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Alzheimer

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Impact de la fragilité sur le pronostic du patient Alzheimer
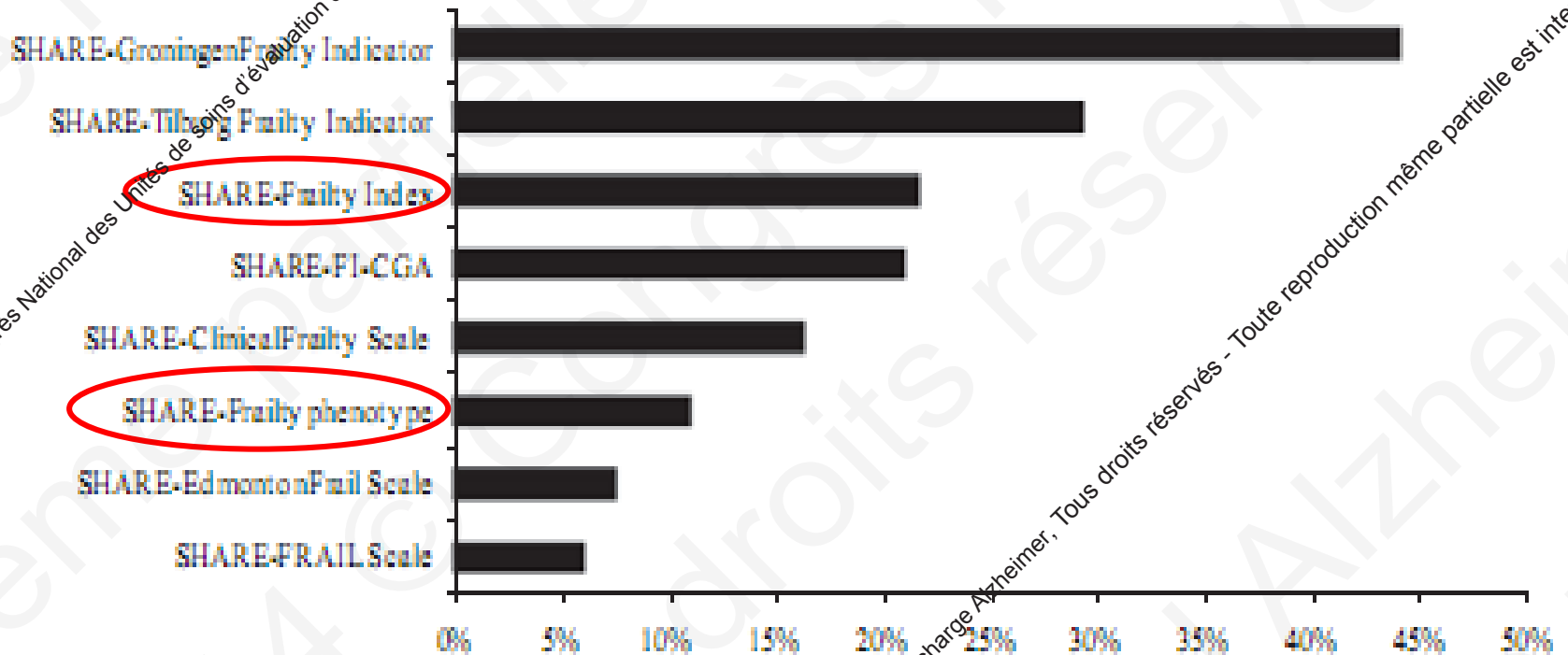
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12 Décembre 2014

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La fragilité

SHARE : 27 527 patients, âge moyen 65.3 ans, 54.8% de femmes

Prévalence de la Fragilité mesurée selon 8 échelles dans SHARE : 6 à 44%.

Theou O et al JAGS, 2013

Fragilité : facteur prédictif d'événements de mauvais pronostic
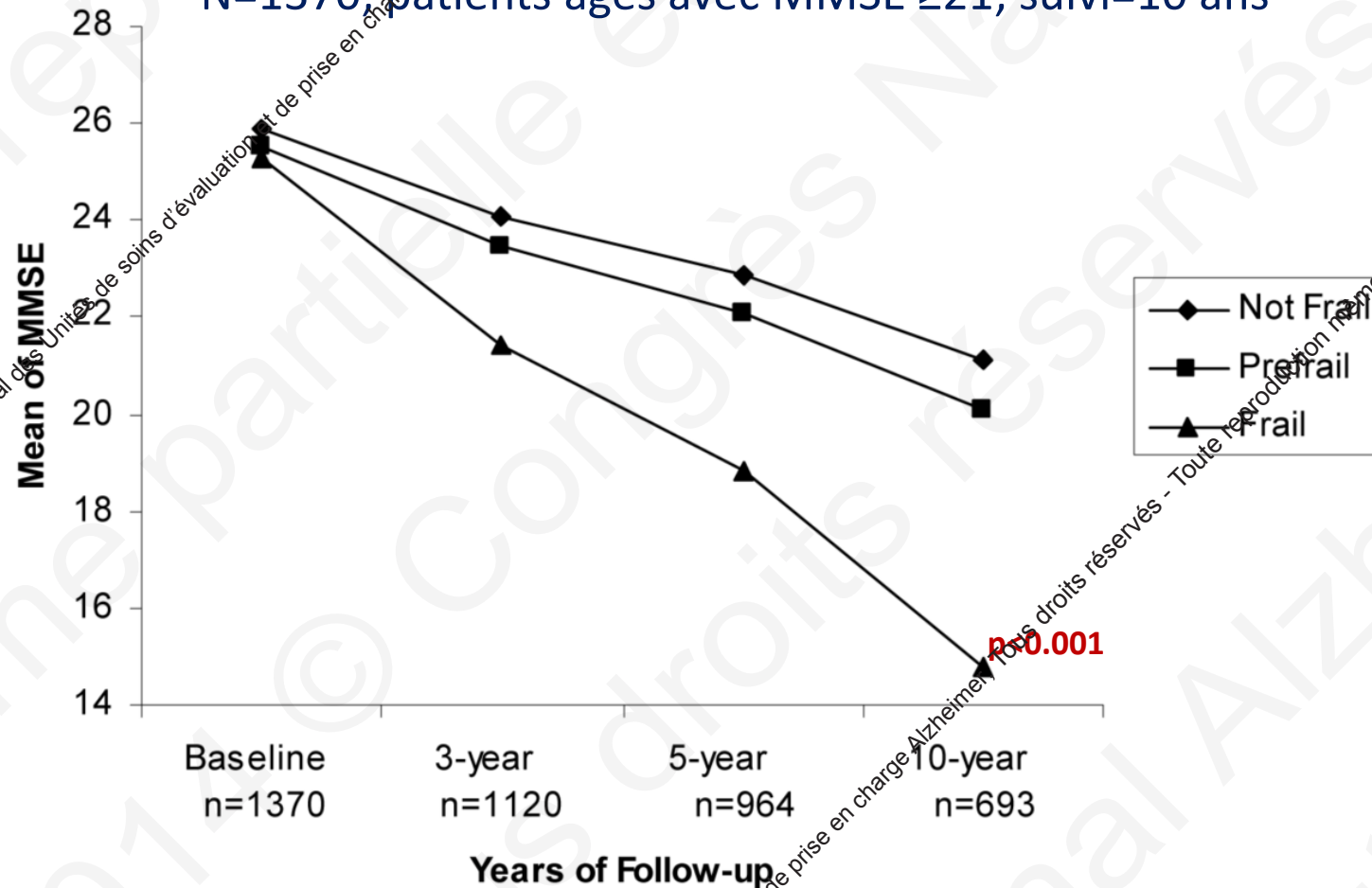
	Year	Country	Participants (n)	Length of follow-up (years)	Falls (HR*/OR† [95% CI])		Worsening disability (HR*/OR† [95% CI])		Hospitalisation (HR*/OR† [95% CI])		Care home admission (HR*/OR† [95% CI])		Mortality (HR*/OR† [95% CI])	
					Inter-mediate frailty	Severe frailty	Inter-mediate frailty	Severe frailty	Inter-mediate frailty	Severe frailty	Inter-mediate frailty	Severe frailty	Inter-mediate frailty	Severe frailty
Cardiovascular Health Study (CHS)[3]	2001	USA	5317	7	1·12* (1·00–1·26)	1·23* (1·50–2·21)	1·55* (1·38–1·75)	1·79* (1·47–2·17)	1·11* (1·03–1·19)	1·27*, (1·11–1·46)	NA	NA	1·28* (1·13–1·55)	1·63* (1·27–2·08)
Canadian Study of Health and Aging (CSHA)[92]	2004	Canada	9008	5	NA	NA	NA	NA	NA	NA	2·54 † (1·67–3·86)	2·60 (1·06–4·96)	2·54† (1·92–3·37)	3·69† (2·26–6·02)
Women's Health and Aging Study (WHAS)[93]	2006	USA	1438	3	0·92* (0·63–1·64)	1·18* (0·63–2·19)	NA	NA	0·99* (0·67–1·47)	0·67* (0·33–1·35)	5·16* (0·81–32·9)	23·98* (4·45–129·2)	3·50* (1·91–6·39)	6·03* (3·00–12·08)
Study of Osteoporotic Fractures (SOF)[94]	2008	USA	6701	4·5	1·23† (1·02–1·48)	2·44† (1·95–3·04)	1·89†, (1·66–2·14)	2·79† (2·31–3·37)	NA	NA	NA	NA	1·54† (1·40–1·69)	2·75* (2·46–3·07)

HR=hazard ratio. NA=not available. OR=odds ratio. *Hazard ratio. †Odds ratio. The comparator for hazard ratios and odds ratios is people who are not frail.

Table: Covariate-adjusted associations between frailty and adverse outcomes (falls, disability, hospitalisation, care home admission, and mortality) from four large prospective cohort studies

Fragilité : facteur prédictif de déclin cognitif

N=1370; patients âgés avec MMSE ≥21; suivi=10 ans

Samper-Ternent et al., **J Am Geriatr Soc 2008**

Searching for an Operational Definition of Frailty: A Delphi Method Based Consensus Statement. The Frailty Operative Definition-Consensus Conference Project

"La fragilité est un syndrome multidimentionnel caractérisé par une décroissance des réserves et une diminution de la résistance au stress.

Absence de définition opérationnel :
- Outil robuste pour prédire la survenue d'événements de mauvais pronostic.
- Indicateur des actions à mener pour agir sur la réversibilité de la fragilité.

British Geriatrics Society.
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COMMENTA

The frai
differen

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Table 1. Main characteristics of the frailty phenotype and the Frailty Index

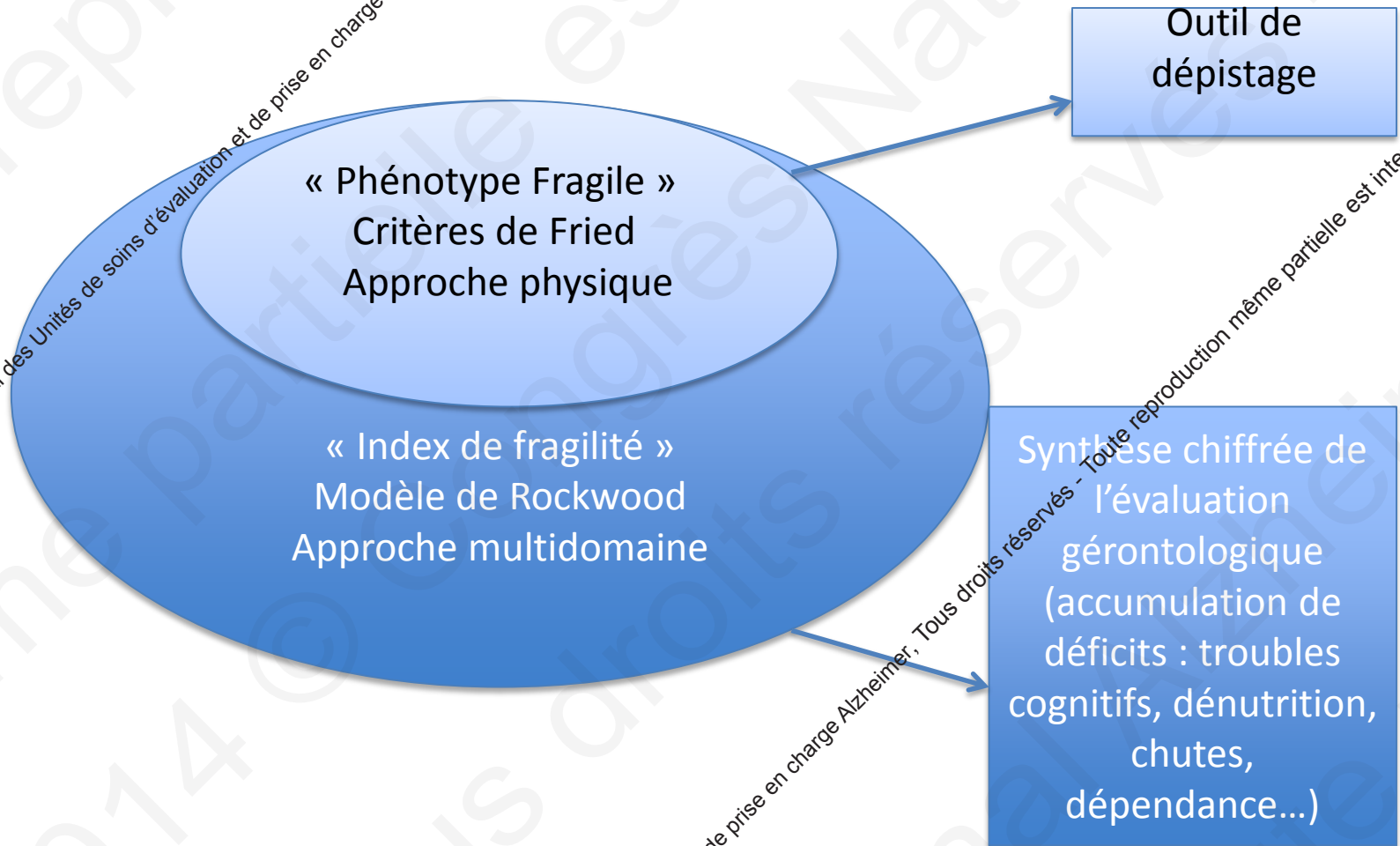| Frailty phenotype	Frailty Index
Signs, symptoms	Diseases, activities of daily living, results of a clinical evaluation
Possible before a clinical assessment	Doable only after a comprehensive clinical assessment
Categorical variable	Continuous variable
Pre-defined set of criteria	Unspecified set of criteria
Frailty as a pre-disability syndrome	Frailty as an accumulation of deficits
Meaningful results potentially restricted to non-disabled older persons	Meaningful results in every individual, independently of functional status or age

Index de Fragilité

Appendix 1: List of variables used by the Canadian Study of Health and Aging to construct the 70-item CSHA Frailty Index

- Changes in everyday activities
- Head and neck problems
- Poor muscle tone in neck
- Bradykinesia, facial
- Problems getting dressed
- Problems with bathing
- Problems carrying out personal grooming
- Urinary incontinence
- Toileting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal problems
- Problems cooking
- Sucking problems
- Problems going out alone
- Impaired mobility
- Musculoskeletal problems
- Bradykinesia of the limbs
- Poor muscle tone in limbs
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls

- Mood problems
- Feeling sad, blue, depressed
- History of depressed mood
- Tiredness all the time
- Depression (clinical impression)
- Sleep changes
- Restlessness
- Memory changes
- Short-term memory impairment
- Long-term memory impairment
- Changes in general mental functioning
- Onset of cognitive symptoms
- Clouding or delirium
- Paranoid features
- History relevant to cognitive impairment or loss
- Family history relevant to cognitive impairment or loss
- Impaired vibration
- Tremor at rest
- Postural tremor
- Intention tremor
- History of Parkinson's disease
- Family history of degenerative disease

- Seizures, partial complex
- Seizures, generalized
- Syncope or blackouts
- Headache
- Cerebrovascular problems
- History of stroke
- History of diabetes mellitus
- Arterial hypertension
- Peripheral pulses
- Cardiac problems
- Myocardial infarction
- Arrhythmia
- Congestive heart failure
- Lung problems
- Respiratory problems
- History of thyroid disease
- Thyroid problems
- Skin problems
- Malignant disease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of the palmomental reflex
- Other medical history

IF = nombre de déficiences/nbre de critères évalués

Rockwood et al., **CMAJ 2005**

Fragilité : deux approches complémentaires

« Phénotype Fragile »
Critères de Fried
Approche physique

« Index de fragilité »
Modèle de Rockwood
Approche multidomaine

Outil de dépistage

Synthèse chiffrée de l'évaluation gérontologique (accumulation de déficits : troubles cognitifs, dénutrition, chutes, dépendance…)

Objectifs

- **Etudier l'Index de Fragilité (FI) chez les patients atteints de maladie d'Alzheimer :**

  - comme facteur prédictif de la survenue d'hospitalisations, d'institutionnalisation et de décès.

  - en comparaison à la sévérité de la démence (score CDR) pour prédire la survenue d'événements de mauvais pronostic.

  - comme facteur associé au déclin cognitif à court terme.

Méthode

- Impact of Cholinergic Treatment Use study (ICTUS) – étude de cohorte multicentrique prospective européenne menée sur deux ans.

- 1379 MA probables stades léger à modéré à domicile avec un aidant informel identifié.

- **Le score FI:** rapport entre les potentiels déficits actuels (ex: déficits présents chez cette personne/30)

- Etude de survie: modèle de Cox

Résultats (1)

Table 2. Baseline characteristics of the study sample ($n = 1,191$)

	Mean (SD) or %
Age (years)	76.2±7.6
Gender (women)	63.8
Body mass index (kg/m^2)	25.2±4.2
Education (years)	8.0±4.7
Diabetes	11.6
Hypertension	39.0
Ischemic heart disease	13.2
Stroke	8.0
Falls	17.1
Seizures	1.1
Depression	24.5
ADAS-Cog (points)	29.5±9.2
MMSE (points)	20.6±3.9
CDR score (points)	
- 0.5	43.2
- 1	44.2
- ≥2	12.6
ADL (/6)	5.5±0.9
IADL (/8)	4.9±2.2
Frailty Index (%)	20.8±12.2

Values are presented as means ± standard deviations (SD) or percentage

Résultats (2)

Table 3. Results from unadjusted and adjusted proportional hazard models testing the relationships of the FI with mortality, hospitalization and institutionalization.

	Mortality	P	Hospitalization	P	Institutionalization	P
	n/N=77/1,191		n/N=185/1,191		n/N=134/1,191	
Frailty Index (continuous)						
Unadjusted	1.023 (1.005, 1.040)	0.011	1.018 (1.006, 1.030)	0.002	1.018 (1.004, 1.033)	0.009
Adjusted for age, gender	1.019 (1.002, 1.037)	0.031	1.017 (1.006, 1.029)	0.004	1.011 (0.997, 1.025)	0.116
Frailty index classification						
Unadjusted						
Not frail (FI<25%)	1		1		1	
Frail (FI≥25%)	2.211 (1.413, 3.457)	0.001	1.557 (1.164, 2.083)	0.003	1.566 (1.112, 2.206)	0.010
Adjusted for age, gender						
Not frail (FI<25%)	1		1		1	
Frail (FI≥25%)	1.409 (0.997, 1.992)	0.052	1.525 (1.137, 2.046)	0.005	2.121 (1.352, 3.325)	0.001

Results are presented as HR and 95%CI. **FI**: Frailty Index; **n/N**: number of events/total study sample

Résultats (3)

Table 4. Results from unadjusted and adjusted proportional hazard models simultaneously testing the independent relationships of the FI and CDR score with mortality, hospitalization and institutionalization.

	Mortality, n/N=77/1,191	P	Hospitalization, n/N=185/1,191	P	Institutionalization, n/N=134/1,191	P
Unadjusted						
Frailty Index (continuous)	1.009 (0.990, 1.028)	0.369	1.019 (1.006, 1.032)	0.003	1.003 (0.988, 1.019)	0.652
CDR score	2.038 (1.349, 3.081)	0.001	0.929 (0.679, 1.272)	0.648	2.028 (1.486, 2.766)	<0.001
Adjusted for age and gender						
Frailty Index (continuous)	1.007 (0.987, 1.027)	0.494	1.019 (1.006, 1.032)	0.004	0.998 (0.983, 1.014)	0.838
CDR score	1.922 (1.256, 2.941)	0.003	0.913 (0.664, 1.254)	0.573	1.955 (1.427, 2.679)	<0.001

Results are presented as HR and 95%CI. **FI**: Frailty Index, **CDR score**: Clinical Dementia Rating score; **n/N**: number of events/total study sample

Résultats (4)

Table 4. Longitudinal modifications of ADAS-Cog and MMSE scores according to the frailty status.

	Baseline MMSE	Δ MMSE Between 1 year follow-up & baseline assessment[1]		Baseline ADAS-Cog	Δ ADAS-Cog Between 1 year follow-up & baseline assessment[1]	
	Mean±SEM	Unadjusted Mean±SEM	Adjusted[2] Mean±SEM	Mean±SEM	Unadjusted Mean±SEM	Adjusted[2] Mean±SEM
Non-frail ≤ 0.25 points (*n*=650)	21.13±0.15	-1.24±0.14	-1.24±0.15	18.74±0.34	3.07±0.29	3.06±0.30
Frail > 0.25 points (*n*=323)	19.58±0.21	-1.89±0.20	-1.91±0.21	23.20±0.48	4.59±0.42	4.66±0.42

SEM: standard error of means

[1] Values are presented as means ± SEM. All statistical differences were significant (all p values<0.05) between frail and non-frail participants.

[2] Adjusted for age, gender and years of education.

Conclusion

- **L'Index de Fragilité (FI) est un outil robuste chez les patients atteints de MA pour prédire à un an :**

  - La survenue d'évènements de mauvais pronostic (hospitalisation, institutionnalisation et mortalité).

  - L'aggravation du déclin cognifif .

Conclusion (2)

- **A la difference des autres instruments, le FI :**

  - Applicable à des populations déjà dépendantes (EHPAD) et avec des maladies hautement fragilisantes (Alzheimer, cancers…).

  - Outil reflet synthétique de l'évaluation gérontologique standardisée et donc des réserves physiologiques.

  - Identifiant les individus à haut risque d'évènements de mauvais pronositic (en particulier un déclin cognitif à court terme) au sein d'une population hétérogène et complexe.

Merci de votre attention.

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