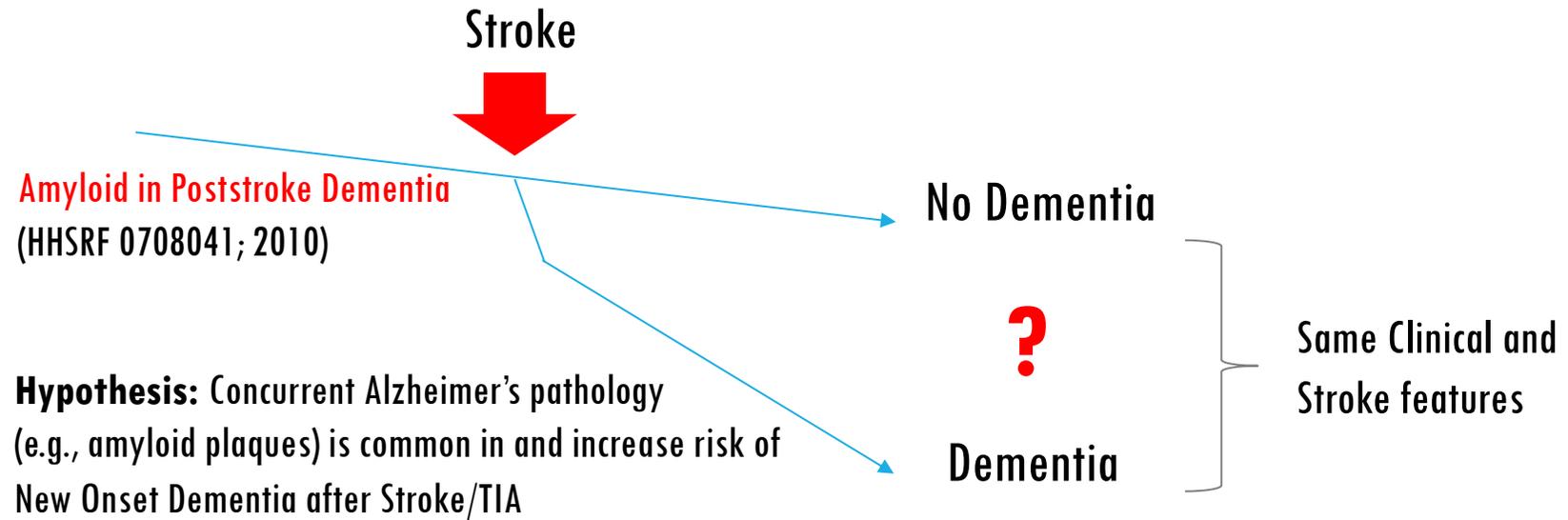
Dr Chi Lai HO



Dr Eric LEUNG

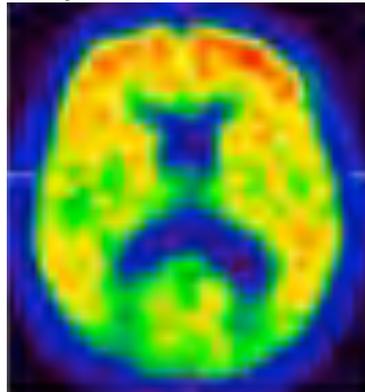
Department of Nuclear Medicine, Hong Kong Sanatorium and Hospital

Strategies for Dementia Prevention depends on Underlying Mechanisms



2nd Commonest Cause of Dementia

Amyloid PET



First *in-vivo* study using Amyloid PET in Stroke

n=72: 2/3 new onset dementia vs 1/3 without dementia
 Amyloid (A): 30% vs 8% p=0.032

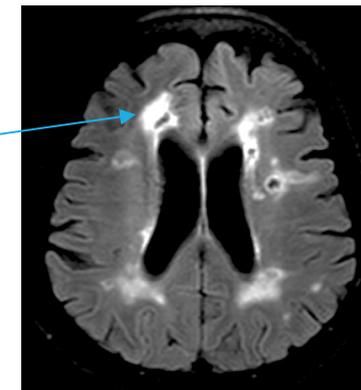
A-

A+ (*rapid decline over years*)

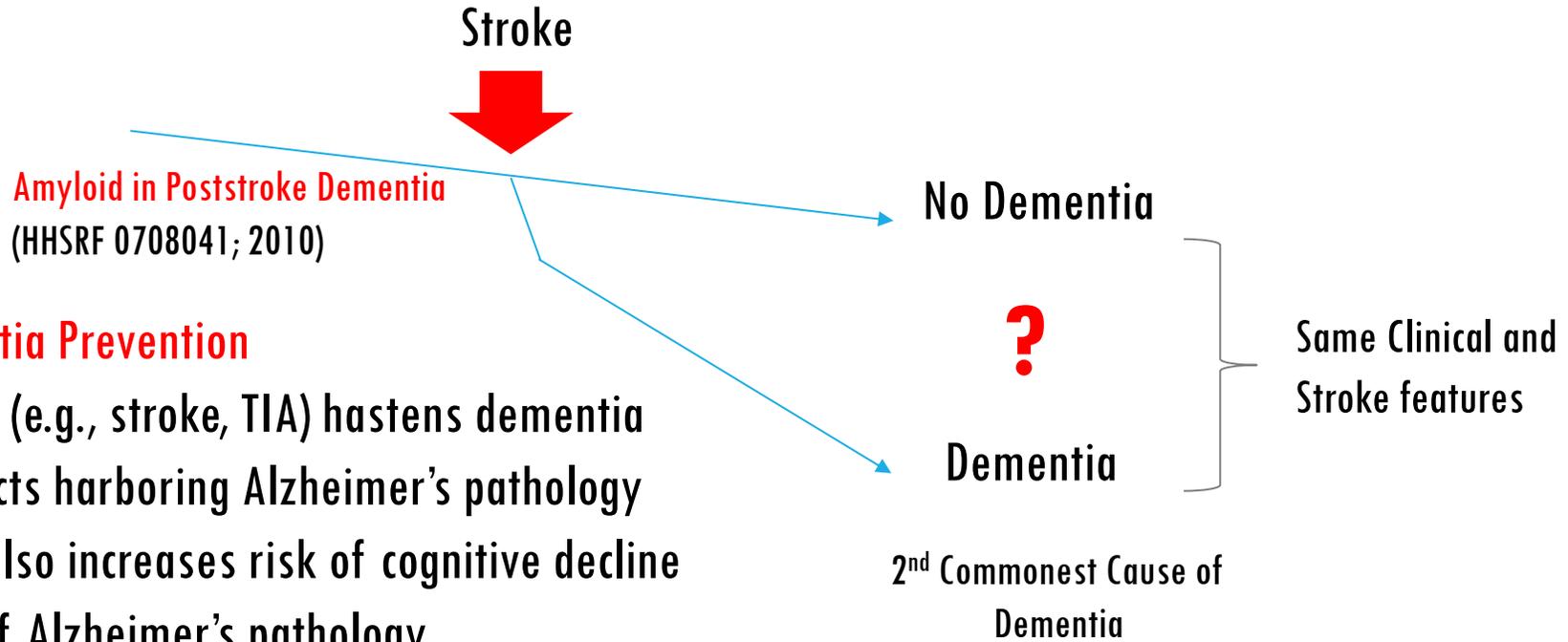
- Concurrent cerebral small vessel disease (SVD) also increases risk of dementia and subsequent cognitive decline independent of amyloid
- Dementia occurs even after TIA/small infarct in subjects harboring Amyloid and/or SVD

(Size and site of stroke lesion were not risk factors)

FLAIR MRI



Strategies for Dementia Prevention depends on Underlying Mechanisms



Insights to Dementia Prevention

- Vascular insult (e.g., stroke, TIA) hastens dementia onset in subjects harboring Alzheimer's pathology
- Cerebral SVD also increases risk of cognitive decline independent of Alzheimer's pathology



- Control of Vascular Risk Factors/Diseases can prevent/delay Dementia in Alzheimer's disease (AD)
- Detection and Intervention at the Pre-dementia Stage of AD and SVD provides the greatest opportunity of preventing Dementia

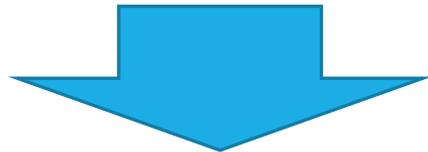
Strategies for Dementia Prevention depends on Underlying Mechanisms



Amyloid in Poststroke Dementia
(HHSRF 0708041; 2010)

Insights to Dementia Prevention

- Vascular insult (e.g., stroke, TIA) hastens dementia onset in subjects harboring Alzheimer's pathology
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- Control of Vascular Risk Factors/Diseases can prevent/delay Dementia in Alzheimer's disease (AD)
- Detection and Intervention at the Pre-dementia Stage of AD and SVD provides the greatest opportunity of preventing Dementia

Related Publications

1. Alzheimer's & Dementia 2015 Jan (IF 21.56)
2. Alzheimer's & Dementia 2016 Nov (IF 21.56)
3. International Journal of Stroke 2021 July (IF 5.179)
4. Stroke 2015 Nov (IF 6.967)
5. JAMA 2015 May (IF 56.272)
6. JAMA 2015 May (IF 56.272)
7. Nature Reviews Neurology 2017 Mar (IF 42.937)

Strategies for Dementia Prevention depends on Underlying Mechanisms



Dr Lisa AU
Neurology



Alzheimer's Disease
International

The global voice on dementia

World Alzheimer Report 2021

Journey through the diagnosis of dementia

ALZHEIMER'S DISEASE INTERNATIONAL | WORLD ALZHEIMER REPORT 2021

Expert essay

The differential diagnosis between Alzheimer's disease and vascular dementia, including the concept of mixed dementia

Lisa W.C. Au, Vincent C.T. Mok

Division of Neurology, Department of Medicine and Therapeutics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, CHINA

Related Publications

1. Alzheimer's & Dementia 2015 Jan (IF 21.56)
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7. **Nature Reviews Neurology 2017 Mar (IF 42.937)**



Excellent Research Award 2017



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Food and Health Bureau

Strategies for Dementia Prevention depends on Underlying Mechanisms



Amyloid in Poststroke Dementia
(HHSRF 0708041; 2010)

Insights to Dementia Prevention

- Vascular insult hastens dementia onset in subjects harboring Alzheimer's pathology
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- Control of Vascular Risk Factors / Diseases can prevent/delay Dementia in Alzheimer's disease (AD)
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7. Nature Reviews Neurology 2017 Mar (IF 42.937)



Detection of Mild Cognitive Impairment (MCI) in Hong Kong

Validation of Cognitive Assessment test for Detection of MCI of AD and SVD in Hong Kong Older People (HHSRF 06070231; 2008)

Montreal Cognitive Assessment (MoCA)

HK-MoCA (10-15 min)

Education	n	MoCA					MoCA 5-Min Protocol				
		Median	IQR	Cutoff at Percentile			Median	IQR	Cutoff at Percentile		
				16th	7th	2nd			16th	7th	2nd
Age 65-69 y											
0-3	64	21	4	17	14	9	22	5	18	15	13
4-6	82	23	5	19	18	13	24	5	20	17	14
7-9	74	24	5	21	19	16	25	6	20	19	13
10-12	82	25	4	22	20	17	26	5	22	20	20
>12	67	27	3	25	23	21	28	3	24	23	18
Age 70-79 y											
0-3	76	19	5	15	14	11	21	6	16	13	12
4-6	82	22	4	18	15	10	23	5	19	16	13
7-9	66	23	4	20	18	15	24	5	19	17	15
10-12	76	24	4	22	19	18	24	4	20	18	15
>12	67	25	5	22	20	16	25	5	21	19	17
Age ≥80 y											
0-6	37	18	6	13	13	10	18	7	13	10	9
>6	21	20	5	17	15	13	21	6	17	15	15

Impairment is determined when score ≤ age and education corrected percentile cutoff. IQR indicates interquartile range; and MoCA, Montreal Cognitive Assessment.

Age & Education Norms

Detection and Intervention at the Pre-dementia Stage of AD and SVD provides the greatest opportunity of preventing Dementia

HK-MoCA-5 min



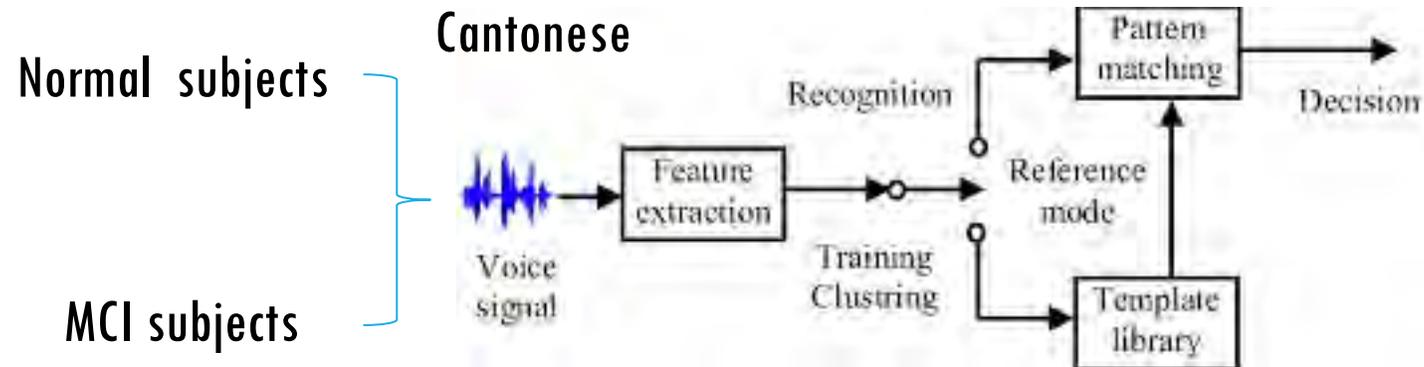
Dr Adrian Wong, Clinical Psychologist, CUHK
Standard Practice of Hospital Authority

Dementia Geriatric Cogn Disorder 2009 August
J Neurol Neurosurg Psychiatry 2013 May
Journal of Clinical Experimental Neuropsychology 2015
Stroke 2015 Dec & Stroke 2015 April

Detection of Mild Cognitive Impairment (MCI) in Hong Kong

CU-MARVEL Study - **C**ognitive assessment **U**sing **M**achine Le**A**rning empowe**R**ed **V**oice ana**L**ysis Study

Theme-Based Research Scheme T45-407/19N; 2020



Prof Helen Meng
System Engineering
and Engineering
Management, CUHK

Detection and Intervention at the Pre-dementia Stage of AD and SVD provides the greatest opportunity of preventing Dementia

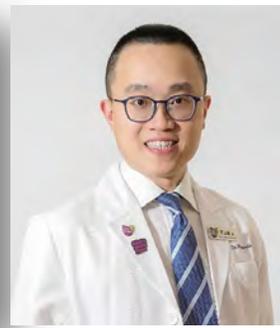
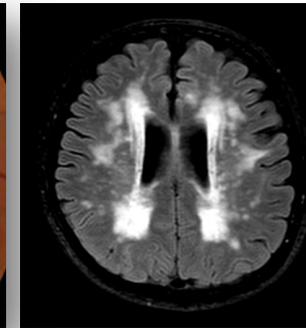
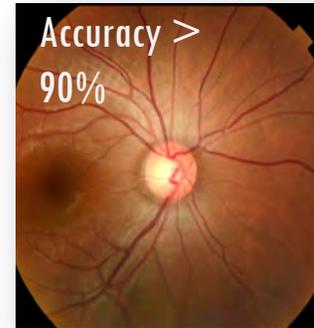
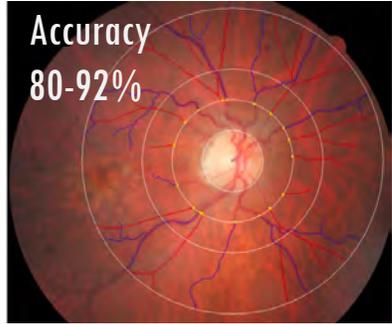
Accurate and Affordable Screening Tests for AD and SVD among MCI

AD

SVD

Machine Learning Derived Retinal Imaging AD Biomarkers (HMRF 04153506; 2017)

Machine Learning Derived Retinal Imaging SVD Biomarkers



J Neurol Neurosurg
Psychiatry 2021

Dr Carol Cheung
Ophthalmology

Dr Lisa AU
Neurology

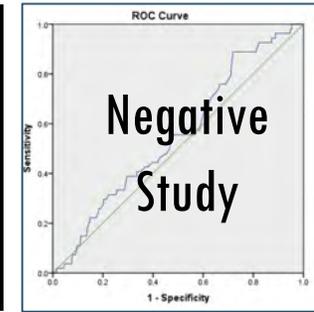
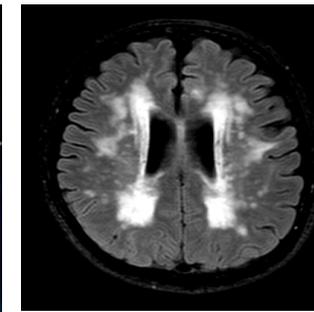
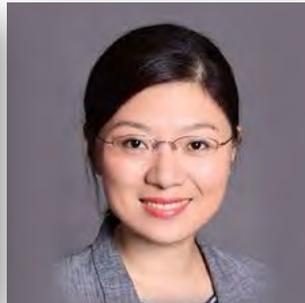
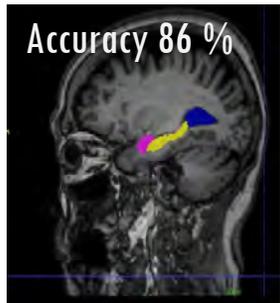
RGC 471911; ITF MRP/037/17X
Annals of Clinical and Translational Neurology 2019
Jan

Prof Benny Zee
School of Public
Health

Dr Alexander
Lau, Neurology

Machine Learning Derived MRI AD Biomarker (HMRF 08190666; 2021)

Transcranial Doppler derived Pulsatility Index (HHSRF 09100131; 2011)



Aging 2021 May
(Pilot Results)

Dr KO Ho
Neurology and School
of Biomedical Sciences

Dr Shi Lin
Imaging and Interventional
Radiology

Journal of the Neurological Sciences 2019 August

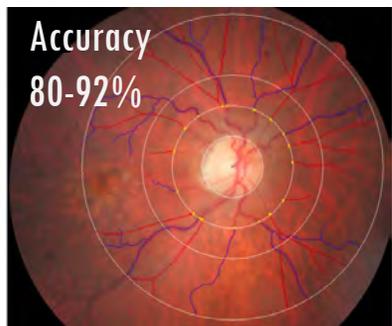
Early Intervention for AD MCI Stage

Emerging Strategies for early AD



AD

Machine Learning Derived Retinal Imaging AD Biomarkers (HMRF 04153506; 2017)

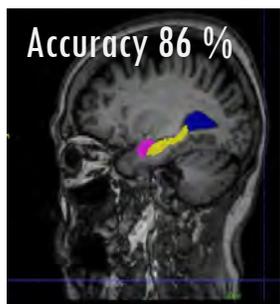


J Neurol Neurosurg
Psychiatry 2021

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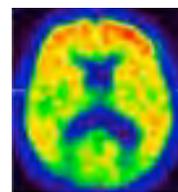


Aging 2021 May
(Pilot Results)

Dr KO Ho
Neurology and School
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Dr Shi Lin
Imaging and Interventional
Radiology

Confirmatory
Test, e.g., PET



1. Multi-domain Life-Style, e.g., Exercise, Diet, Cognitive training
2. Control of Cardiovascular Risk Factors, e.g., Aggressive BP control (systolic < 130 mmHg), (*Remarks: Glucagon Like Peptide 1 receptor agonist (GLP-1 RA) in DM*)
3. Medical Nutrition Drink/Supplement (e.g., Fortasyn Connect, Omega 3 fatty acids *800 mg docosahexaenoic acid/225 mg eicosapentaenoic acid*)
4. Anti-amyloid, e.g., Aducanumab

Alzheimer's disease

Philip Scheltens, Bart De Strooper, Miia Kivipelto, Henne Holstege, Gael Chételat, Charlotte E Teunissen, Jeffrey Cummings, Wiesje M van der Flier

In this Seminar, we highlight the main developments in the field of Alzheimer's disease. The most recent data *Lancet 2021; 397: 1577-90*



Early Intervention for SVD at Pre-dementia Stage

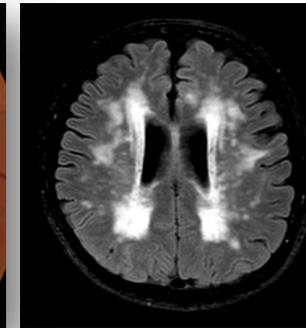
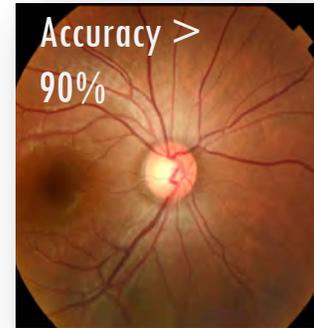
Emerging Strategies

1. Aerobic Exercise —

CU-AEROBIC RCT (**A**erobic **E**xercise in **O**lder **P**eople with **S**ubclinical Sporadic **C**erebral SVD) (**H**MRF 03140936; 2016)
 Alzheimer's & Dementia — Translational Research & Clinical Intervention Dec 2021

SVD

Machine Learning Derived Retinal Imaging SVD Biomarkers

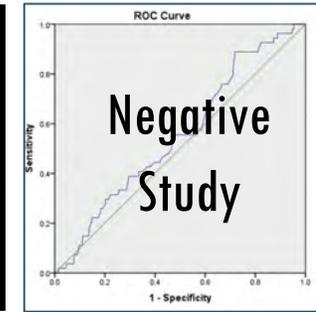
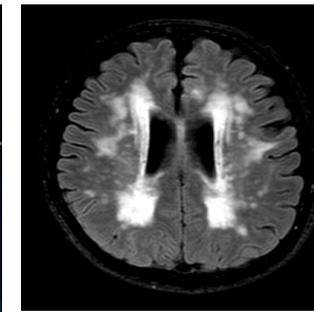


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 Annals of Clinical and Translational Neurology 2019
 Jan

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 School of Public
 Health

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 Lau, Neurology

Transcranial Doppler derived Pulsatility Index (HHSRF 09100131; 2011)



Journal of the Neurological Sciences 2019 August

Early Intervention for SVD at Pre-dementia Stage

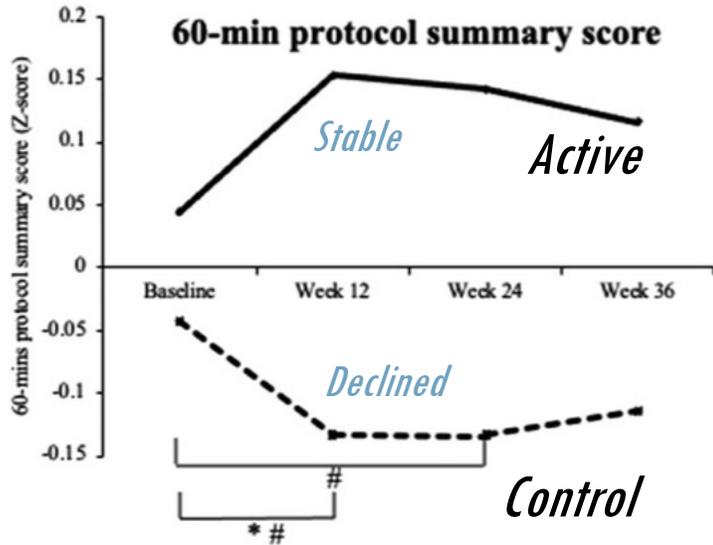
Emerging Strategies

1. Aerobic Exercise —

CU-AEROBIC RCT (Aerobic Exercise in Older People with Subclinical Sporadic Cerebral SVD) (HMRF 03140936; 2016)

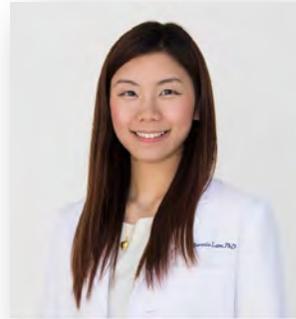
Alzheimer's & Dementia — Translational Research & Clinical Intervention Dec 2021

a. Global cognition



Vigorous exercise 60 min/session
x2 session/week for 6 months

Dr Bonnie Lam



Dr Adrian Wong

Received: 28 April 2021 | Revised: 22 October 2021 | Accepted: 2 November 2021 | Published online: 23 December 2021
DOI: 10.1002/trc2.12224

RESEARCH ARTICLE

Translational Research
Clinical Interventions

Aerobic exercise in older people with subclinical sporadic cerebral small vessel disease: A randomized clinical trial

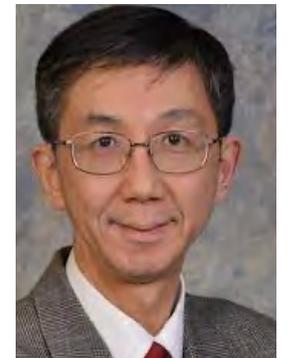
Adrian Wong^{1,2} | Bonnie Yin Ka Lam^{1,2} | Margaret Kit Yi Mak³ | Linda Chiu Wa Lam⁴ |
Lisa Wing Chi Au^{1,2} | Brian Ka Fung Yiu^{1,2} | Chun Wong¹ | Hor Yee Tong¹ |
Sin Ki Yeung¹ | Winnie Chiu Wing Chu⁵ | Lin Shi^{5,6} | Thomas Wai Hong Leung¹ |
Yannie Oi Yan Soo¹ | Alexander Yuk Lun Lau^{1,2} | Bonaventure Yiu Ming Ip¹ |
Timothy Chi Yui Kwok¹ | Ho Ko^{1,2,7} | Vincent Chung Tong Mok^{1,2}



Prof Margaret Mak
Rehabilitation Sciences, PolyU



Prof Linda Lam
Psychiatry, CUHK



Prof Timothy Kwok
Geriatric, CUHK

Early Intervention for SVD at Pre-dementia Stage

Emerging Strategies

1. Aerobic Exercise (**HMRF 03140936**; 2016)
2. Aggressive BP Control aiming Systolic BP < 130mmHg
3. Statins (e.g., ROCAS/Regression of Cerebral Artery Stenosis Study)
4. B Vitamins (GRF CU04317; 2004) (2 mg folic/25 mg B6,/0.5 mg B12)
5. Avoid Cilostazol (Anti-thrombotic) (GRF CHUK 14111414) — worsens cognition



Dr Bonaventure Ip

Nature Reviews Disease
2018

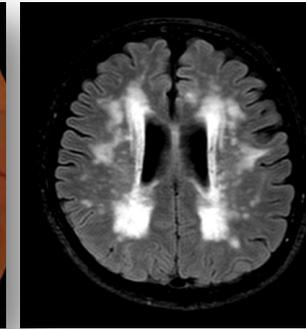
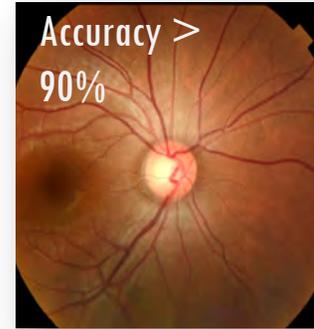
PRIMER

Vascular cognitive impairment

Wiesje M. van der Flier^{1,2}, Ingmar Skoog³, Julie A. Schneider⁴, Leonardo Pantoni⁵, Vincent Mok⁶, Christopher L. H. Chen⁷ and Philip Scheltens¹

SVD

Machine Learning Derived Retinal Imaging SVD Biomarkers

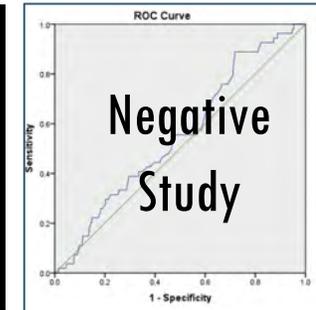
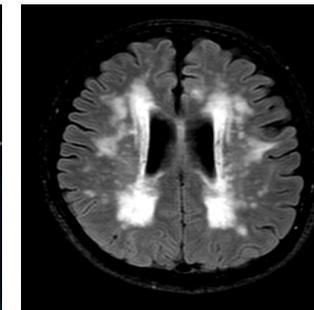


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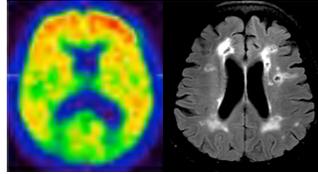
Transcranial Doppler derived Pulsatility Index (HHSRF 09100131; 2011)



Journal of the Neurological Sciences 2019 August

Strategies for Dementia Prevention

Early AD/SVD



Cognitive Function

Normal

Normal cognition

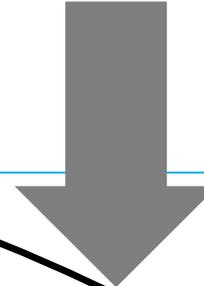
Mild

Mild Cognitive Impairment (MCI)

Severe

*Dementia
(i.e., severe cognitive impairment)*

Stroke/TIA



Amyloid in Poststroke Dementia
(HHSRF 0708041; 2010)

0

1

2

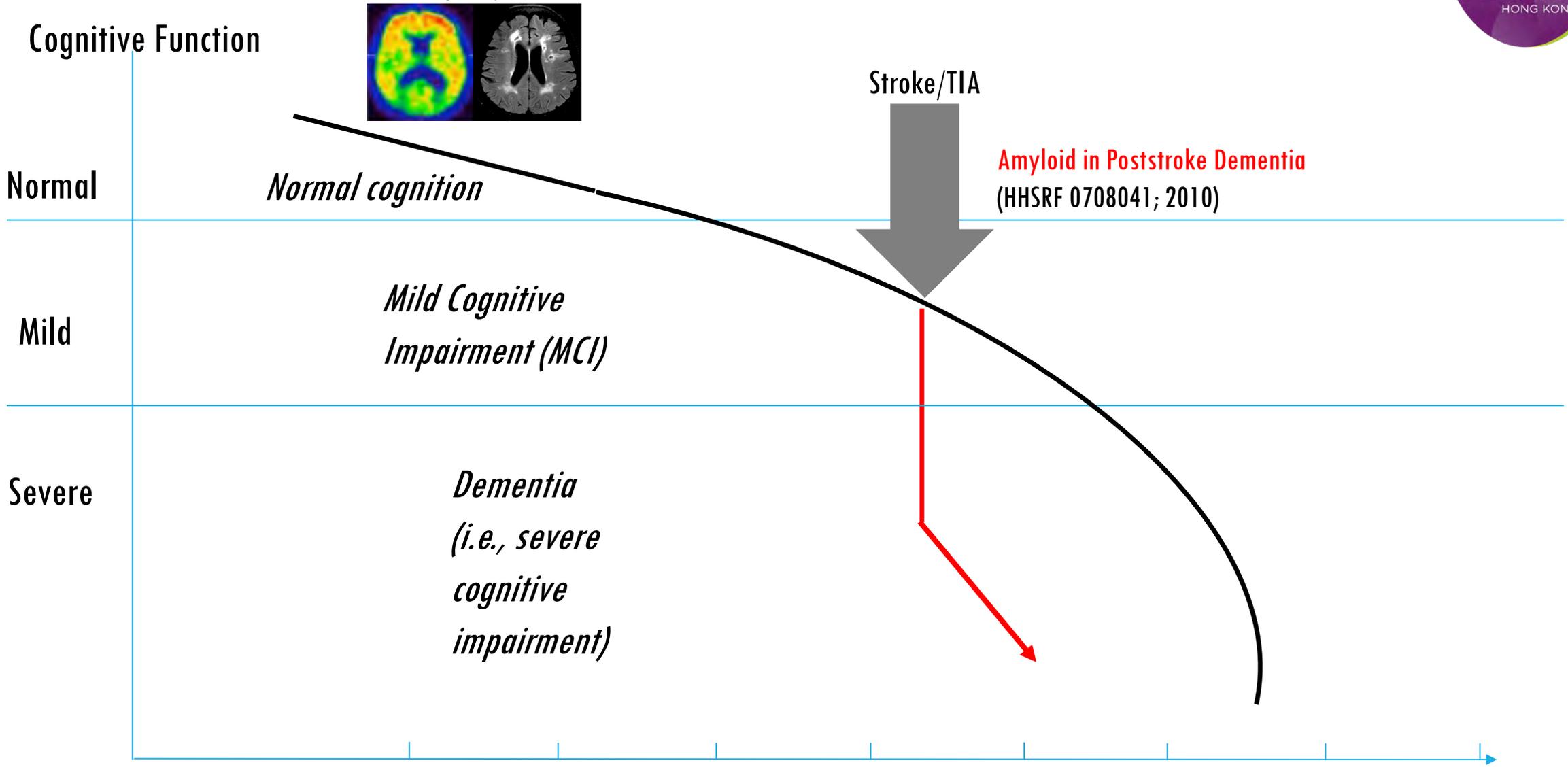
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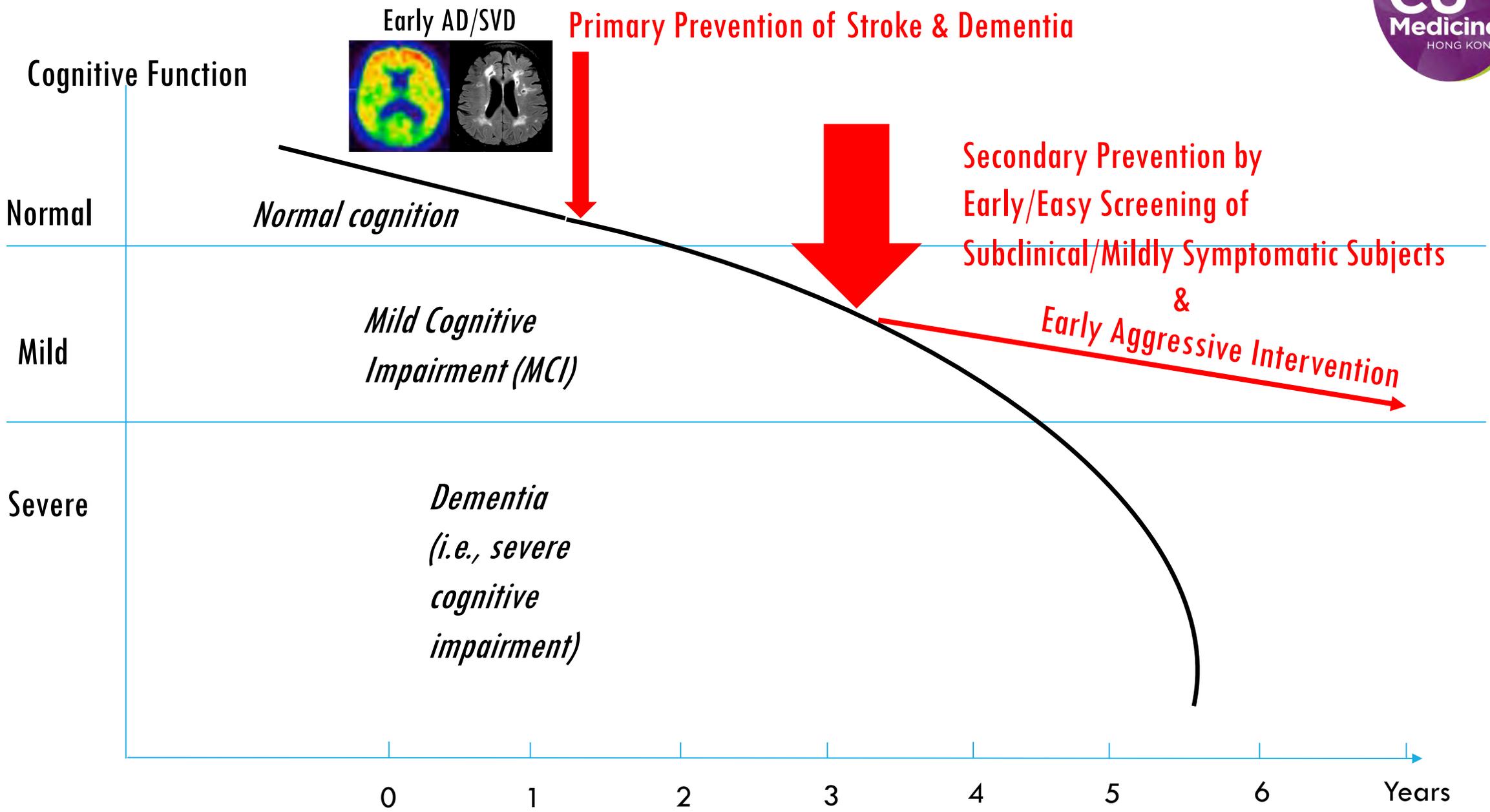
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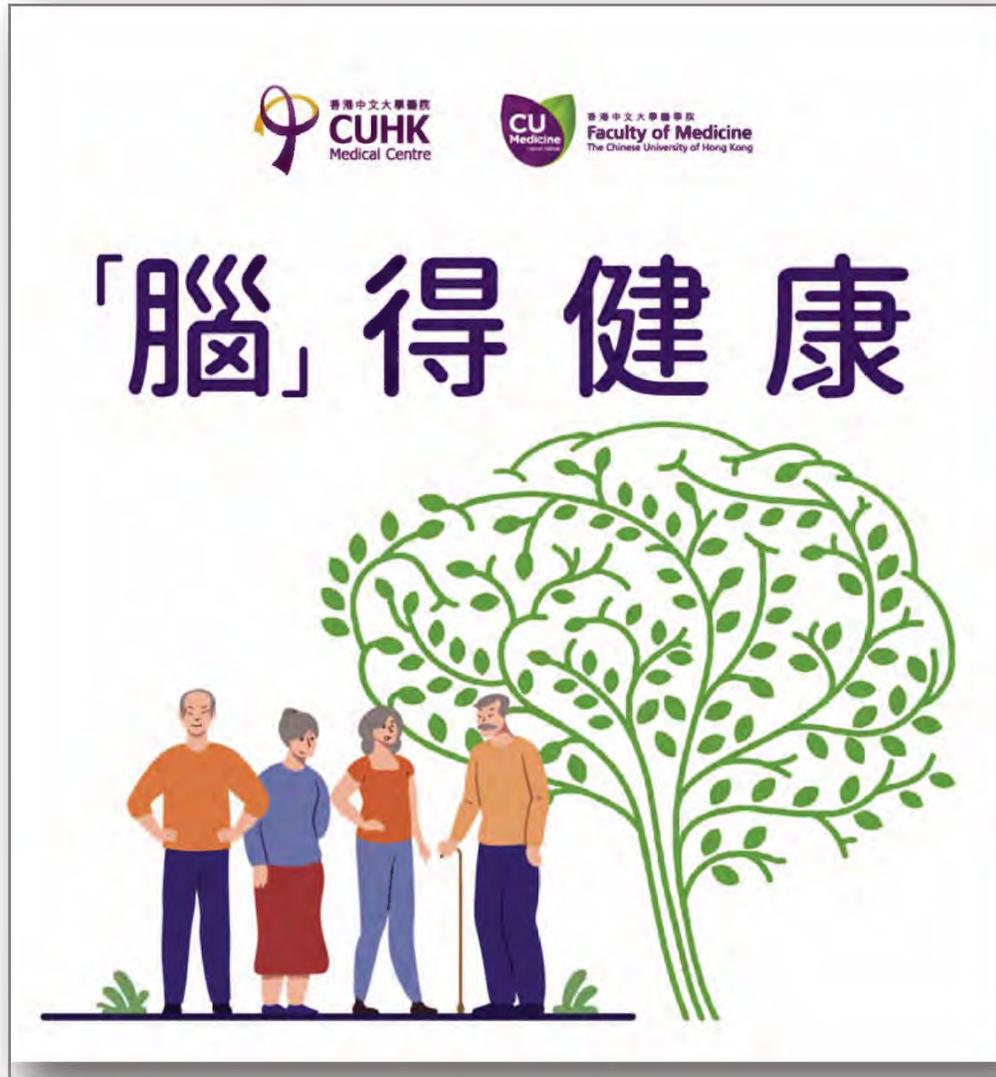
Years



Strategies for Dementia Prevention



Strategies for Dementia Prevention



3000 copies freely distributed to Older People via network of NGOs



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及早治療和預防認知障礙症

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CUHK Medical Centre

中大醫學院

CUHK Medicine

中大腦神經科

CUHK Neurology



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請立即訂閱中大腦神經科的電子通訊。

Acknowledgements:

Division of Neurology, Department of Medicine and Therapeutics

Emeritus Professor Lawrence KS WONG



Dr Adrian WONG

Dr KO Ho

Dr Lisa AU

Dr Bonnie LAM

Dr Alexander LAU

Dr Bonaventure IP

Ms Pauline KWAN

Division of Geriatric, Department of Medicine and Therapeutics

Professor Timothy KWOK

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Professor Linda LAM

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Professor Winnie CHU

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Professor Margaret MAK



Hong Kong University of Science and Technology

Professor Nancy IP



Hong Kong Sanatorium and Hospital

Department of Nuclear Medicine

Dr HO Chi Lai

Dr Eric LEUNG



Research Fund Secretariat

HHSRF 0708041

HHSRF 06070231

HHSRF 09100131

HMRF 04153506

HMRF 03140936

HMRF 08190666

Excellent Research Award 2017

10th Anniversary Award 2021

University Grant Commission

GRF CU04317

GRF CHUK 14111414

Theme-Based Research Scheme T45-407/19N

Information Technology Fund

ITF Midstream Research Programme/037/17X

Philanthropic Donation

Therese Pei Fong Chow Research Centre for Prevention of Dementia (In Memory of Donald HK Chow)



Food and Health Bureau
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Brain Health Brings Health

