



Association des Aidants  
et Malades à Corps de Lewy

# Colloque A2MCL maladie à corps de Lewy

8 novembre 2024

**LE VINATIER**

PSYCHIATRIE UNIVERSITAIRE  
LYON MÉTROPOLE





Module 2

# Maladie à corps de Lewy et fragilité

Module présidé par :

**Pr Claire ROUBAUD BAUDRON**  
*Gériatre – CHU CMRR Bordeaux*

**Dr Guillaume ALBARET**  
*Gériatre - CHU CMRR Bordeaux*



# Module 2

## MCL, fragilité et capacités intrinsèques ?

**Dr Antoine GARNIER-CRUSSARD**

*Gériatre, Lyon, MCU-PH*

*Hospices Civils de Lyon, Université Lyon 1,  
INSERM U1237*



# Liens d'intérêt

- **Activités non rémunérées** : Investigateur ou coinvestigateur pour des études des laboratoires Novo Nordisk, Biogen, UCB Pharma, Lilly, TauRX Therapeutics, Roche, Alzheon, VIFOR, Medesis Pharma, GlaxoSmithKline
- **Activités rémunérées** : néant
- **Avantages divers (transports, repas...)** : néant

antoine garnier-crussard

# Remerciements



Federica Sanopo



Marie Signoret



Mihaela Nodit



Marie Collin



Justine Bonnet-Chateau



Victor Gilles



# Vieillessement = **hétérogénéité**

## Mme Robuste.

- o 82 ans
- o Antécédents
  - o Hypertension artérielle
  - o Diabète de type 2

## Mme Fragile.

- o 82 ans
- o Antécédents
  - o Hypertension artérielle
  - o Diabète de type 2

### Grippe + surinfection bactérienne

- o Antibiothérapie 7 jours
- o Fatigue 10 jours

- o Confusion, chute
- o Fracture du col du femur
- o Hospitalisation 45 jours, entrée en EHPAD

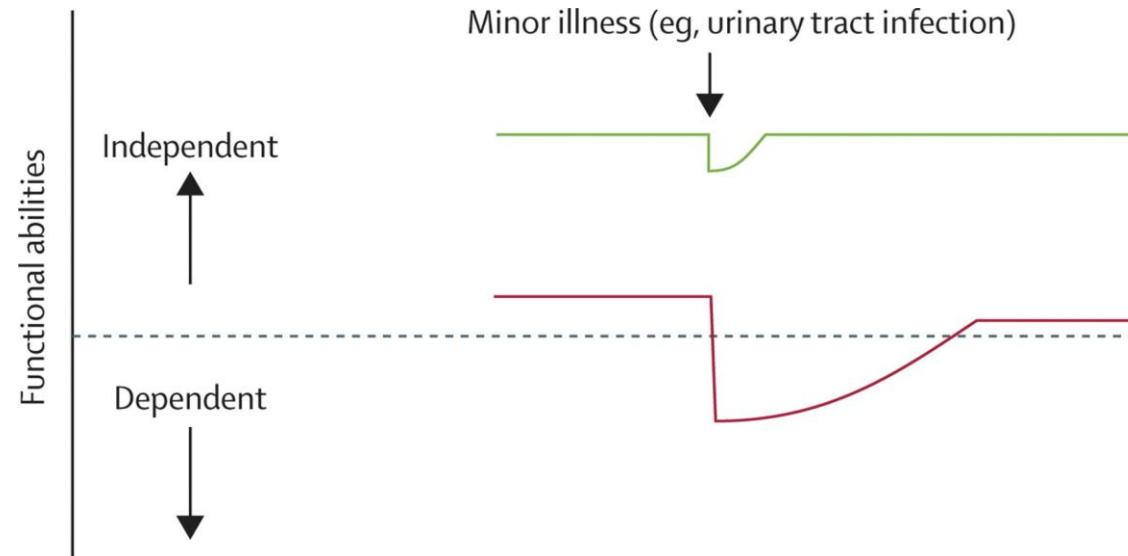
**Quelles différences entre ces deux dames ?**

**L'âge et les comorbidités ne suffisent pas à comprendre...**

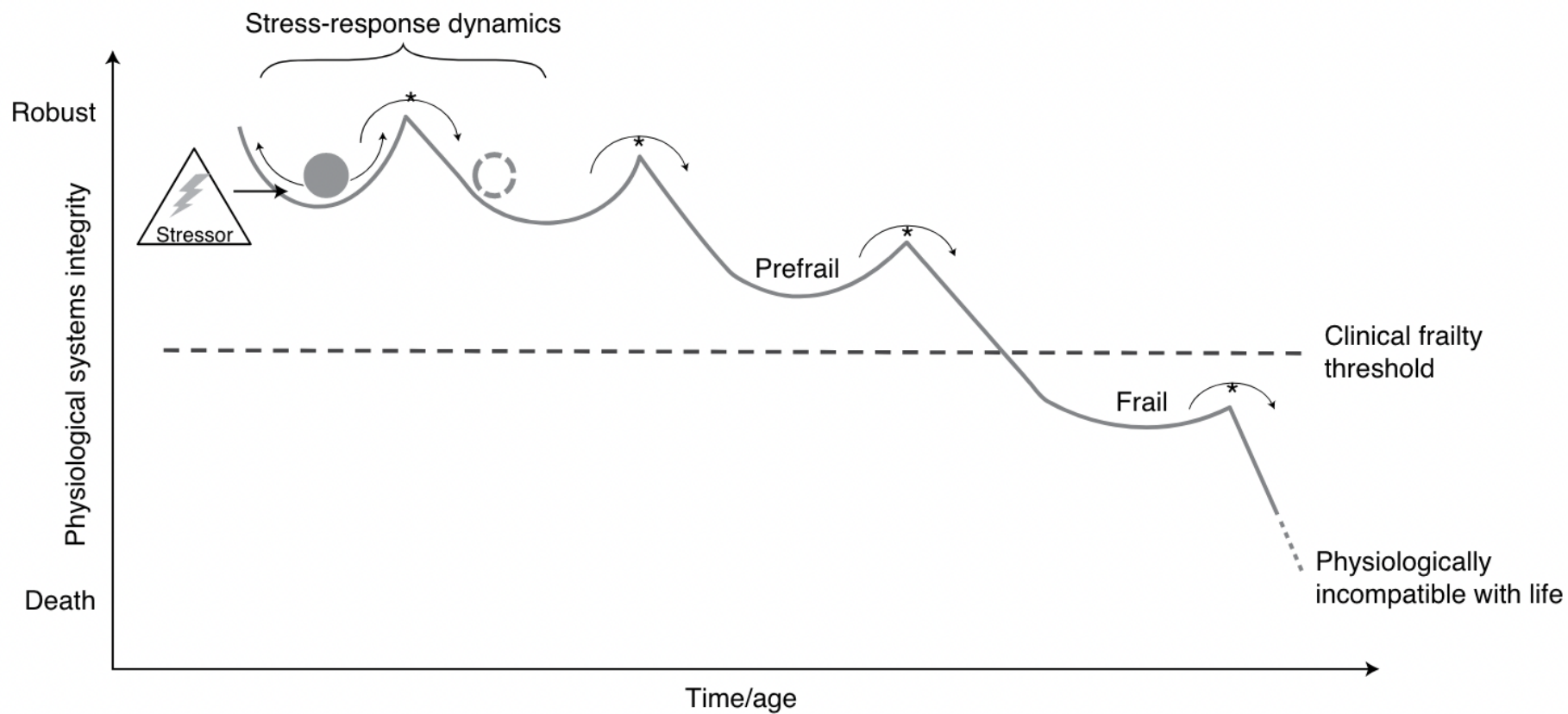
**Comment mesurer cet écart ?**

# Fragilité

## Diminution des réserves physiologiques et augmentation de la vulnérabilité



# Fragilité



*Histoire naturelle de la MCL ?*



## Comment la mesurer ?

Des **modèles** essaient de capturer ce **concept** théorique de fragilité et ont permis le développement d'**outils de mesure** en clinique

Modèle **phénotypique**

Modèle **d'accumulation de déficits**

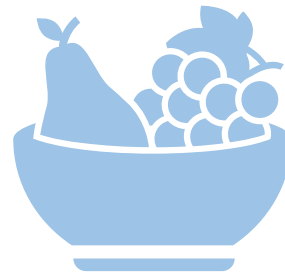


Frailty Index



# Fragilité

## Comment la réduire ?



Intervention multi-domaines  
Activité physique

### SYSTEMATIC REVIEW

#### Comparative effectiveness of non-pharmacological interventions for frailty: a systematic review and network meta-analysis

XUEMEI SUN<sup>1</sup>, WENQI LU<sup>1</sup>, YINYAN GAO<sup>1</sup>, LANG QIN<sup>1</sup>, HUI FENG<sup>2</sup>, HONGZHUAN TAN<sup>1</sup>, QIONG CHEN<sup>3,4</sup>, LINXIN FENG<sup>5,6</sup>, MEIWE XUYI WU<sup>7,8</sup>

### RESEARCH ARTICLE

Open Access

The impact of interventions on management of frailty in hospitalized frail older adults: a systematic review and meta-analysis

Zahra Rezaei-Shahavarloo<sup>1</sup>, Foroozan Atashzadeh-Shoorideh<sup>2</sup>, Robbert J. J. Gobbens<sup>1,3,5</sup>, Abbas Ebadati<sup>6,7</sup> and Ghohramess Ghahramani Harouni<sup>8</sup>

# Fragilité

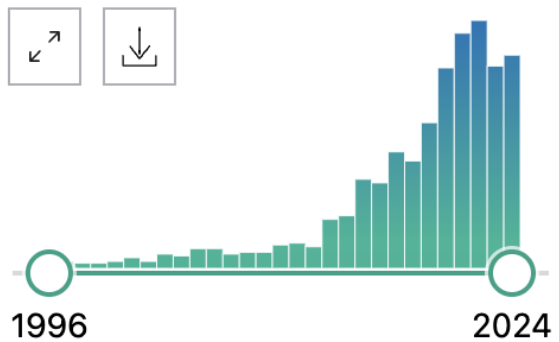


(frailty) AND (alzheimer)

[Advanced](#) [Create alert](#) [Create RSS](#)

896 results

RESULTS BY YEAR

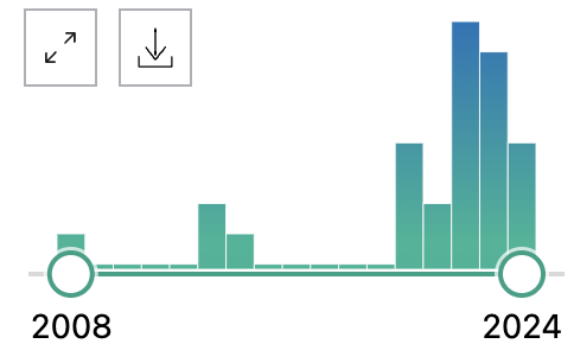


(frailty) AND (lewy body)

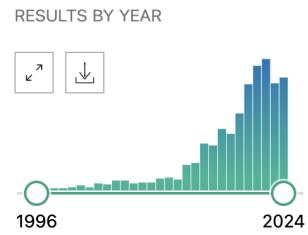
[Advanced](#) [Create alert](#) [Create RSS](#)

27 results

RESULTS BY YEAR



# Fragilité dans la maladie d'Alzheimer



## Les protéinopathies n'expliquent pas à elles seules les phénotypes cliniques

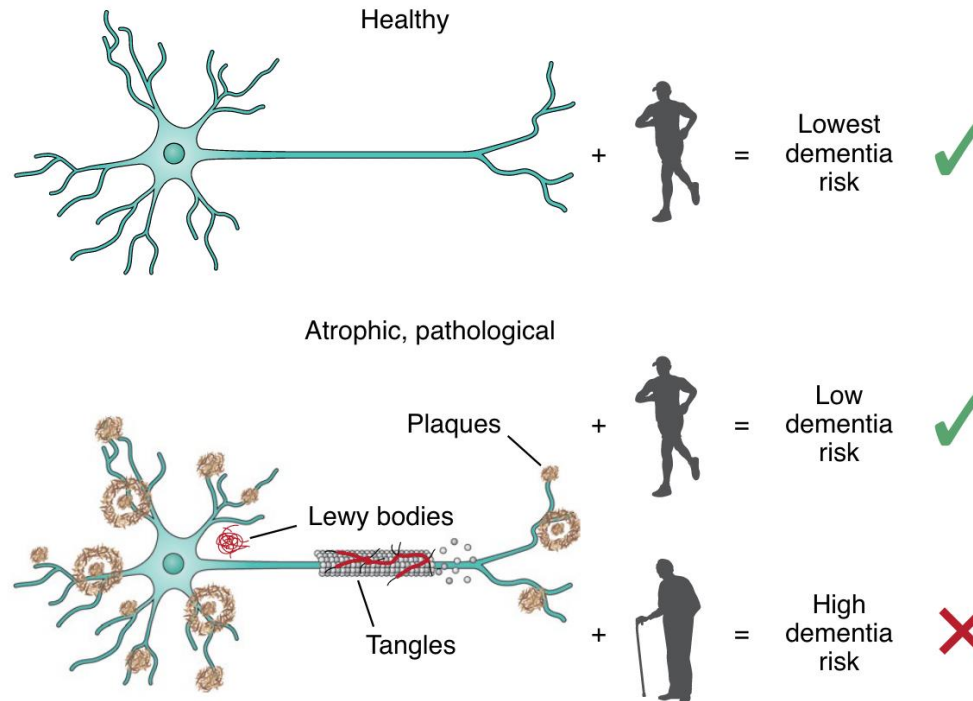
J Frailty Aging 2022;  
Published online May 31, 2022, <http://dx.doi.org/10.14283/jfa.2022.43>

Editorial

© Serdi 2022

### Could there Be Frailty in the Discrepancy between Lesions and Symptoms of Alzheimer's Disease?

M. Canevelli<sup>1</sup>, G. Bruno<sup>1</sup>, M. Valletta<sup>1</sup>, M. Cesari<sup>2,3</sup>



Wallace et al., *Lancet Neurol* 2019  
Wallace et al., *Neurology* 2020  
Howlett et al., *Nature Aging* 2021  
Canevelli, *J Frailty Aging* 2022



# Fragilité dans la maladie à corps de Lewy

	<b>MCL (N=55)</b>
Age	80.2 (6.02)
Genre (F)	28 (50.9%)
MMSE	19.3 (5.34)

## Caractéristiques de la maladie

Hallucinations	43 (78.2%)
Syndrome parkinsonien	44 (80.0%)
Fluctuations	30 (81.1%)
RBD	32 (58.2%)

## Fragilité

Fragiles	29 (52.7%)
Pré-fragiles	20 (36.4%)
Robustes	6 (10.9%)

## SYSTEMATIC REVIEW

### Prevalence of frailty in 62 countries across the world: a systematic review and meta-analysis of population-level studies

Age	Physical frailty	
Minimum cut-off (at study entry)	Number of studies (sample size)	Prevalence (95% CI)
.....	.....	.....
Frailty		
50–59+	37 (136,456)	6% (4–8%)
60–69+	150 (268,989)	12% (11–14%)
70–79+	92 (99,865)	18% (16–19%)
80–89+	75 (23,297)	28% (26–30%)
90+	9 (945)	46% (33–61%)



# Fragilité dans la maladie à corps de Lewy

	<b>MCL (N=55)</b>
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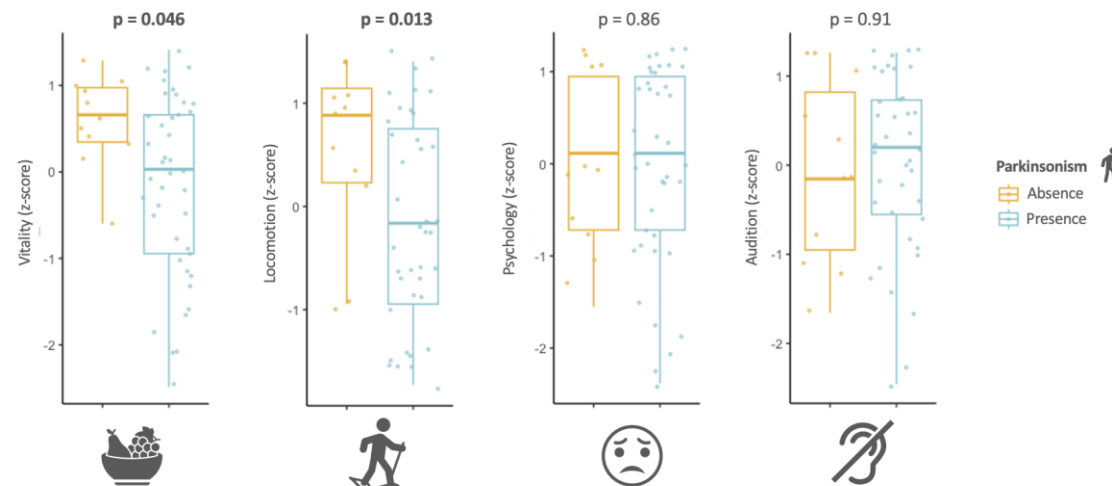
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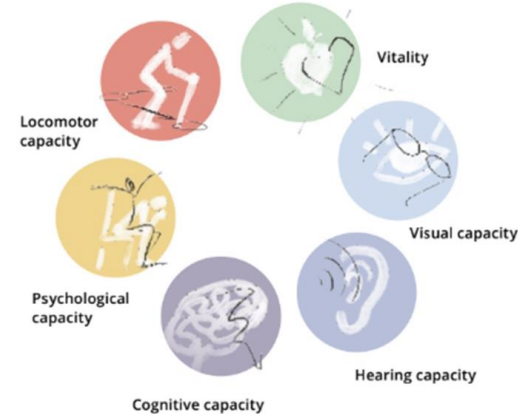
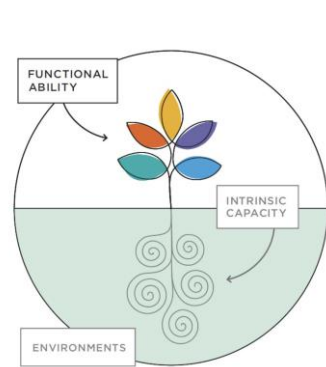
Fragiles	29 (52.7%)
Pré-fragiles	20 (36.4%)
Robustes	6 (10.9%)

	OR	95% CI	p-value
Hallucinations	0.93	0.22-3.80	0.92
Parkinsonism	5.00	1.09-29.27	<b>0.0496</b>
Fluctuations	5.88	0.73-128.09	0.14
RBD	0.52	0.16-1.69	0.28



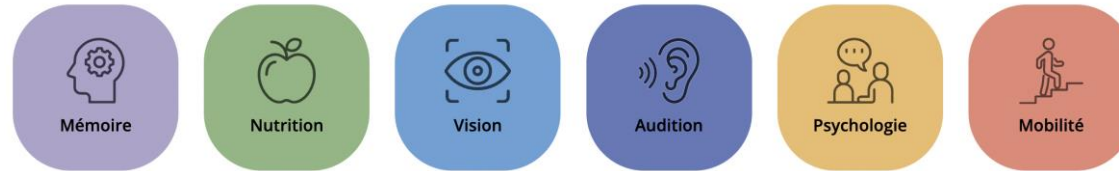
# Capacités Intrinsèques

Ensemble des **capacités mentales et physiques**, qui lui permettent de maintenir ses capacités fonctionnelles

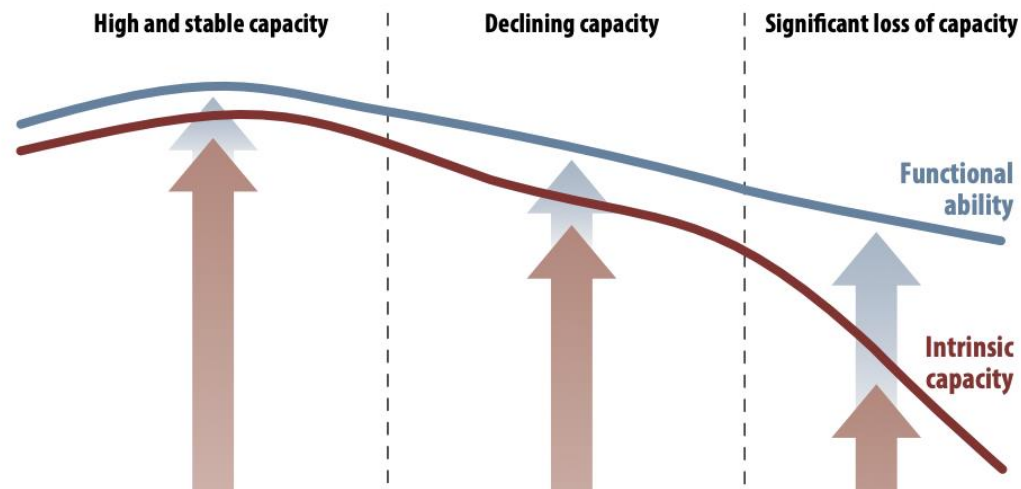


→ **vieillir en santé** = avoir les capacités suffisantes pour faire **ce qui a du sens et de la valeur** pour nous (≠ vieillir sans maladie !)

# ICOPE: integrated care for older people

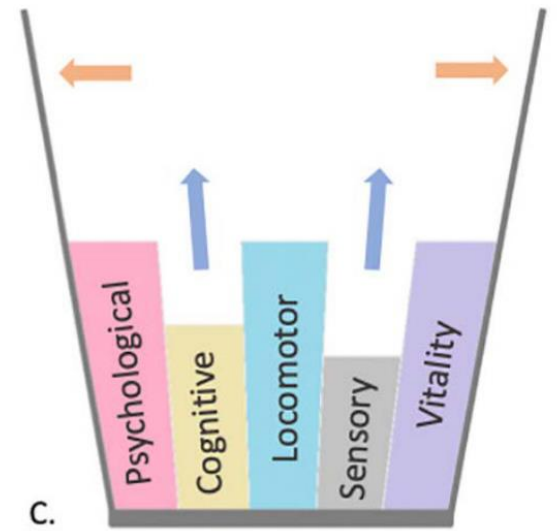
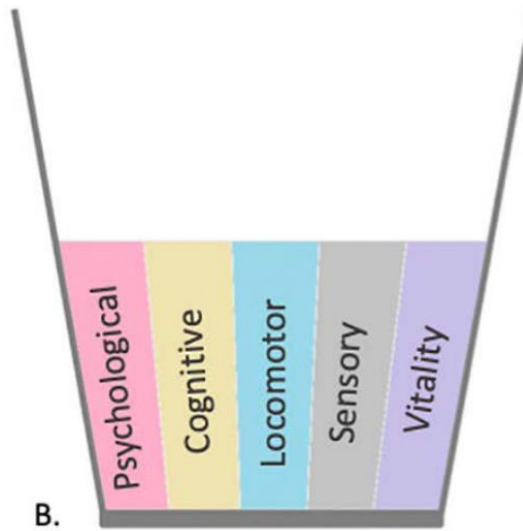
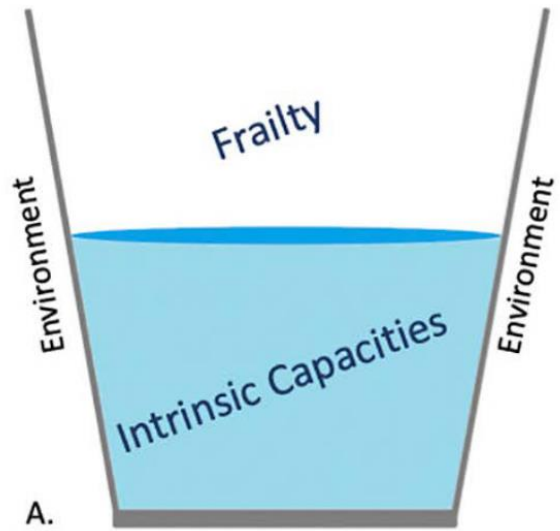


Repérage puis confirmation des baisses de capacités intrinsèques en population (>60 ans), aboutissant à une prise en charge précoce et individualisée





# Fragilité et capacités intrinsèques



# Capacités Intrinsèques

## → Associés au **déclin fonctionnel et à la mortalité**

### Association of intrinsic capacity with functional decline and mortality in older adults: a systematic review and meta-analysis of longitudinal studies

Juan Luis Sánchez-Sánchez, Wan-Hsuan Lu, Daniel Gallardo-Gómez, Borja del Pozo Cruz, Philipe de Souto Barreto, Alejandro Lucia\*, Pedro L Valenzuela\*

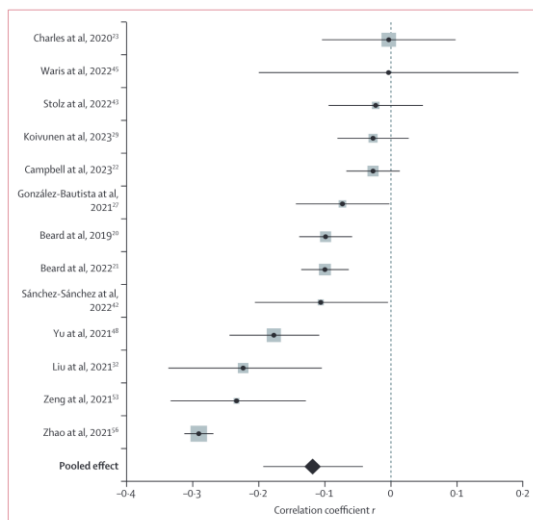


Figure 2: Association between intrinsic capacity and impairment in basic activities of daily living. Bars indicate 95% CIs.

**BADL**

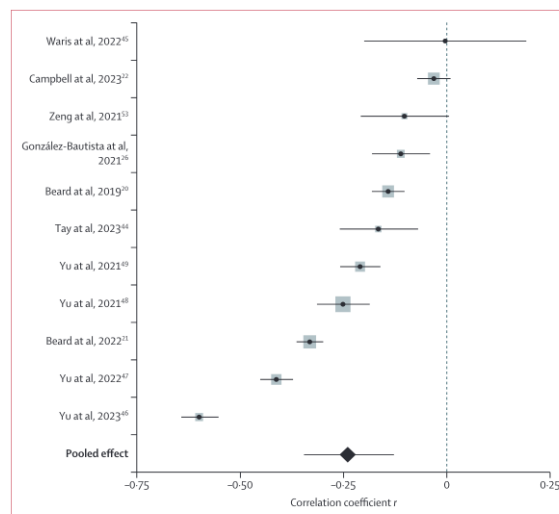


Figure 3: Association between intrinsic capacity and impairment in instrumental activities of daily living. Bars indicate 95% CIs.

**IADL**

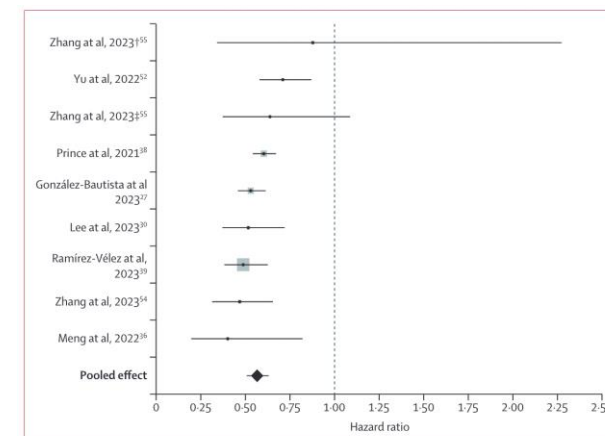


Figure 4: Association between intrinsic capacity and mortality. Bars indicate 95% CIs. †Data from the National Institute for Longevity Sciences-Longitudinal Study of Aging (Japan). ‡Data from the Longitudinal Aging Study of Taipei (Taiwan).

**Mortalité LE VINATIER**  
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# Capacités Intrinsèques → Une **cible d'intervention...**

JIM Original Article

doi: 10.1111/joim.13710

## Sustained improvement of intrinsic capacity in community-dwelling older adults: The +AGIL Barcelona multidomain program

■ Maria Cristina Ferrara<sup>1</sup>, Laura Mónica Pérez<sup>2</sup>, Aida Ribera Sole<sup>2,3</sup>, Lorena Villa-García<sup>2,4,5,6</sup>, Joan Ars<sup>2,3,4,7</sup>, Luis Soto-Bagaría<sup>2</sup>, Giuseppe Bellelli<sup>1,8</sup>, Matteo Cesari<sup>9</sup>, María Belén Enfedaque<sup>10</sup> & Marco Inzitari<sup>2,4,11</sup>



Journal of the American Medical Directors Association

Volume 25, Issue 5, May 2024, Pages 757-763.e4



Original Study

## Enhancing Intrinsic Capacity and Related Biomarkers in Community-Dwelling Multimorbid Older Adults Through Integrated Multidomain Interventions: Ancillary Findings From the Taiwan Integrated Geriatric (TIGER) Trial

Wei-Ju Lee MD, PhD<sup>a,b</sup>, Li-Ning Peng MD, PhD<sup>a,c</sup>, Ming-Hsien Lin MD<sup>a,c</sup>, Sunyoung Kim MD<sup>d</sup>, Fei-Yuan Hsiao PhD<sup>e,f</sup>, Liang-Kung Chen MD, PhD<sup>a,c,g</sup>



Age and Ageing 2022; 51: 1–10  
<https://doi.org/10.1093/ageing/afac303>

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RESEARCH PAPER

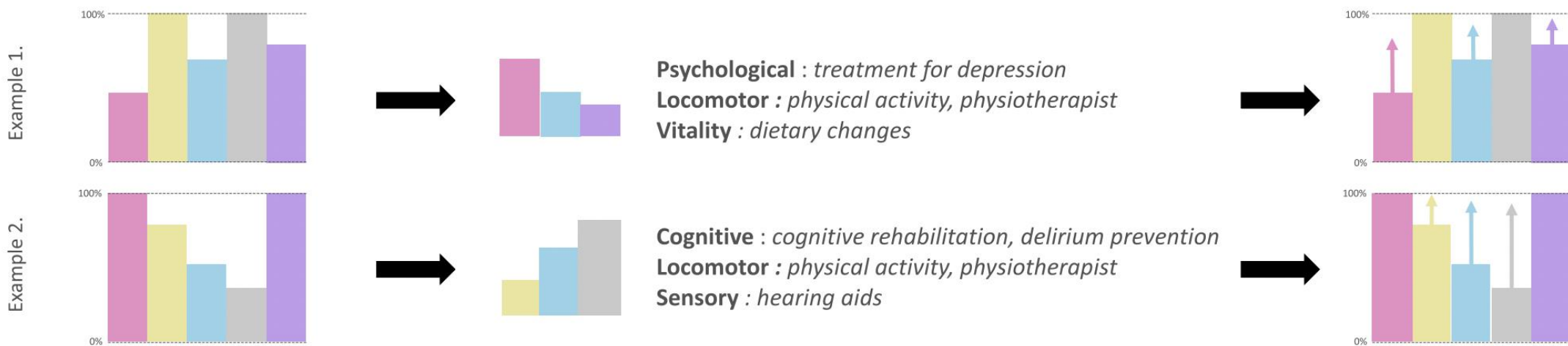
## Effects of a 12-week Vivifrail exercise program on intrinsic capacity among frail cognitively impaired community-dwelling older adults: secondary analysis of a multicentre randomised clinical trial

JUAN LUIS SÁNCHEZ-SÁNCHEZ<sup>1,2,3</sup>, PHILIPPE DE SOUTO BARRETO<sup>1,4</sup>, IVÁN ANTÓN-RODRIGO<sup>5,6</sup>, FERNANDA RAMÓN-ESPINOZA<sup>7</sup>, ITXASO MARÍN-EPELDE<sup>8</sup>, MARINA SÁNCHEZ-LATORRE<sup>8</sup>, DÉBORA MORAL-CUESTA<sup>8</sup>, ÁLVARO CASAS-HERRERO<sup>8,9,10</sup>

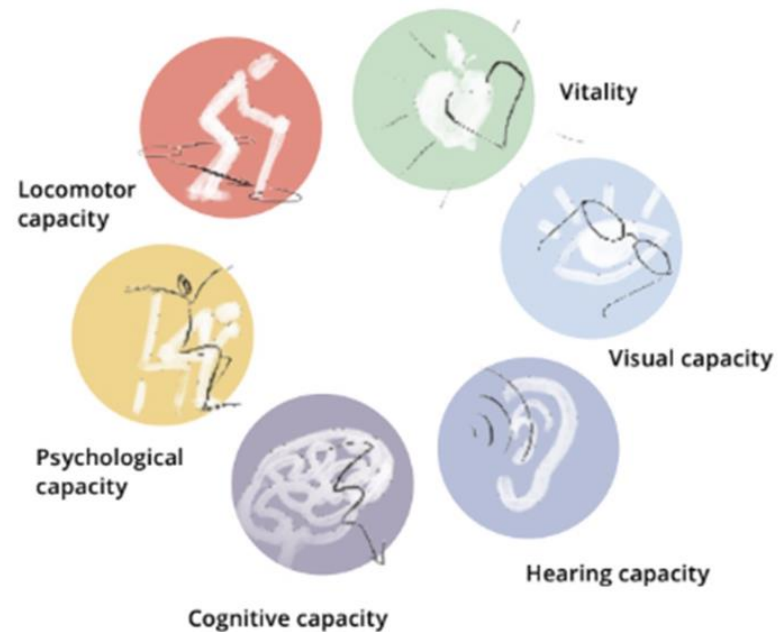
# Capacités Intrinsèques

→ Une **cible d'intervention...personnalisée** !

## B. Individual Assessment of IC



# Capacités Intrinsèques et maladie à corps de Lewy



Locomotion: SPPB

Vitality/Nutrition: MNA

Psychologie: Mini-GDS

Audition: HVEC

**Table 1.** Study sample characteristics

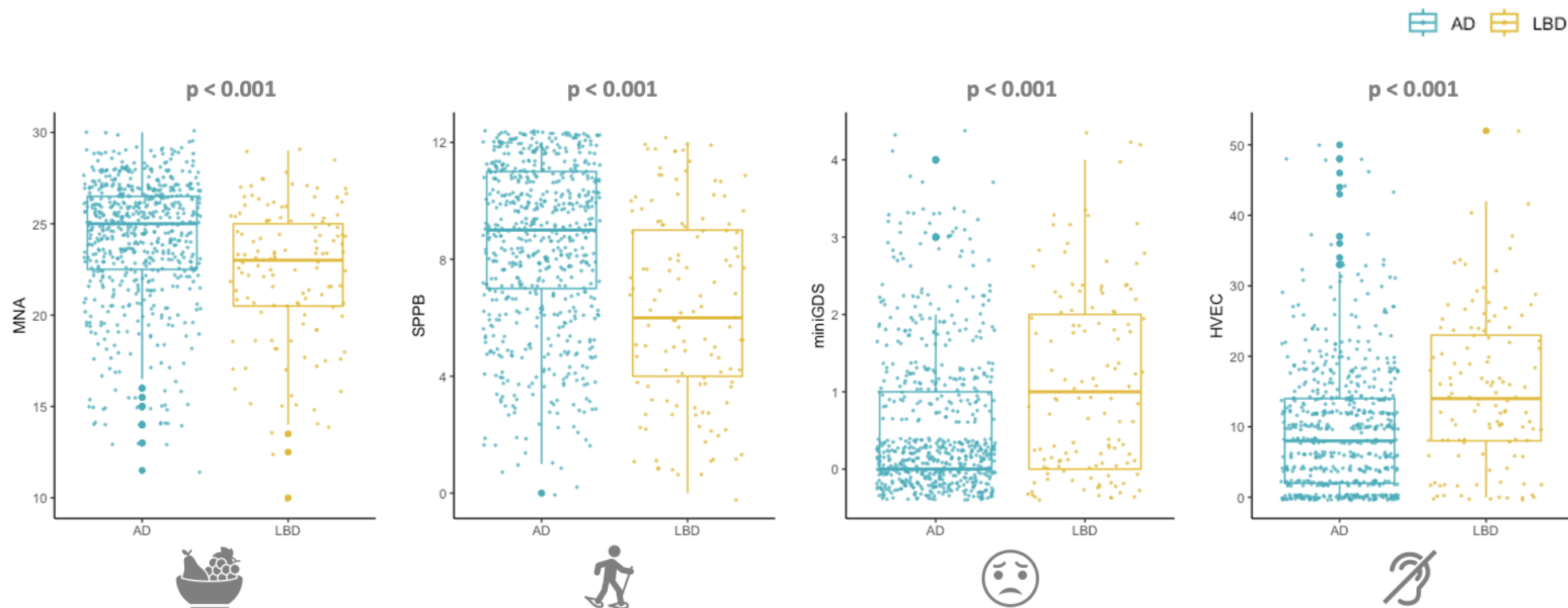
	<b>AD (N=644)</b>	<b>LBD (N=154)</b>	<b>Overall (N=798)</b>
Age	81.6 (6.30)	80.3 (6.39)	81.4 (6.33)
Gender (F)	417 (64.8%)	75 (48.7%)	492 (61.7%)
MMSE	20.3 (5.05)	17.9 (5.97)	19.9 (5.31)
Missing	0 (0%)	8 (5.2%)	8 (1.0%)
IADL	4.64 (2.18)	3.08 (2.36)	4.35 (2.30)
Missing	0 (0%)	4 (2.6%)	4 (0.5%)
ADL	5.42 (1.05)	4.47 (1.75)	5.22 (1.28)
Missing	118 (18.3%)	17 (11.0%)	135 (16.9%)
Hallucinations	-	123 (79.9%)	-
Parkinsonism	-	117 (76.5%)	-
Fluctuations	-	89 (76.7%)	-
RBD	-	90 (61.6%)	-
FP-CIT SPECT	-	52 (73.2%)	-
Hypertension	297 (46.1%)	71 (46.1%)	368 (46.1%)
Diabetes	102 (15.8%)	32 (20.8%)	134 (16.8%)
Cancer	97 (15.1%)	29 (18.8%)	126 (15.8%)

Abbreviations: **MMSE** = Mini Mental State Examination (for the Cognition domain of IC, score/30, higher score indicates better cognitive performance); **ADL**= Activities of Daily Living (score/6, higher score indicates better basal autonomy); **IADL**= Instrumental Activities of Daily Living (score/8, higher score indicates better instrumental autonomy); **RBD** = Rapid Eye Movement sleep behavior disorder



## Figure 1. Relationships between intrinsic capacities and diagnostic

Intrinsic capacity domains (vitality assessed by MNA, locomotion assessed by SPPB, psychology assessed by miniGDS, and audition assessed by HVEC) are represented on Y-Axis. Results of multivariate models adjusted for age, gender, and cognition (MMSE) are indicated.



Abbreviations: **MMSE** = Mini Mental State Examination; **SPPB** = Short Physical Performance Battery (for the Locomotion domain of IC, score/12, higher score indicates better locomotor performance); **MNA** = Mini Nutritional Assessment (for the Vitality domain of IC, score/24, score indicates better nutrition); auditory part of the **HVEC** = Hearing, Vision, Equilibrium and Cognition (for the Sensory domain of IC, score /60, higher score indicates lower auditive performance); **miniGDS** = mini-Geriatric Depression Scale (for the Psychology domain of IC, score/4, higher score indicates risk of depression);

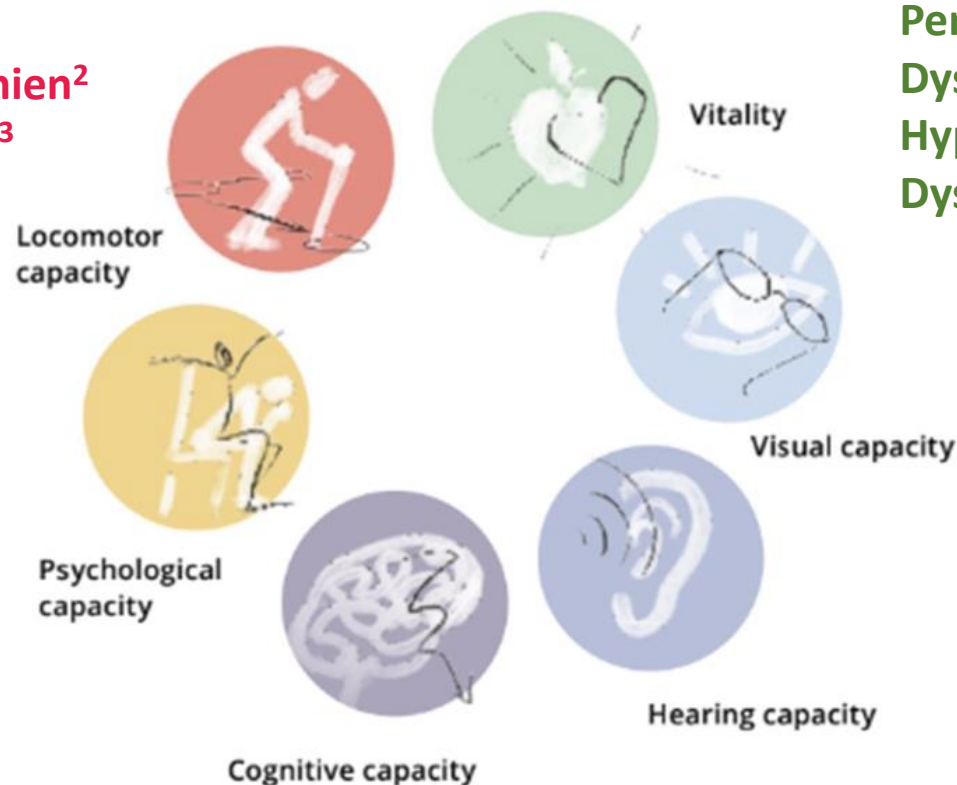


# Capacités Intrinsèques et MCL

→ Fragilité ou caractéristiques de la maladie ?

Syndrome parkinsonien<sup>2</sup>  
Instabilité posturale<sup>3</sup>  
Chutes répétées<sup>3</sup>

Dépression<sup>3</sup>  
Anxiété<sup>3</sup>



Perte poids  
Dysphagie  
Hyposmie, dysgueusie  
Dysautonomie (constipation)

Photophobie  
Troubles auditifs (lien  $\alpha$ -syn?)

Troubles cognitifs<sup>1</sup>

<sup>1</sup> McKeith: "essential criteria"

<sup>2</sup> McKeith: "core clinical feature"

<sup>3</sup> McKeith: "supportive clinical features"



# Capacités Intrinsèques, fragilités et MCL → Apparition dans les futurs critères ?

## Clinical diagnosis of Alzheimer's disease: recommendations of the International Working Group

Bruno Dubois\*, Nicolas Villain\*, Giovanni B Frisoni, Gil D Rabinovici, Marwan Sabbagh, Stefano Cappa, Alexandre Bejanin, Stéphanie Bombois, Stéphane Epelbaum, Marc Teichmann, Marie-Odile Habert, Agneta Nordberg, Kaj Blennow, Douglas Galasko, Yaakov Stern, Christopher C Rowe, Stephen Salloway, Lon S Schneider, Jeffrey L Cummings, Howard H Feldman

### Panel 3: Towards a personalised Alzheimer's disease risk profile in asymptomatic at-risk people

#### Factors that can increase the risk of progression to Alzheimer's disease

- Increased age
- Frailty
- Female sex
- Low education level
- Heterozygous APOE ε4 status
- Polygenic risk factors beyond APOE
- Family history of Alzheimer's disease
- Memory complaint or subjective cognitive decline
- Magnitude of brain lesions, inferred from pathophysiological biomarker results especially if searched with PET
- Presence of markers of neurodegeneration (ie, isolated hippocampal atrophy on MRI, <sup>18</sup>F-fluorodeoxyglucose-PET hypometabolism, or elevated CSF neurofilament light chain)
- Copathology

# Capacités Intrinsèques, fragilités et MCL

→ Vers un programme spécifique ?



→ Interventions mixtes (pharmaco/non pharmaco)



PHRCi en preparation (TNC léger)



En conclusion

**La fragilité et les baisses de capacités intrinsèques...**

**...sont fréquentes dans la MCL**

**...participent à la vulnérabilité des patient(e)s**

**...sont potentiellement modifiables !**

MERCI POUR VOTRE  
ATTENTION



## Module 2

# MCL, fragilité et capacités intrinsèques ?

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*Gériatre, Lyon, MCU-PH*

*Hospices Civils de Lyon, Université Lyon 1,  
INSERM U1237*





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