



Come rendere fruibili le innovazioni terapeutiche nel prossimo futuro ?

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The scenary

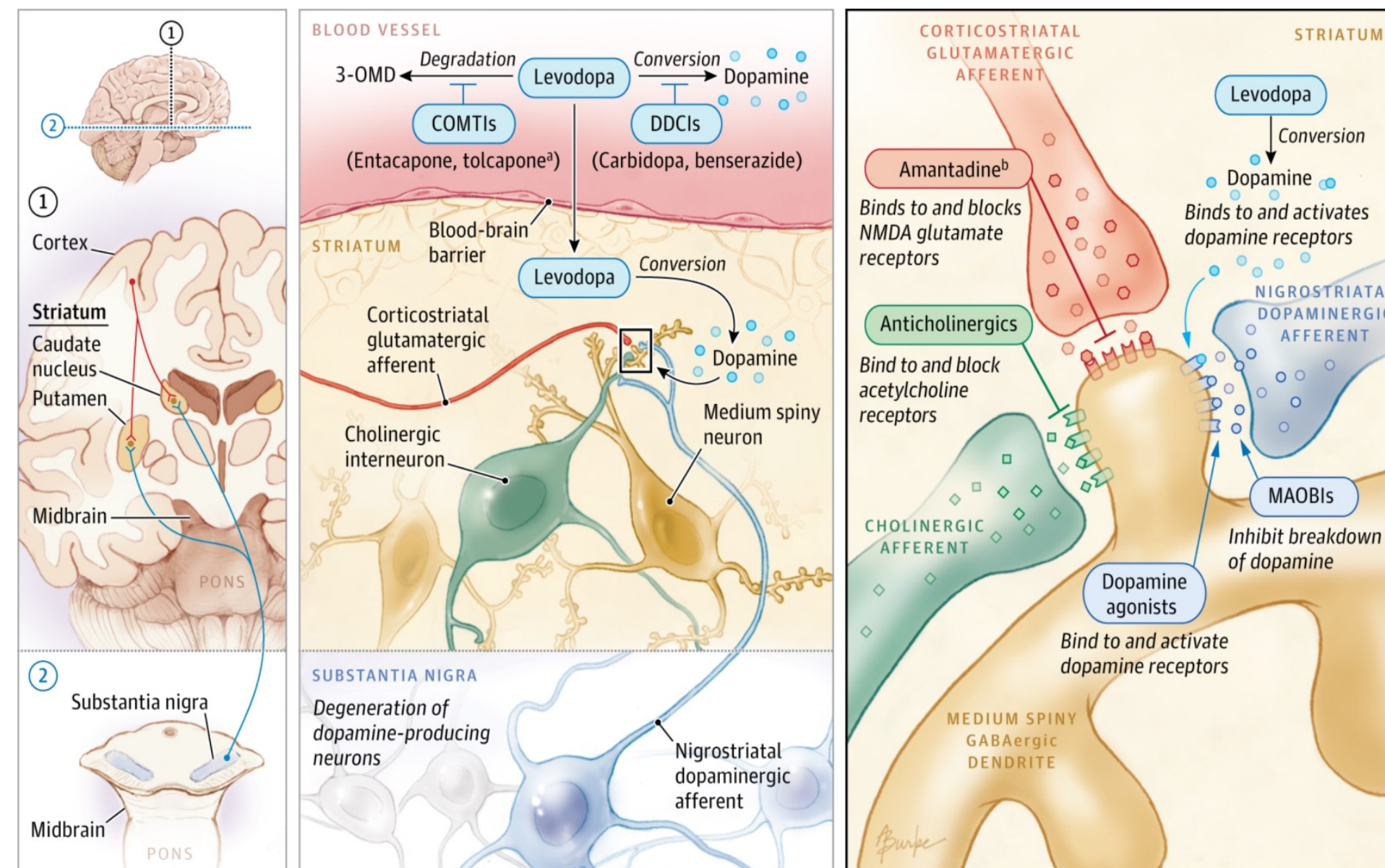
- Prodromal phase
- Diagnosis
- Early treatment
- Follow the patient
- Check complications
- Advanced phase
- Palliative care

→ 20 years?

What does the patient need?

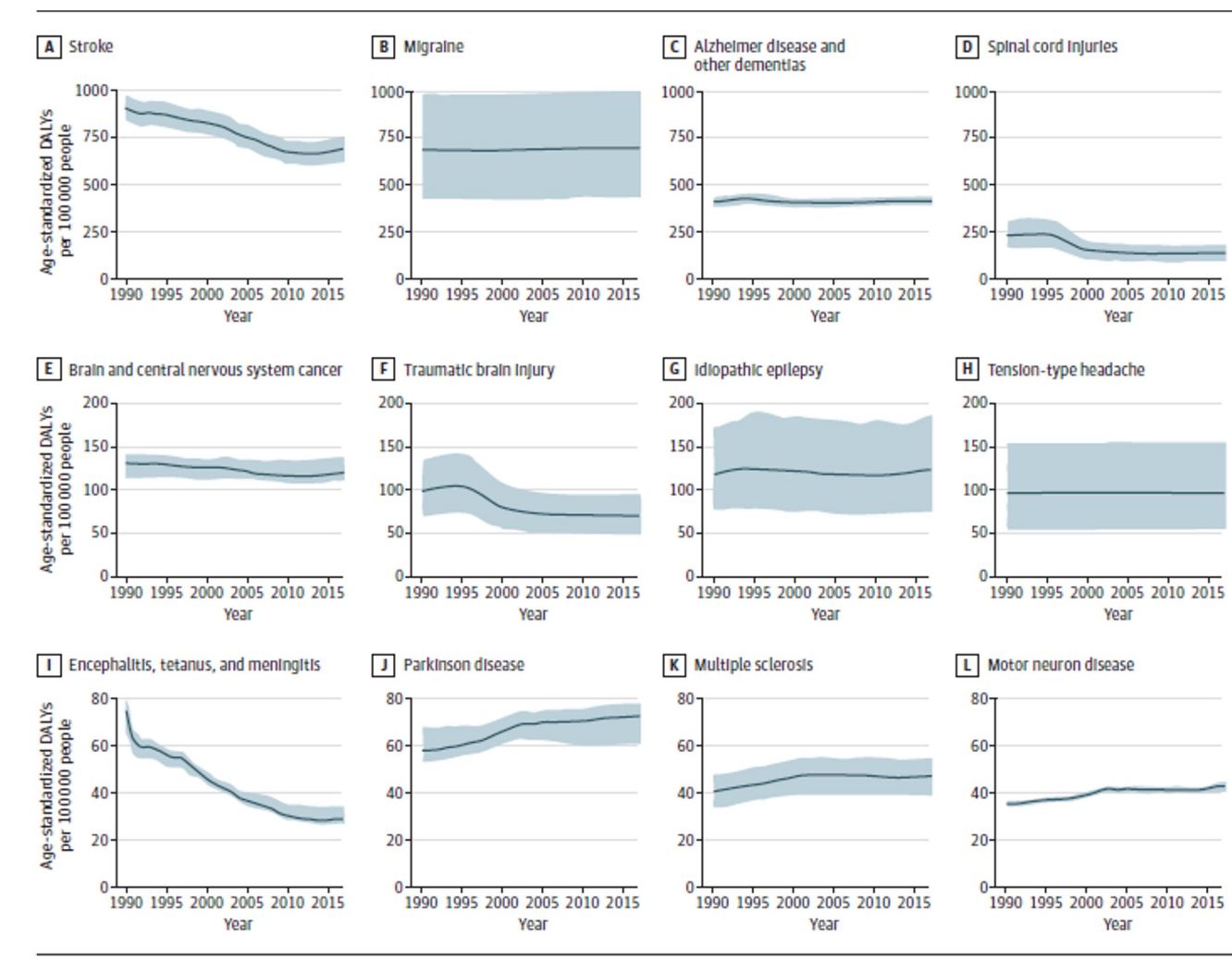
1. Drugs
2. Physical activity
3. Physiotherapy, occupational therapy, logotherapy
4. Psychological support (also for caregiver)
5. Assessment of working abilities, certifications for invalidity ...
6. others

Drugs that are available now



JAMA Neurology | **Original Investigation**
Burden of Neurological Disorders Across the US
From 1990-2017
A Global Burden of Disease Study

GBD 2017 US Neurological Disorders Collaborators



VIEWPOINT

The Parkinson Pandemic—A Call to Action

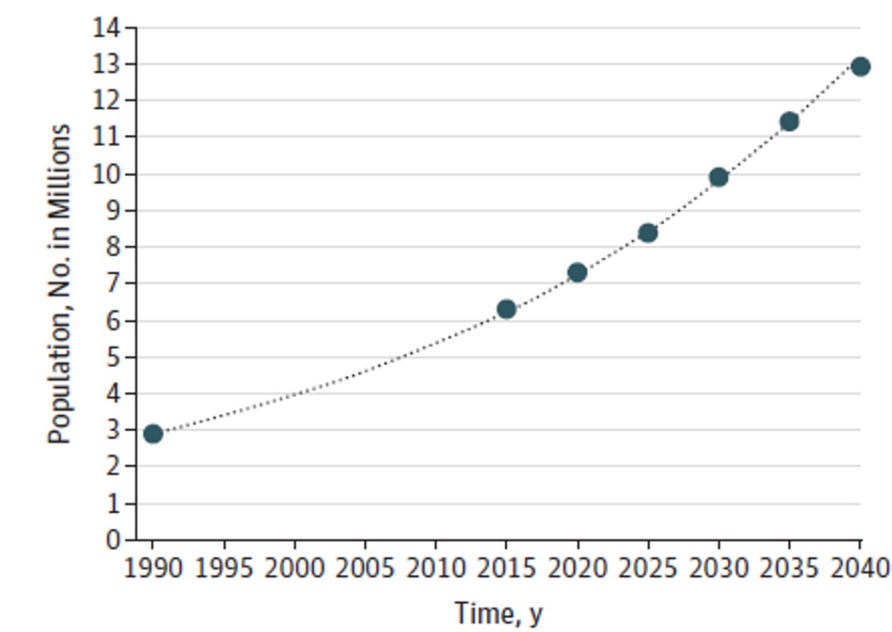
Pandemic features

- Exponential growth
- No one is immune
- Involvement of large geographic areas
- Migration

Causes

- aging populations
- increasing longevity
- declining smoking rates
- industrialization
- longer-lasting disease

Figure. Estimated and Projected Number of Individuals With Parkinson Disease, 1990-2040



Sources: Global Burden of Disease Study (1990 and 2015) and projections based on published² and public³ sources.

JAMA Neurology Published online November 13, 2017

PD prevalence: age and sex effect

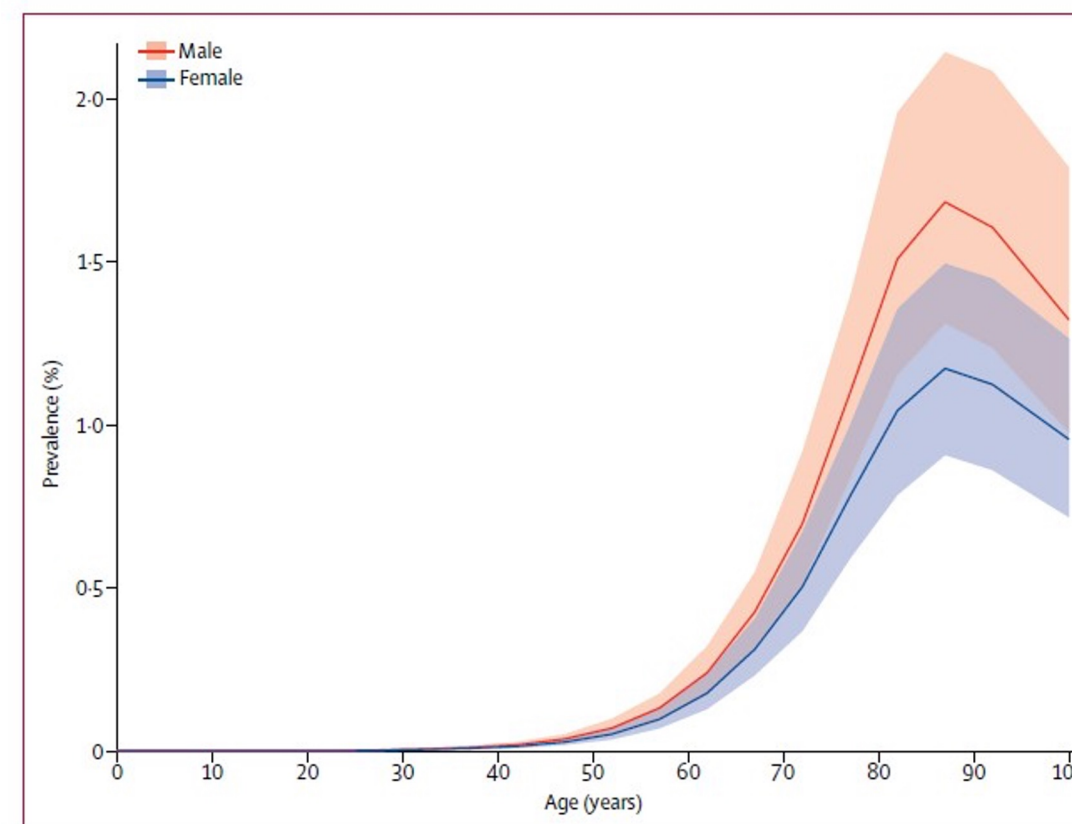


Figure 2: Global prevalence of Parkinson's disease by age and sex, 2016
Prevalence is expressed as the percentage of the population that is affected by the disease. Shading indicates 95% uncertainty intervals.

Lancet Neurol 2018; 17: 939-53

PD prevalence: the weight of disability

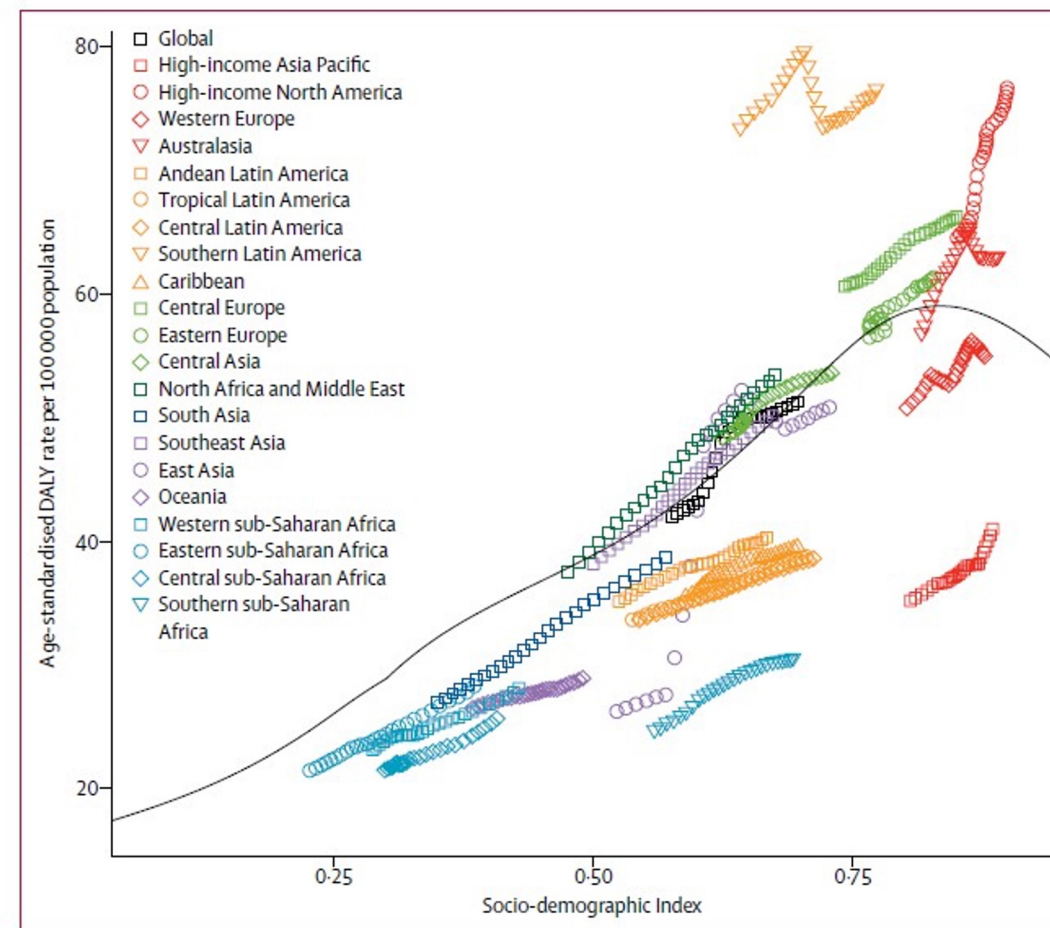


Figure 4: Age-standardised DALY rates for Parkinson's disease by 21 Global Burden of Disease regions by Socio-demographic Index, 1990-2016
 Expected values based on Socio-demographic Index and disease rates in all locations are shown as the black line. The black line represents expected values of age-standardised DALY rates for each value of Socio-demographic Index and is based on a Gaussian process regression of results for all Global Burden of Disease locations over the entire 1990-2016 estimation period. DALY=disability-adjusted life-year.

Lancet Neurol 2018; 17: 939-53

What about Italy?

Prevalence: 193.7/100,000

Incidence: 40/100.000

significant age-dependent trend, with higher rates in older groups

strong association of PD with male sex, but only in older age groups

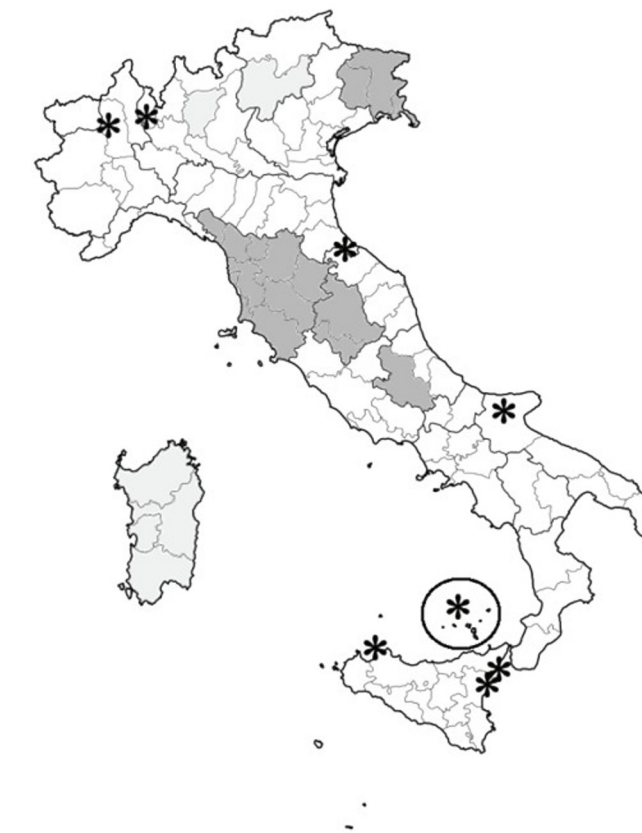
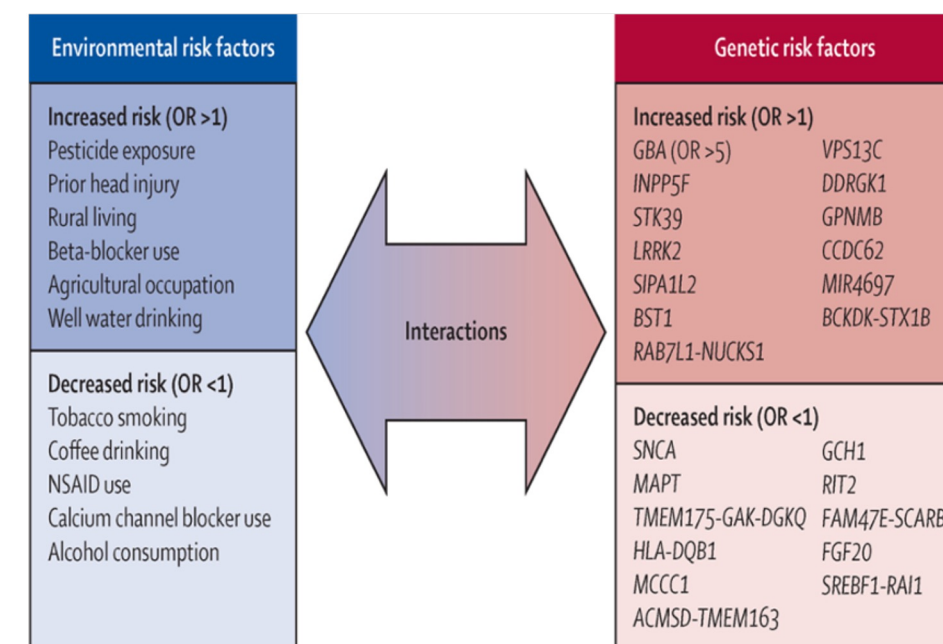


Figure 2. Geographic locations of studies performed on the prevalence of Parkinson's disease in Italy (1979 - 2019), and included in the meta-analysis. Deep gray = data retrieved at provincial and/or regional level, by sex and age groups; light grey = data retrieved at provincial and/or regional level, cumulative; * = data retrieved at municipal level.

Riccò et al., 2020

PD: risk and protective factors

- The etiology of Parkinson disease is likely multifactorial
- A complex interaction between underlying genetic susceptibility and combination of risk and protective factors contribute to determine the development of PD



Kalia et al., 2015

PD risk and protective factors

Non modifiable vs modifiable

Non modifiable factors

- Age
- Male sex
- Familiarity for PD
- Ethnicity
- Genetic factors*

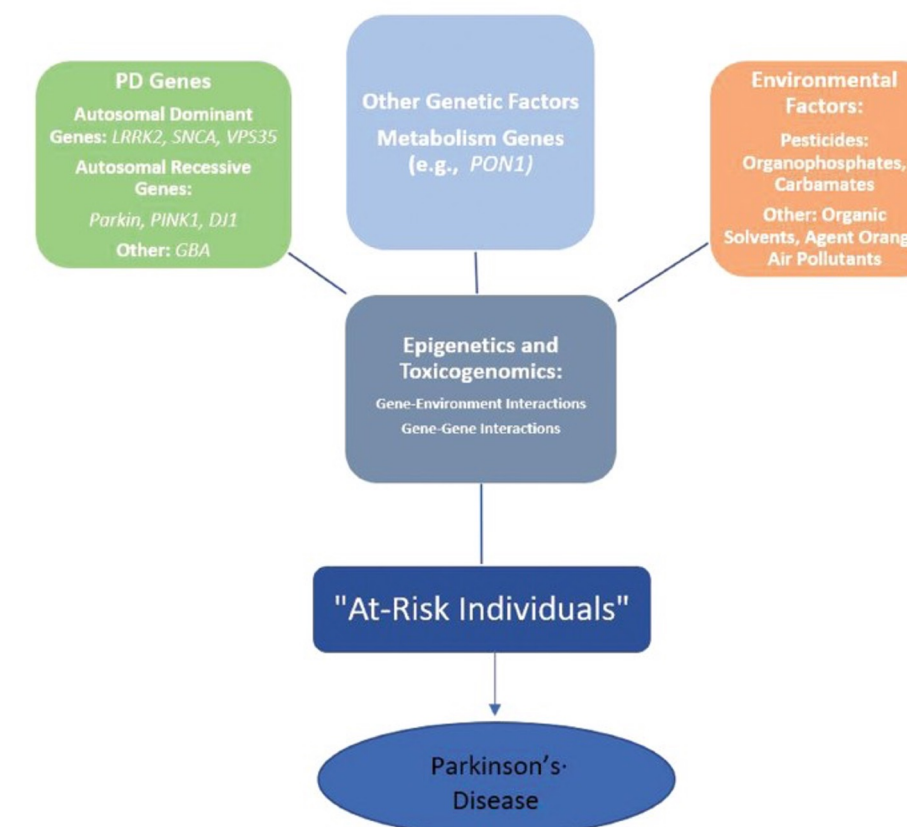


Fig. 1 Interplay between genes and environment and their effect on the development of Parkinson's disease.

Genetic-targeted approach to PD

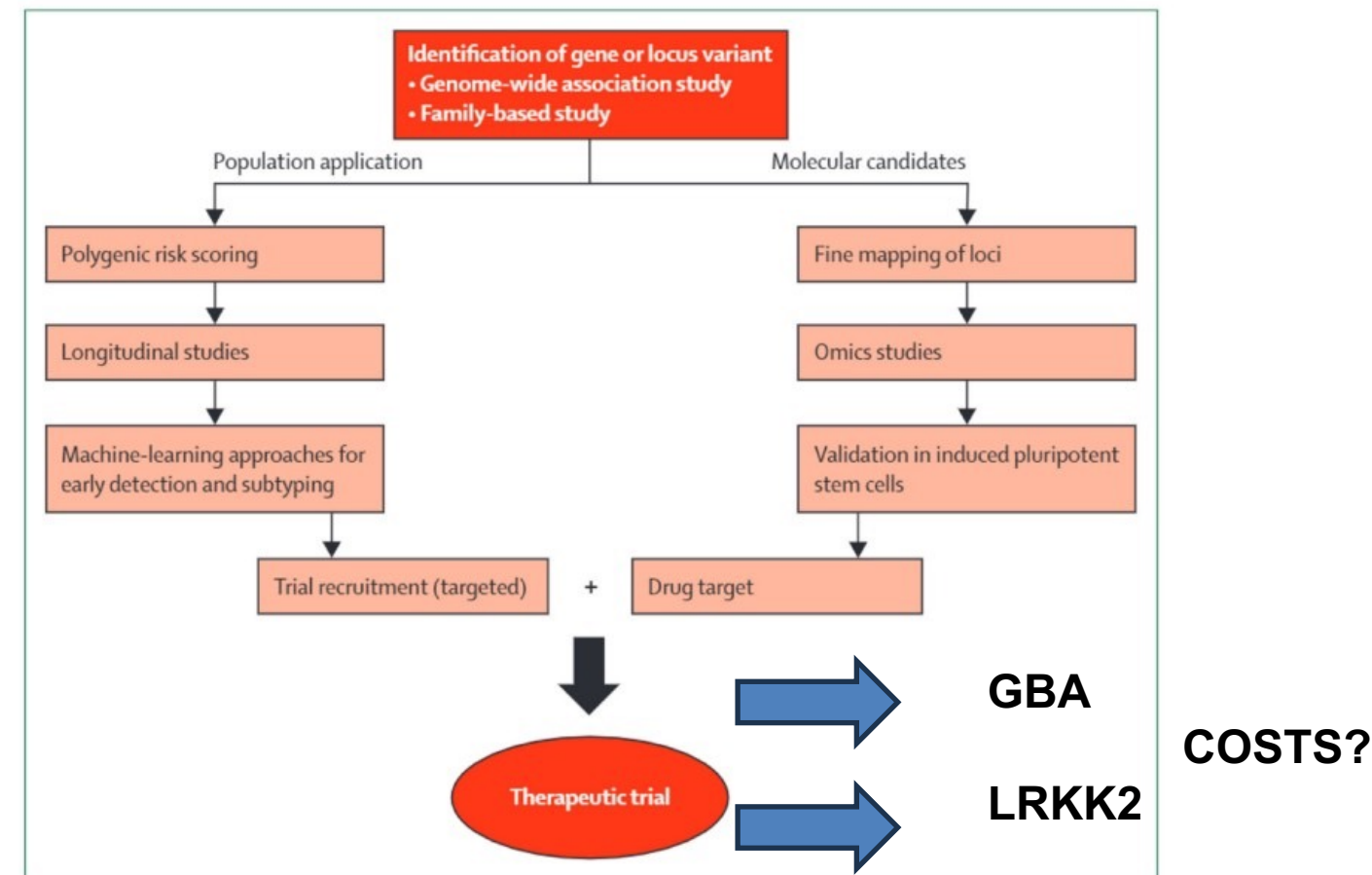
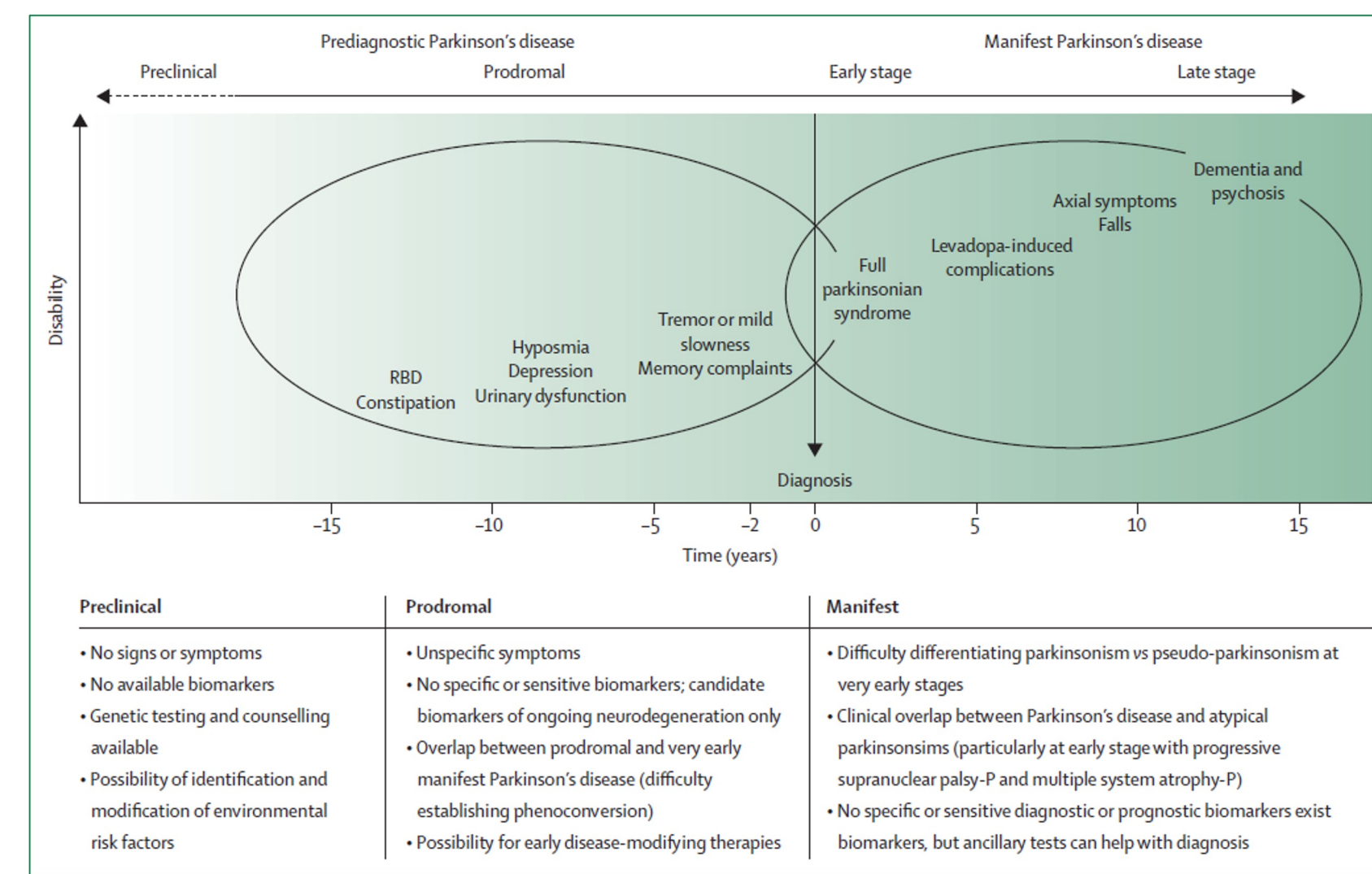


Figure 2:
 Schematic for genetics-driven drug discovery

Lancet Neurol. 2020 February ; 19(2): 170–178.
 doi:10.1016/S1474-4422(19)30287-X.

PD: the prodromal phase



www.thelancet.com/neurology Vol 20 May 2021

The scenary

- **Prodromal phase**
- Diagnosis
- **Early treatment**
- Follow the patient
- Check complications
- Advanced phase
- Palliative care

→ 20 years?

α -syn-targeting therapeutic strategies

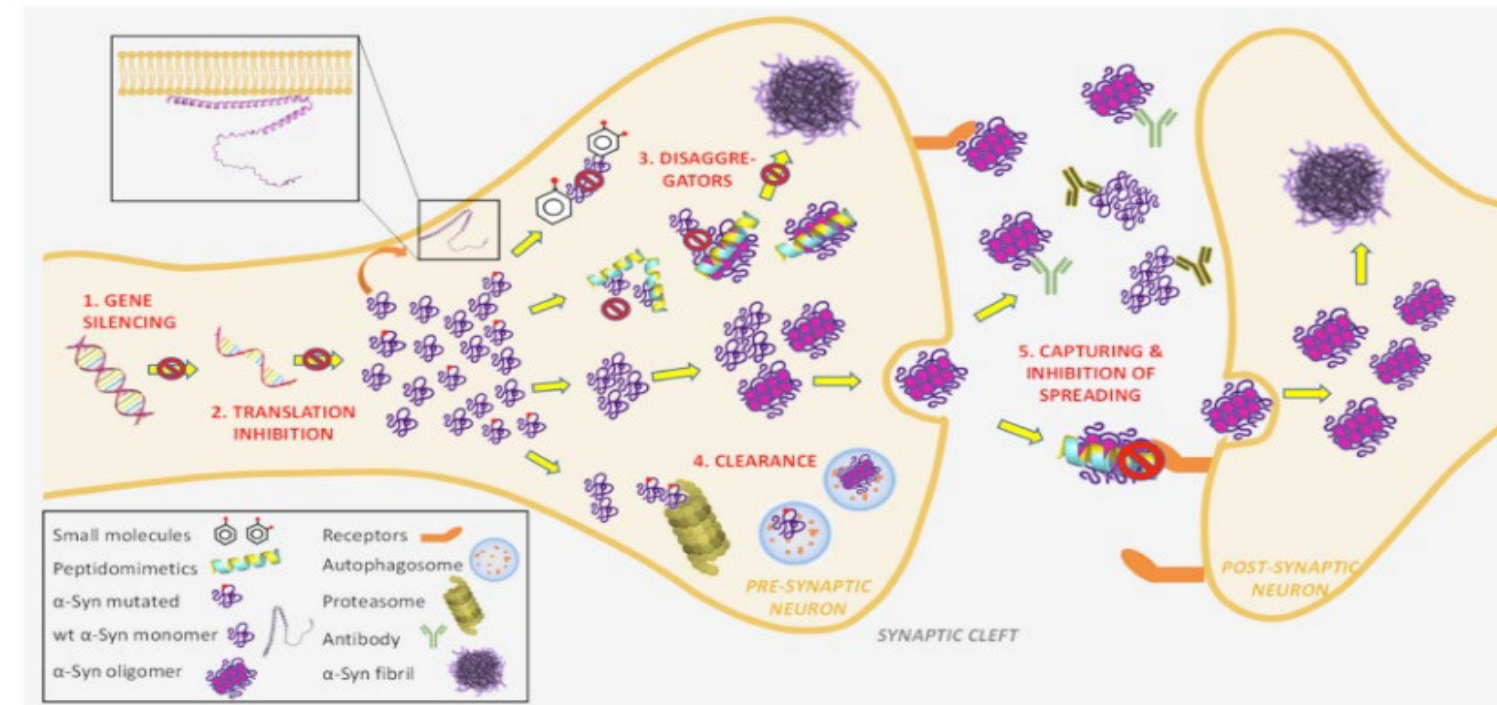


Figure 3. Five major developing α -Syn-targeting therapeutic strategies. They include reducing α -Syn transcription (1) and translation (2), inhibiting α -Syn aggregation by disaggregators involving low-molecular-weight compounds identified by high-throughput screening and rationally designed peptides or peptidomimetics (3), enhancing α -Syn clearance and degradation through autophagy and the ubiquitin-proteasome system (4), and capturing the toxic α -Syn forms in the extracellular space and blocking their transcellular spreading via immunotherapies (5).

Cells 2022, 11, 1732. <https://doi.org/10.3390/cells11111732>

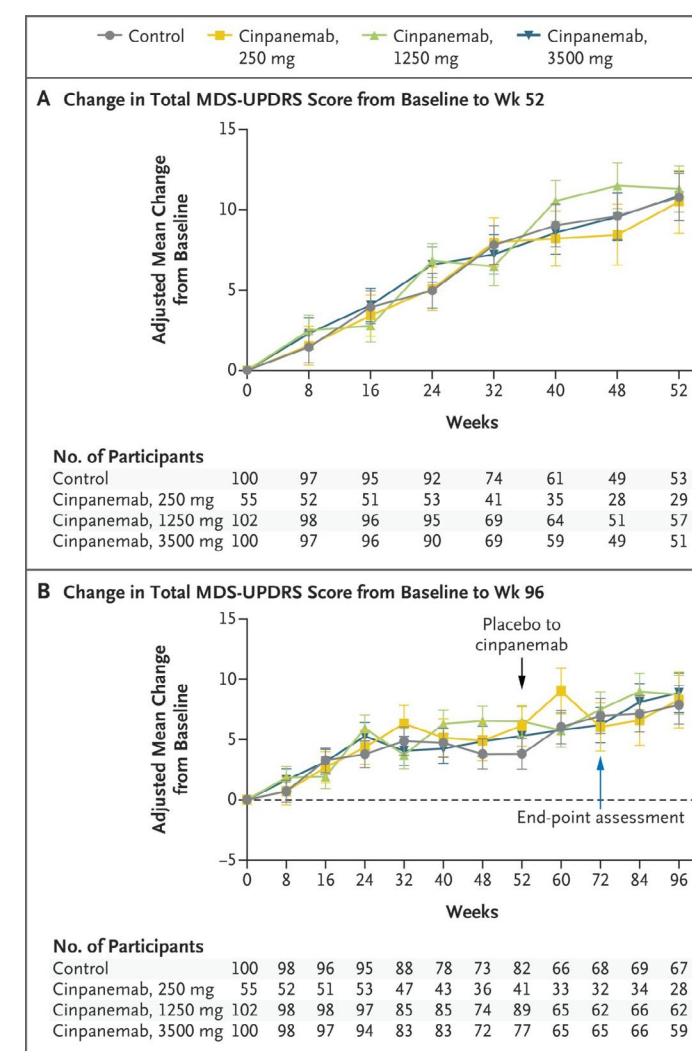
Original Article

Trial of Cinpanemab in Early Parkinson's Disease

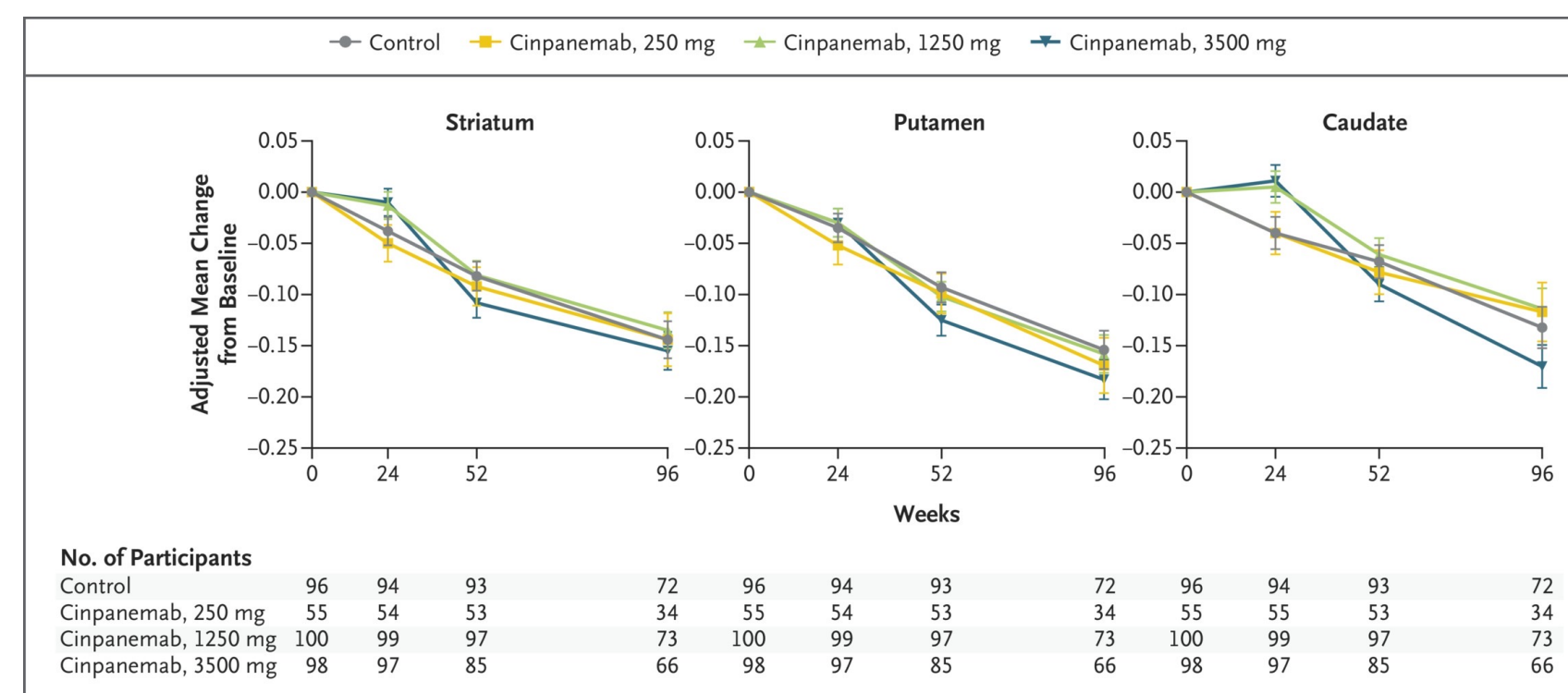
Anthony E. Lang, M.D., Andrew D. Siderowf, M.D., Eric A. Macklin, Ph.D., Werner Poewe, M.D., David J. Brooks, M.D., D.Sc., Hubert H. Fernandez, M.D., Olivier Rascol, M.D., Nir Giladi, M.D., Fabrizio Stocchi, M.D., Caroline M. Tanner, M.D., Ph.D., Ronald B. Postuma, M.D., David K. Simon, M.D., Ph.D., Eduardo Tolosa, M.D., Brit Mollenhauer, M.D., Jesse M. Cedarbaum, M.D., Kyle Fraser, Ph.D., James Xiao, Ph.D., Karleyton C. Evans, M.D., Danielle L. Graham, Ph.D., Inbal Sapir, Ph.D., Jennifer Inra, M.D., R. Matthew Hutchison, Ph.D., Minhua Yang, M.S., Tara Fox, M.S., Samantha Budd Haeberlein, Ph.D., Tien Dam, M.D., for the SPARK Investigators



Adjusted Mean MDS-UPDRS Total Scores to Week 52 and Week 96.



Adjusted Mean Change from Baseline to Week 96 in the DaT-SPECT Striatal Binding Ratio (Pooled Delayed Start).



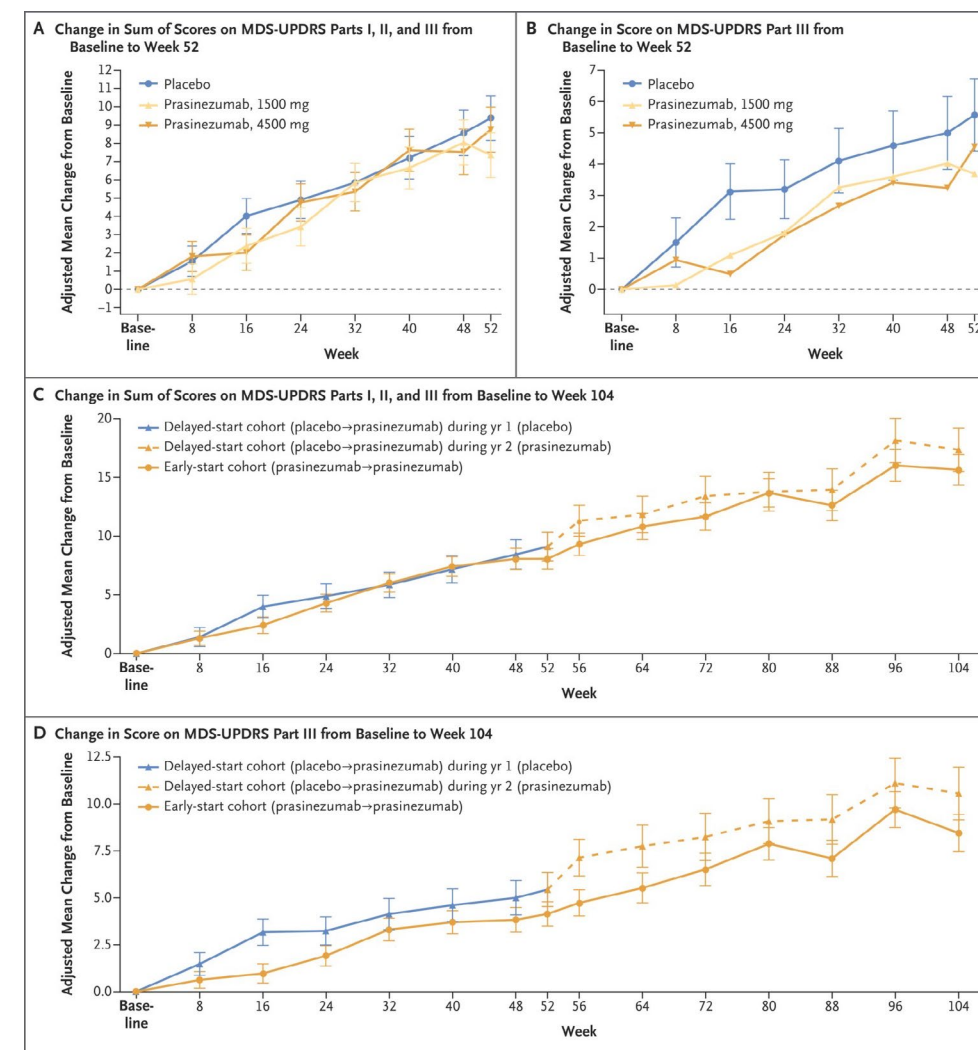
Original Article

Trial of Prasinezumab in Early-Stage Parkinson's Disease

Gennaro Pagano, M.D., Ph.D., Kirsten I. Taylor, Ph.D., Judith Anzures-Cabrera, Ph.D., Maddalena Marchesi, M.D., Tanya Simuni, M.D., Kenneth Marek, M.D., Ph.D., Ronald B. Postuma, M.D., Nicola Pavese, M.D., Ph.D., Fabrizio Stocchi, M.D., Ph.D., Jean-Philippe Azulay, Ph.D., Brit Mollenhauer, M.D., Lydia López-Manzanares, M.D., David S. Russell, M.D., Ph.D., James T. Boyd, M.D., Anthony P. Nicholas, M.D., Ph.D., María R. Luquin, Ph.D., Robert A. Hauser, M.D., Thomas Gasser, M.D., Werner Poewe, M.D., Ph.D., Benedicte Ricci, Ph.D., Anne Boulay, Ph.D., Annamarie Vogt, Ph.D., Frank G. Boess, Ph.D., Juergen Dukart, Ph.D., Giulia D'Urso, Ph.D., Rebecca Finch, M.Sc., Stefano Zanigni, M.D., Ph.D., Annabelle Monnet, M.Sc., Nathalie Pross, Ph.D., Andrea Hahn, M.Sc., Hanno Svoboda, Ph.D., Markus Britschgi, Ph.D., Florian Lipsmeier, Ph.D., Ekaterina Volkova-Volkmar, Ph.D., Michael Lindemann, Ph.D., Sebastian Dziadek, Ph.D., Štefan Holiga, Ph.D., Daria Rukina, Ph.D., Thomas Kustermann, Ph.D., Geoffrey A. Kerchner, M.D., Ph.D., Paulo Fontoura, M.D., Ph.D., Daniel Umbricht, M.D., Ph.D., Rachelle Doody, M.D., Ph.D., Tania Nikolcheva, M.D., Ph.D., Azad Bonni, M.D., Ph.D., for the PASADENA Investigators and Prasinezumab Study Group



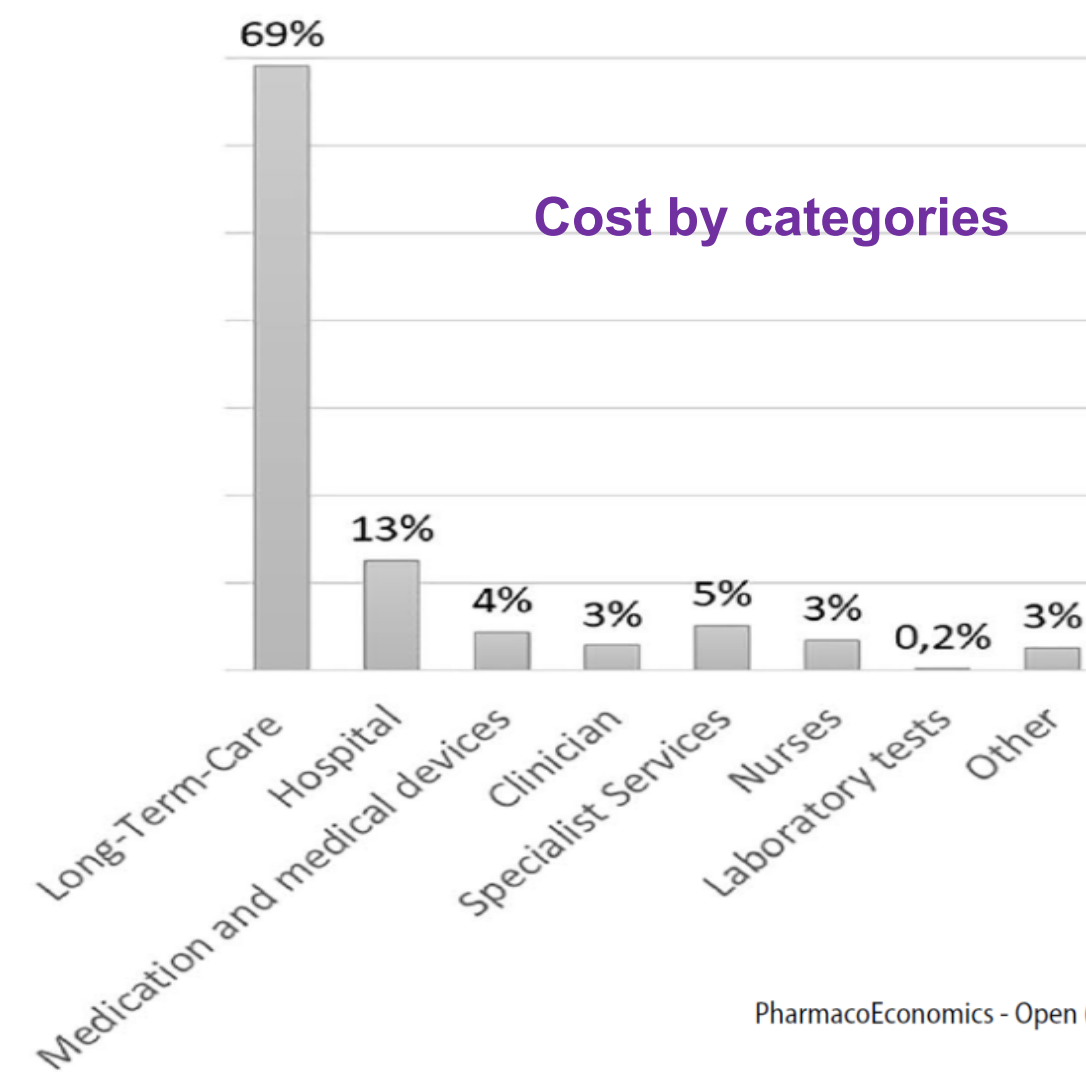
Change in MDS-UPDRS Scores over Time.



Some thoughts.....

- So at the moment we don't have drugs able to stop progression of the disease, but research is ongoing....
- We may have soon drugs for specific subtypes (genetic)
- Are these drugs going to impact on health services?
- Probably yes, but what are the real costs of PD for national health services?

**Prevalence and Cost of Care for Parkinson's Disease in Luxembourg:
 An Analysis of National Healthcare Insurance Data**



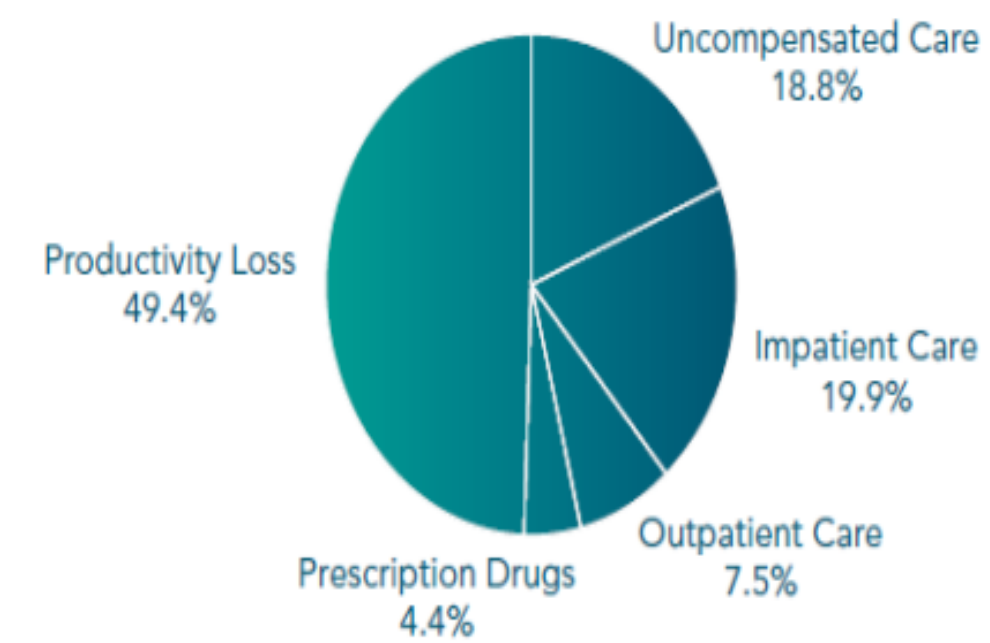
ECONOMIC AND SOCIAL COSTS

		malato	famiglia	società
costi intangibili	Dolore fisico	✓		
	Disagio psicologico	✓	✓	
	Problemi esistenziali	✓	✓	
costi indiretti	Perdita di autonomia	✓	✓	
	Necessità assistenza	✓	✓	✓
	Riduzione capacità lavorativa	✓	✓	✓
costi diretti	Cure mediche: visite, esami, farmaci		(✓)	✓
	Presidi, ausili, modifiche ambientali		(✓)	✓
	Assistenza infermieristica		(✓)	✓

Carta dei diritti del parkinsoniano

Costs in Parkinson disease

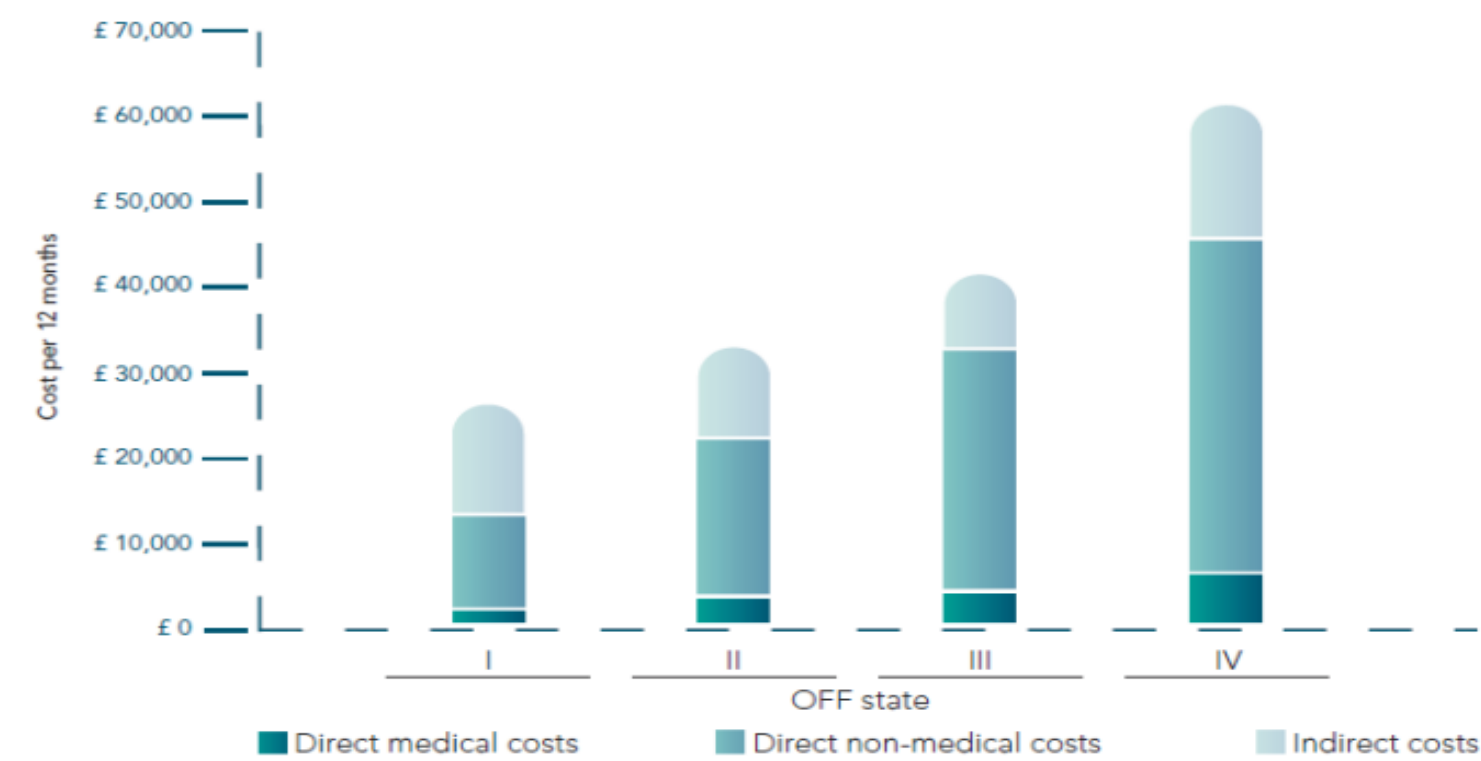
GRAFICO 3: COMPONENTI DEL COSTO TOTALE DELLA MP (HUSE ET AL, 2005) (26)



Carta dei diritti del parkinsoniano

Yearly costs depending on hours OFF

GRAFICO 4: DISTRIBUZIONE DEI COSTI ANNUALI MEDI IN FUNZIONE DEL TEMPO SPESO IN OFF

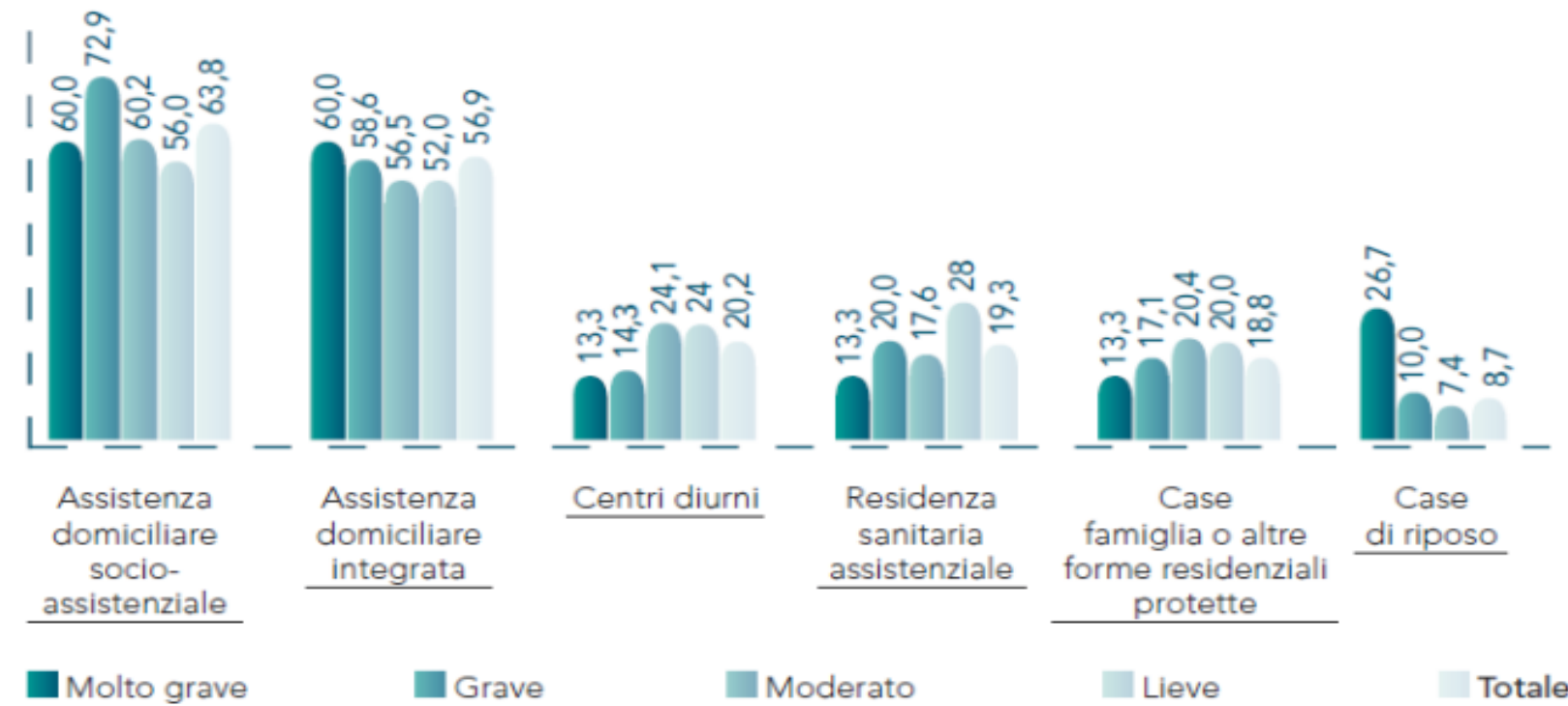


Legenda: (0-25% OFF I, 26-50% OFF II, 51-75% OFF III e 76-100% OFF IV)

Carta dei diritti del parkinsoniano

Most important health services as perceived by patients/caregivers

GRAFICO 9: I SERVIZI SOCIO-SANITARI RITENUTI PIÙ VALIDI (8)

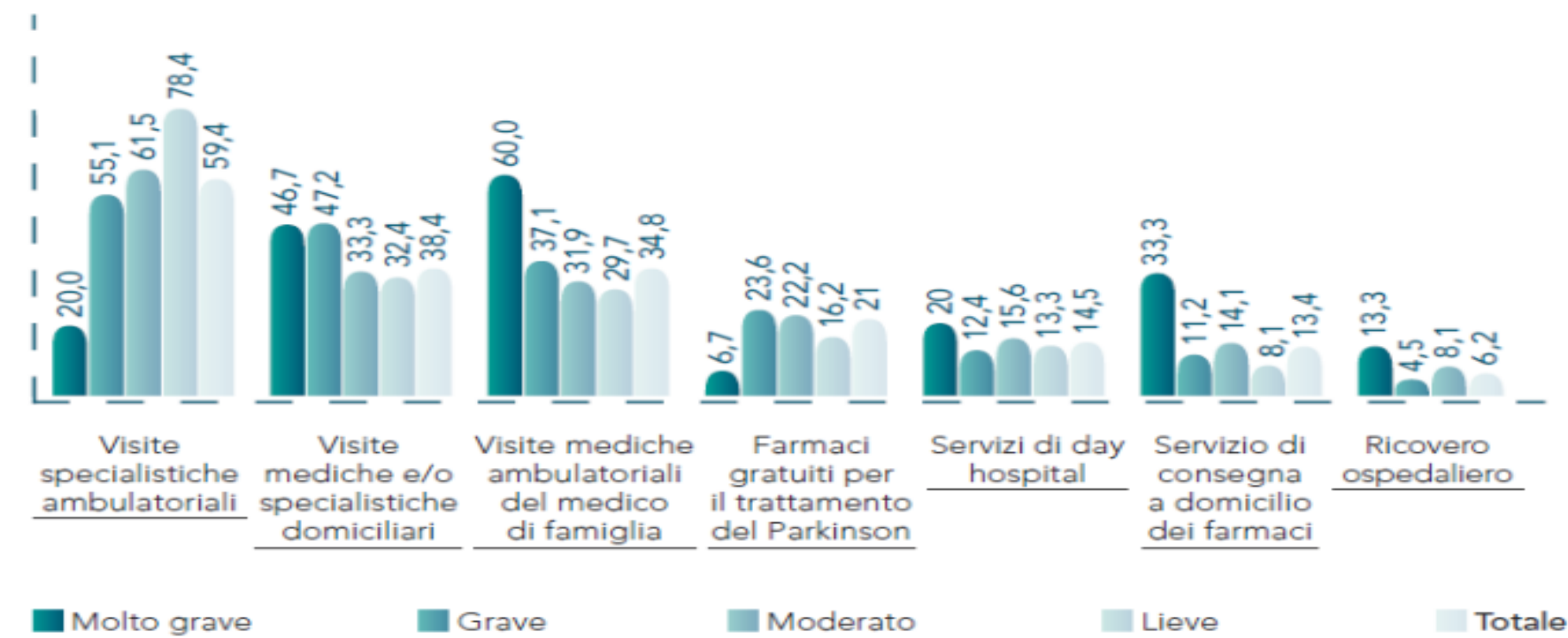


Il totale non è uguale a 100 perchè erano possibili più risposte

Carta dei diritti del parkinsoniano

Most important health services as perceived by patients/caregivers

GRAFICO 8: I SERVIZI SANITARI RITENUTI PIÙ VALIDI (8)



Carta dei diritti del parkinsoniano

RESEARCH ARTICLE

Health Care Utilization in the Last Year of Life in Parkinson Disease and Other Neurodegenerative Movement Disorders

Erica D. McKenzie, MD*, Veronica A. Bruno, MD, MPH*, Andrew Fong, Pin Cai, Madalene Earp, Richard M. Camicioli, MD, Ingrid de Kock, MD, Daniela Buttenschoen, MD, Aynharan Sinnarajah, MD, MPH†, and Janis Miyasaki, MD, MEd†

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- **Place of death:**
 - 45% hospital, long term care 36%, home 8%, residential hospice 4%
- **Emergency visit in 1 year**
 - >1:64%, >3: 14%
- **Hospitalization in 1 year**
 - >1:55%, > 30 days in hospital 33%
- **Very low access to outpatient care**

Cost and Early Complication Analysis Following Total Hip Arthroplasty in Parkinson's Disease Patients: A Propensity-matched Database Study

Abstract

Background: Parkinson's Disease is a well-known neuromuscular disorder, which affects the stability and gait of elderly patients. With the progressive increase in the life span of patients with PD, the problem of degenerative arthritis and the consequent need for total hip arthroplasty (THA) in this cohort are rising. There is paucity of data in the existing literature regarding the healthcare costs and overall outcome following THA in PD patients. The current study was planned to assess the hospital expenditure, details regarding hospital stay, and complication rates for patients with PD, who underwent THA.

Methods: We investigated the National Inpatient Sample data to identify PD patients, who underwent hip arthroplasty from 2016 to 2019. Using propensity score, PD patients were matched 1:1 to patients without PD by age, gender, non-elective admission, tobacco use, diabetes, and obesity. Chi-square and T-tests were used for analyzing categorical and non-categorical variables, respectively (Fischer-Exact test was employed for values <5).

Results: Overall, 367,890 (1927 patients with PD) THAs were performed between 2016 and 2019. Before matching, PD group had significantly greater proportion of older patients, males, and non-elective admissions for THA ($P < 0.001$). After matching, PD group had higher total hospital costs, longer hospital stay, greater blood loss anemia, and prosthetic dislocation ($P < 0.001$). The in-hospital mortality was similar between the two groups.

Conclusion: Patients with PD undergoing THA required greater proportion of emergent hospital admissions. Based on our study, the diagnosis of PD showed significant association with greater cost of care, longer hospital stay, and higher post-operative complications.

Level of evidence: II

Keywords: Parkinson's disease, Total hip arthroplasty

Arch Bone Jt Surg. 2023; 11(1): 47-52.

RESEARCH ARTICLE

Journal of Geriatric Psychiatry WILEY

Incremental health care resource utilization and costs associated among patients with Parkinson's disease psychosis and incident dementia: An analysis of medicare beneficiaries

Krithika Rajagopalan¹ | Nazia Rashid² | Daksha Gopal¹ | Dilesh Doshi²



Int J Geriatr Psychiatry. 2023:e6017.

Caregiver burden by Parkinson's disease severity

Measure	Early PD	Intermediate PD	Advanced PD
Caregiver perceived score	24,7 ± 17.1	29.5 ± 17.0	34.5 ± 17.6
Medication intake due to caregiving	14%	25%	35%
Caregiver treatment satisfaction	5.3 ± 1.3	4.9 ± 1.1	4.4 ± 1.4

Journal of Neurology (2023) 270:2162–2173

Cost-Effectiveness of Carbidopa-Levodopa Enteral Suspension for Advanced Parkinson's Disease in the United States

Movement Disorders, 2023

Rajesh Pahwa,^{1*} Aristide Merola,² Michael Soileau,³ Ali Alobaidi,⁴ A. Simon Pickard,⁵ Prasanna L. Kandukuri,⁴ Yanjun Bao,⁴ John Strezewski,⁴ Julia Oddsdottir,⁶ Weiwei Xu,⁷ and David Standaert⁸

TABLE 1 Base case results per patient and cost breakdown

Parameters	CLES	SoC	Incremental
Costs (\$)	1,031,791.62	1,025,180.24	6611.39
QALYs	4.61	3.76	0.86
LYs	11.82	10.57	1.25
ICER (incremental cost per QALY)	–	–	7711.34
ICER (incremental costs per LY)	–	–	5286.47
Cost breakdown			
Treatment-related costs (\$)	449,695.99	172,109.30	277,586.69
Hospitalizations (\$)	99,401.32	164,815.85	–65414.53
ER visits (\$)	262,354.35	407,705.43	–145,351.09
Consultations (\$)	9523.48	11,508.31	–1984.82
Scan tests (\$)	1878.32	1056.55	821.78
Professional caregiver (\$)	159,341.88	208,559.72	–49,217.84
Respite care (\$)	49,596.27	59,425.07	–9828.80
Total costs (\$)	1,031,791.62	1,025,180.24	6611.39

Abbreviations: CLES, carbidopa/levodopa enteral suspension; SoC, standard-of-care; QALY, quality-adjusted life year; LY, life year; ICER, incremental cost-effectiveness ratio; ER, emergency room.

*Movement
Disorders*

CLINICAL PRACTICE

REVIEW

Cost-Effectiveness of Deep Brain Stimulation With Movement Disorders: A Systematic Review

Tho Thi Hai Dang, MHEcon,^{1*} David Rowell, PhD, MHEcon (Adv),² and Luke B. Connelly, PhD, MEcon^{1,2,3}

The infrequent use of randomized, controlled trials to evaluate DBS efficacy, the paucity of data reporting the long-term effectiveness and/or utility of DBS, and the uncertainty surrounding cost data limit our ability to report cost-effectiveness summaries that are robust.

Conclusions

- Act on risk/protective factors
- Develop a better model of integrated care
 - Access to rehabilitation, logotherapy, occupational therapy, facilitate the provision of drugs for standard care, offer new devices for advanced disease treatment

Conclusions

- New therapies may be dedicated to specific subtypes of disease – precision medicine
 - Example, Genetic forms
- The real cost of PD are in long term care
- Innovative drugs possibly acting to stop disease progression will decrease indirect costs, caregiver burden, will increase quality of life

Costs of advanced therapies in PD

- Considerable variation in the cost of STN (€11,807–€41,276; £9371–£32,759; \$17,363–\$60,700). One study with a BMT control arm reported the cost-utility of DBS at €34,389 per quality-adjusted life year (£27,293; \$50,572)
- Mean discounted lifetime costs were €126,200 for BMT and €133,200 for DBS. Lifetime ICUR for DBS was €6700 per QALY, and €9800 and €2500 per UPDRS-II and III scores point gained
- DBS + BMT offers value for money to UK payers for the treatment of PD, with an ICER of £20,678/QAL
- with CSAI were £78,251.49 in UK and €104,500.08 in Germany. Costs associated with LCIG are £130,011.34 in UK, and €175,004.43 in Germany). Costs for DBS are £87,730.22 in UK, and €105,737.08 in Germany. BMT-associated costs are £76,793.49 in UK, and €90,011.91 in Germany Y gained compared to BMT alone over a 5-year period

- Provider costs were similar for GPi- and STN-DBS (GPi: \$138,044 vs. STN: \$131,822). Societal costs were also similar (GPi: \$171,061 vs. STN: \$167,706).
- A 1-point improvement in the UPDRS-III score was associated with an ICER of \$926 in the first year and \$421 in the second year.
- Year 1 costs for surgery were higher than in standard of care, at £19,069 vs. £9813. A difference of £9256 (95% CI: £7,625, £10,887).
- DBS costs 10.3 million Japanese yen (US \$85,100). The ICER was 3.1 million yen (\$25,600). The ICER was 8.5 million yen (\$70,200) for early DBS, 3.1 million yen (\$25,600) for intermediate DBS, and 3.3 million yen (\$27,200) for late-stage DBS.

- In general, LCIG and DBS are more effective compared to BMT alone, but with a significantly higher cost for the healthcare system. On average, CSAI is more cost-effective than LCIG, and LCIG is in turn more cost-effective than DBS. Hence, the absolute costs of DBS appear greater than those of BMT, CSAI, and LCIG.
- we found that pharmaceutical companies involved in device-aided therapies funded most studies referring device-aided treatments likely due to cost of devices, implantation and management, thus increasing the risk of an excess of favorable outcomes reported.

Delitti in materia di violazione del diritto d'autore (Art. 25-novies, D.Lgs. n. 231/2001) [articolo aggiunto dalla L. n. 99/2009]

- Messa a disposizione del pubblico, in un sistema di reti telematiche, mediante connessioni di qualsiasi genere, di un'opera dell'ingegno protetta, o di parte di essa (art. 171, legge n.633/1941 comma 1 lett. a) bis)
- Reati di cui al punto precedente commessi su opere altrui non destinate alla pubblicazione qualora ne risulti offeso l'onore o la reputazione (art. 171, legge n.633/1941 comma 3)
- Abusiva duplicazione, per trarne profitto, di programmi per elaboratore; importazione, distribuzione, vendita o detenzione a scopo commerciale o imprenditoriale o concessione in locazione di programmi contenuti in supporti non contrassegnati dalla SIAE; predisposizione di mezzi per rimuovere o eludere i dispositivi di protezione di programmi per elaboratori (art. 171-bis legge n.633/1941 comma 1)
- Riproduzione, trasferimento su altro supporto, distribuzione, comunicazione, presentazione o dimostrazione in pubblico, del contenuto di una banca dati; estrazione o reimpiego della banca dati; distribuzione, vendita o concessione in locazione di banche di dati (art. 171-bis legge n.633/1941 comma 2)
- Abusiva duplicazione, riproduzione, trasmissione o diffusione in pubblico con qualsiasi procedimento, in tutto o in parte, di opere dell'ingegno destinate al circuito televisivo, cinematografico, della vendita o del noleggio di dischi, nastri o supporti analoghi o ogni altro supporto contenente fonogrammi o videogrammi di opere musicali, cinematografiche o audiovisive assimilate o sequenze di immagini in movimento; opere letterarie, drammatiche, scientifiche o didattiche, musicali o drammatico musicali, multimediali, anche se inserite in opere collettive o composite o banche dati; riproduzione, duplicazione, trasmissione o diffusione abusiva, vendita o commercio, cessione a qualsiasi titolo o importazione abusiva di oltre cinquanta copie o esemplari di opere tutelate dal diritto d'autore e da diritti connessi; immissione in un sistema di reti telematiche, mediante connessioni di qualsiasi genere, di un'opera dell'ingegno protetta dal diritto d'autore, o parte di essa (art. 171-ter legge n.633/1941)
- Mancata comunicazione alla SIAE dei dati di identificazione dei supporti non soggetti al contrassegno o falsa dichiarazione (art. 171-septies legge n.633/1941)
- Fraudolenta produzione, vendita, importazione, promozione, installazione, modifica, utilizzo per uso pubblico e privato di apparati o parti di apparati atti alla decodificazione di trasmissioni audiovisive ad accesso condizionato effettuate via etere, via satellite, via cavo, in forma sia analogica sia digitale (art. 171-octies legge n.633/1941).

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