

Ontwikkelingen Ziekte van Parkinson

Bart Post
Neuroloog

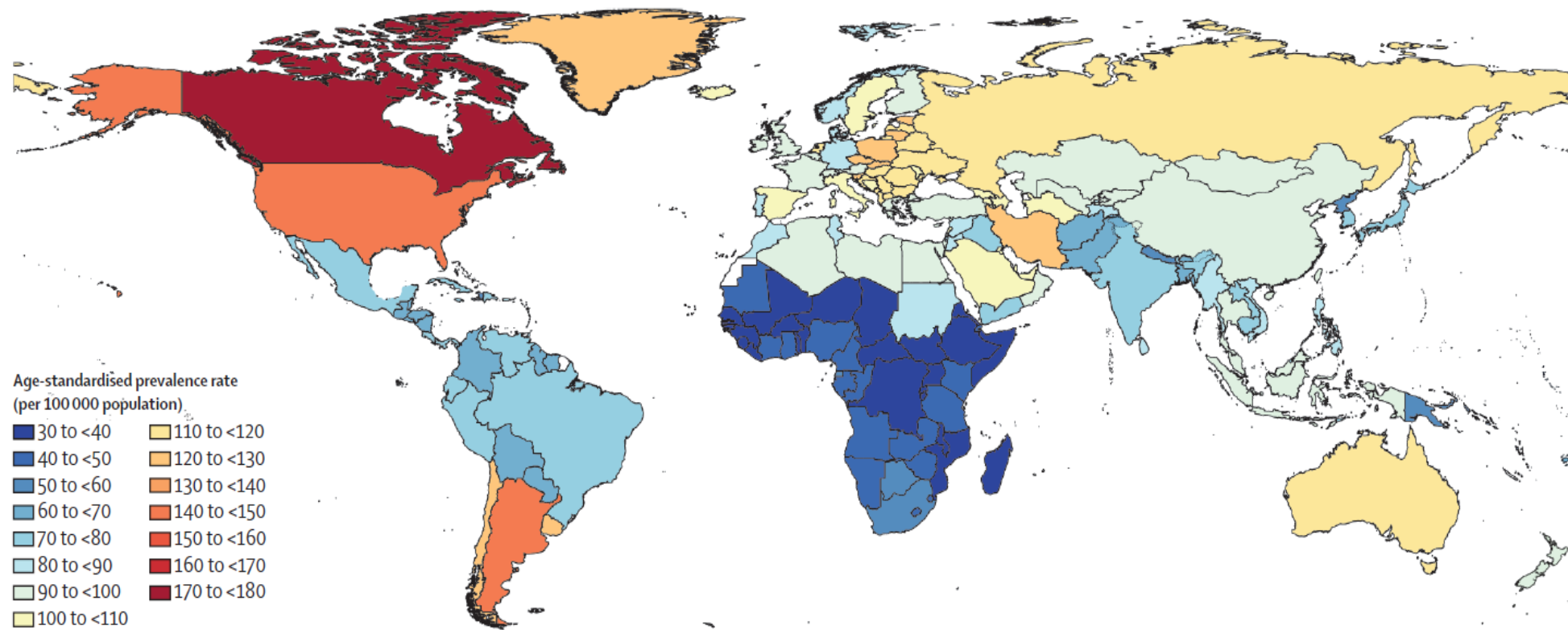
Today's Random Medical News

from the New England
Journal of
Panic-Inducing
Gobbledygook

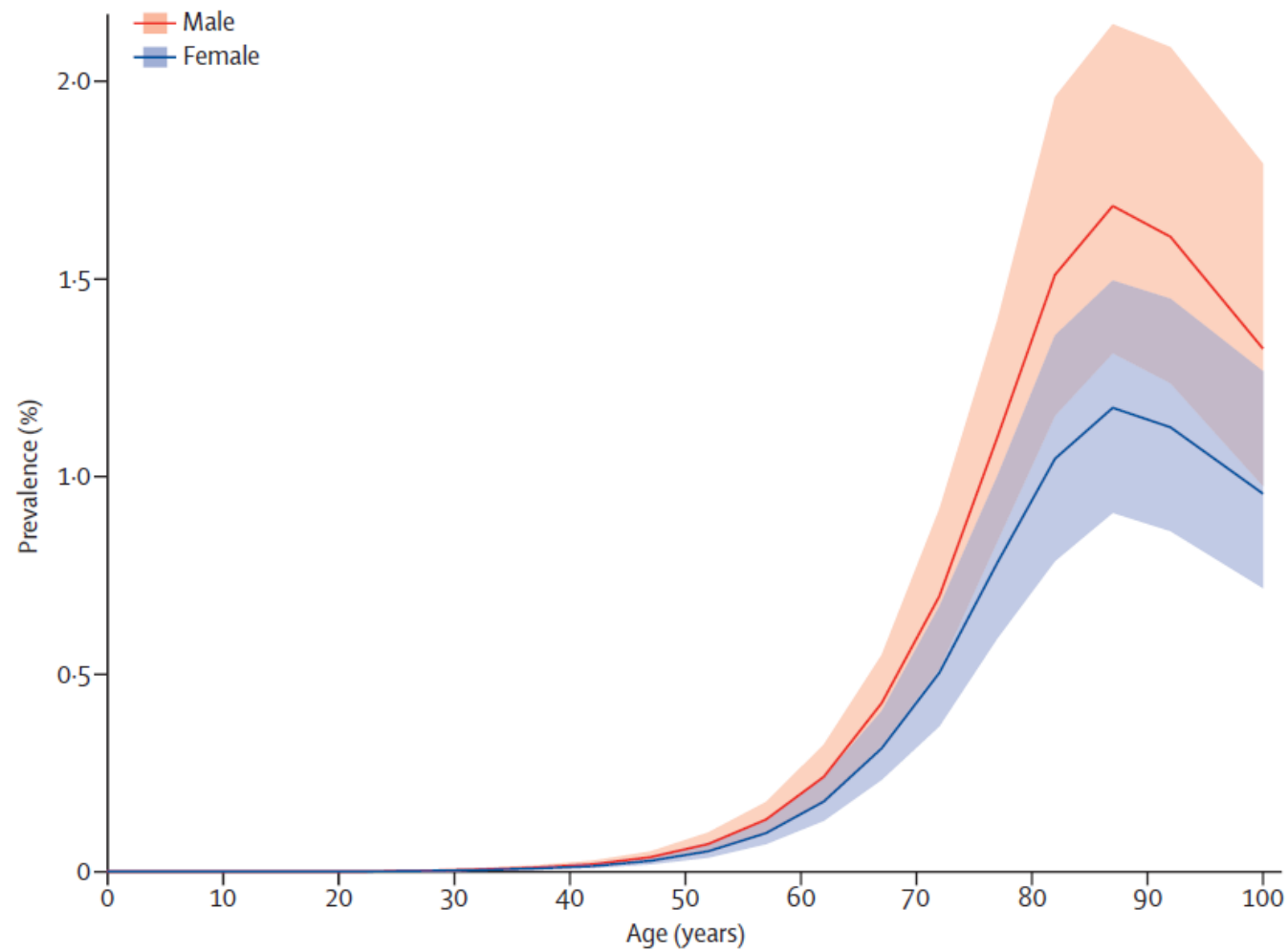
JIM BORGMAN



Global, regional, and national burden of Parkinson's disease, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016



Dorsey, Lancet, 2018



Dorsey, Lancet, 2018

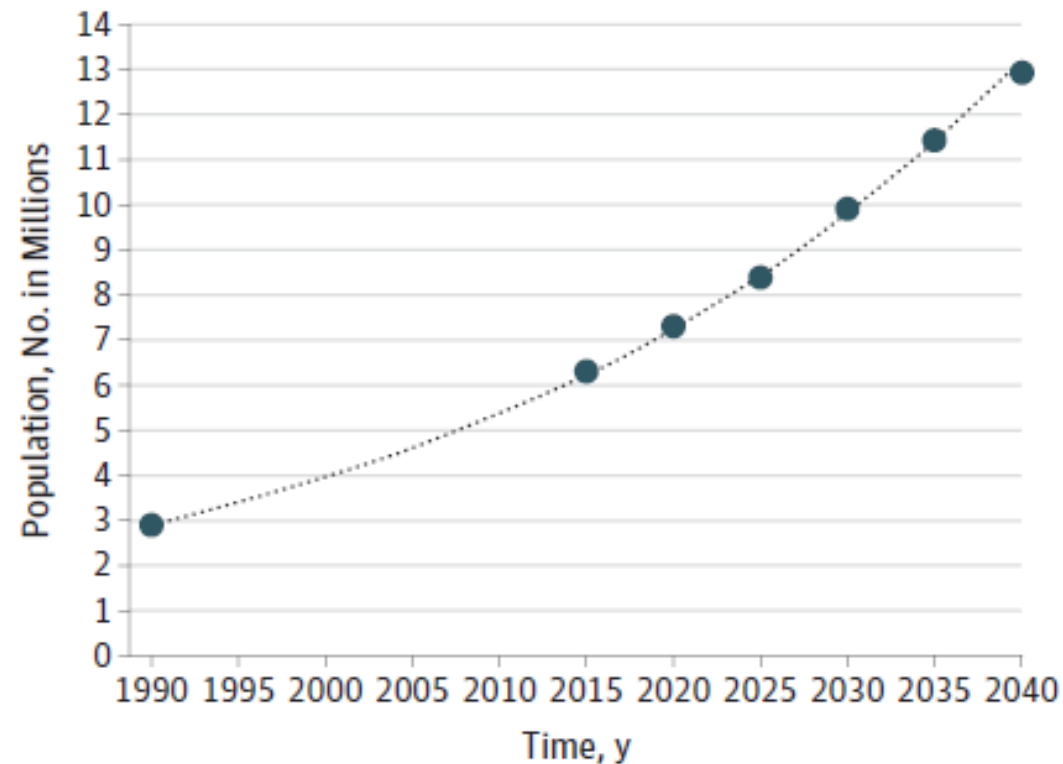
The Parkinson Pandemic—A Call to Action

VIEWPOINT

E. Ray Dorsey, MD
Center for Health and
Technology,
Department of
Neurology, University
of Rochester Medical
Center, Rochester,
New York.

**Bastiaan R. Bloem,
MD, PhD**
Radboud University
Medical Center,
Donders Institute for
Brain, Cognition and
Behavior, Department
of Neurology,
Nijmegen,
the Netherlands.

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



Dorsey, JAMA neurology, 2018



OPEN ACCESS



Check for updates

Projections for prevalence of Parkinson's disease and its driving factors in 195 countries and territories to 2050: modelling study of Global Burden of Disease Study 2021

Dongning Su,^{1,2} Yusha Cui,^{1,2} Chengzhang He,^{3,4} Peng Yin,⁵ Ruhai Bai,⁶ Jinqiao Zhu,^{1,2} Joyce S T Lam,⁷ Junjiao Zhang,^{1,2} Rui Yan,^{1,2} Xiaoqing Zheng,^{1,2} Jiayi Wu,^{1,2} Dong Zhao,⁸ Anxin Wang,^{9,10} Maigeng Zhou,⁵ Tao Feng^{1,2}

Su, BMJ, 2025

Radboudumc

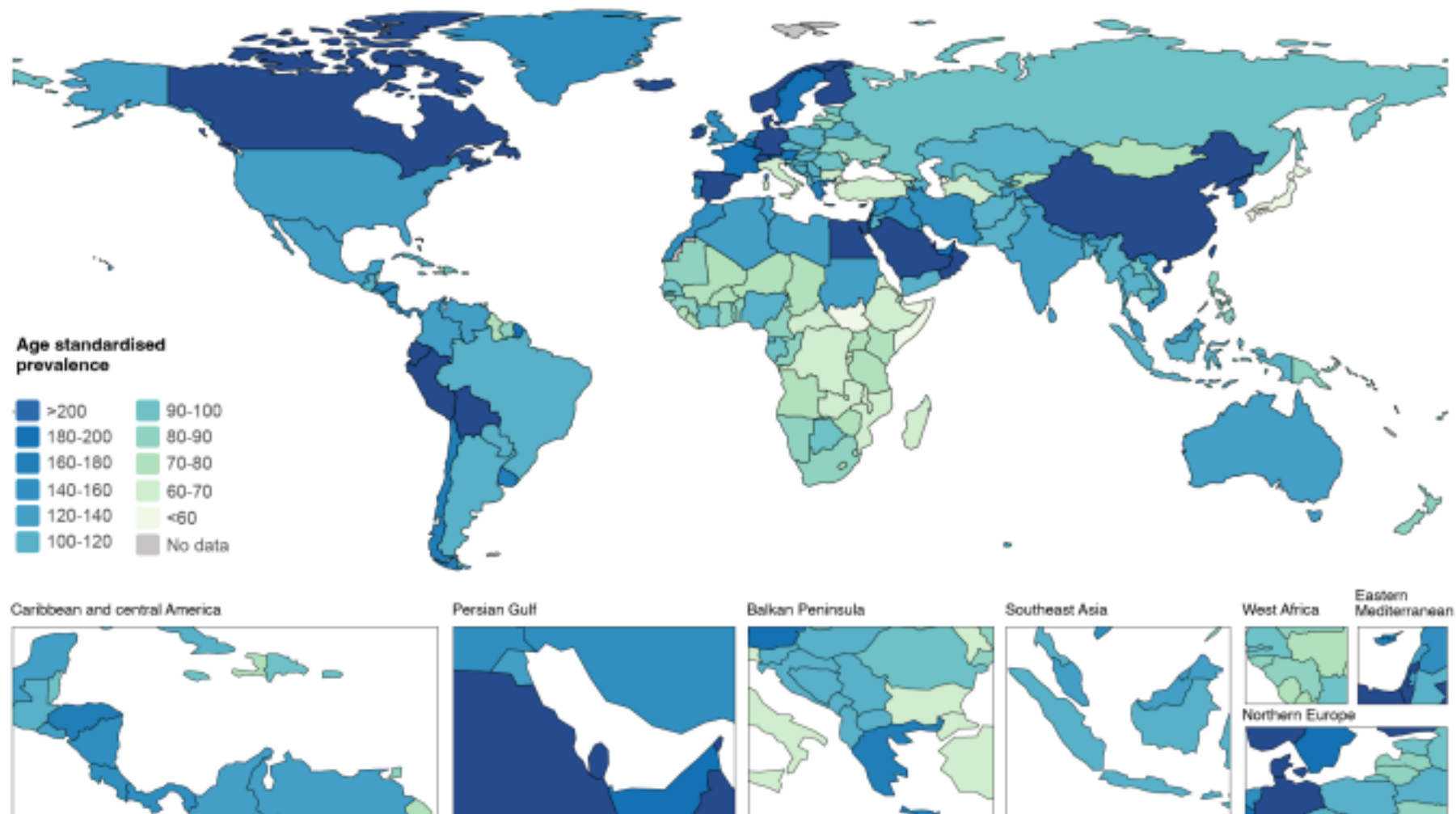
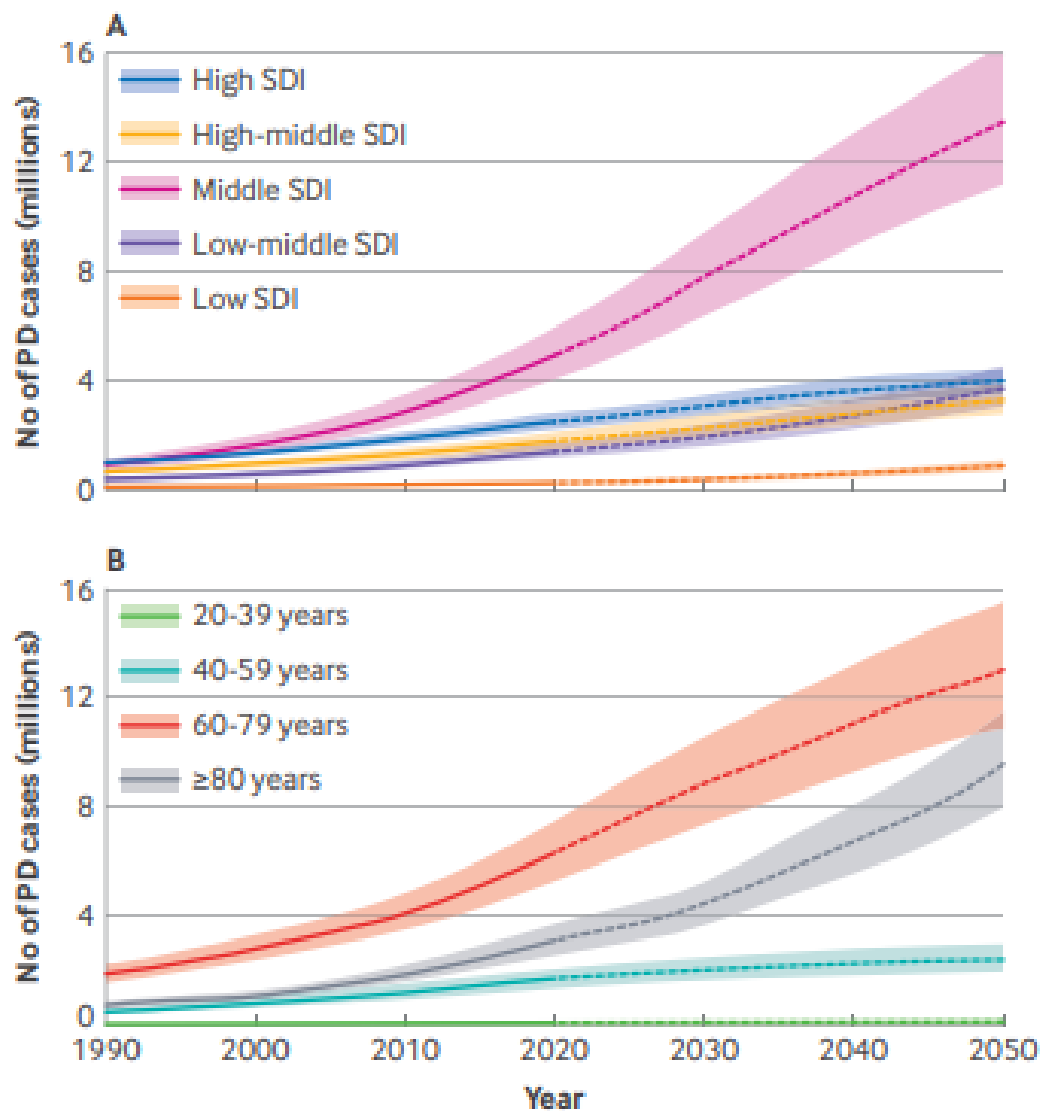
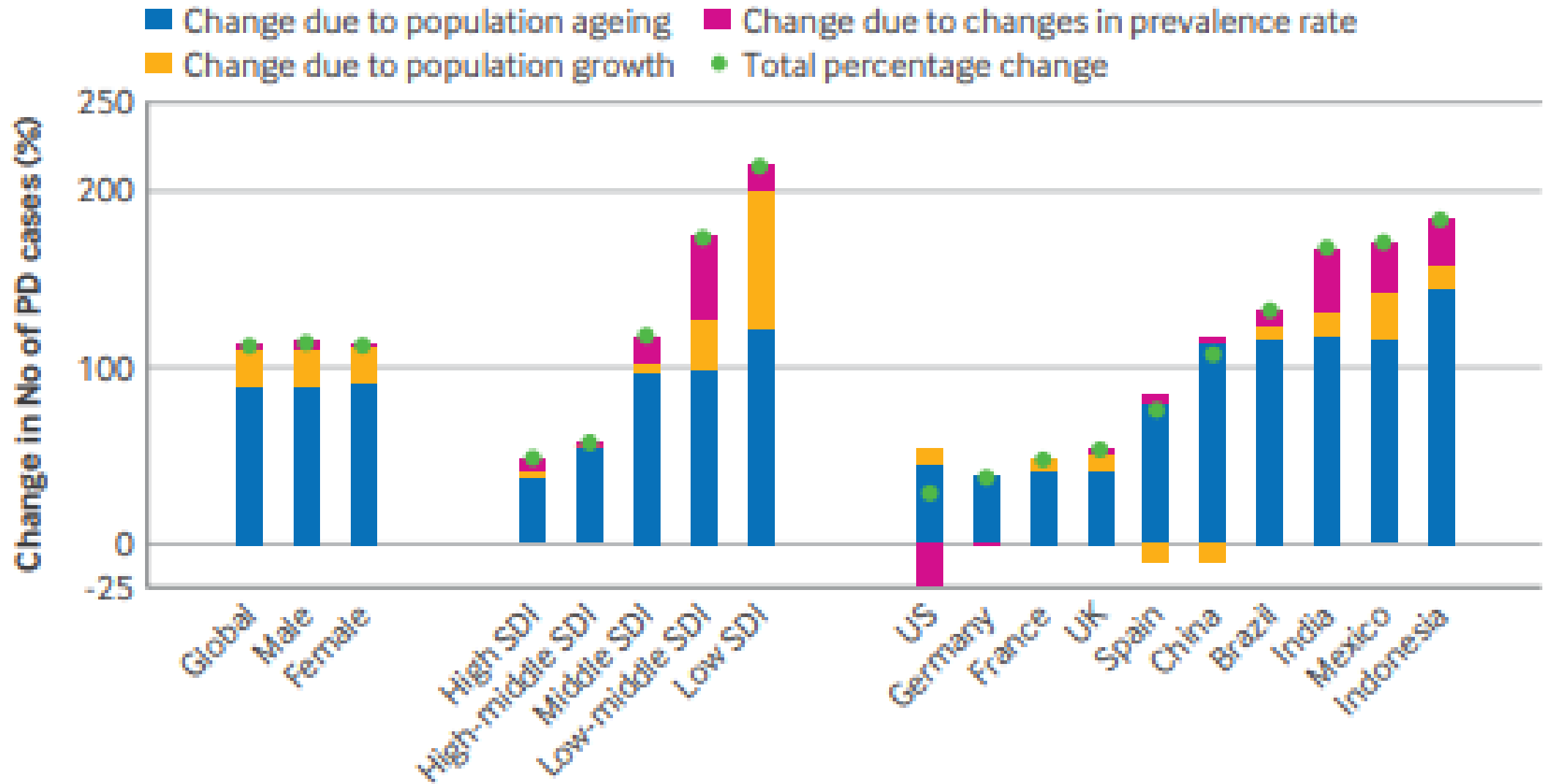
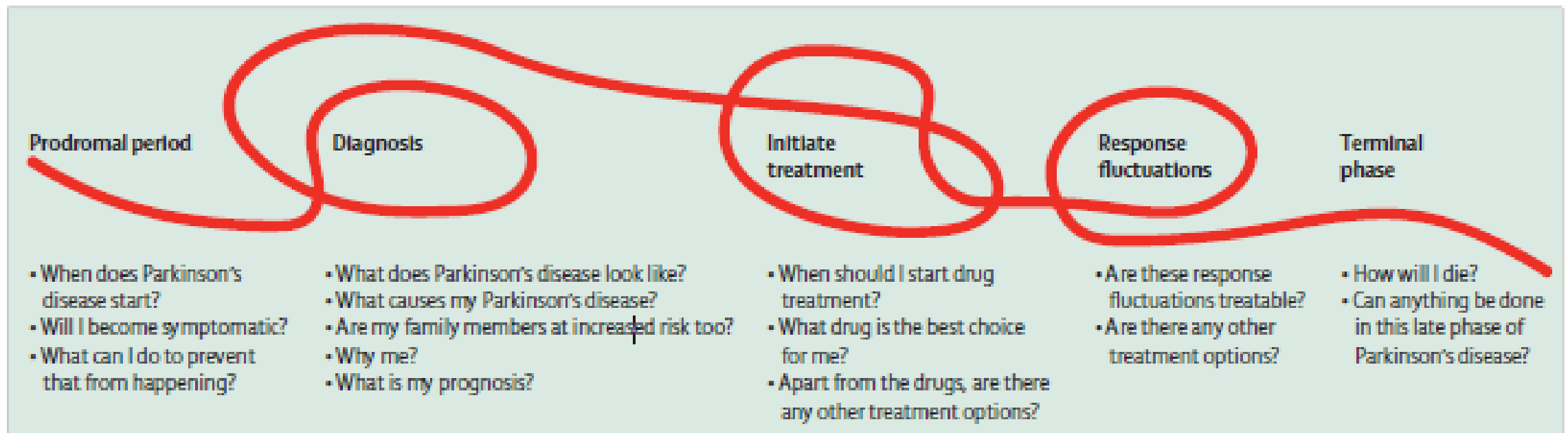


Fig 5 | Projected age standardised prevalence (per 100 000) of Parkinson's disease in 2050, by country and territory for both sexes combined

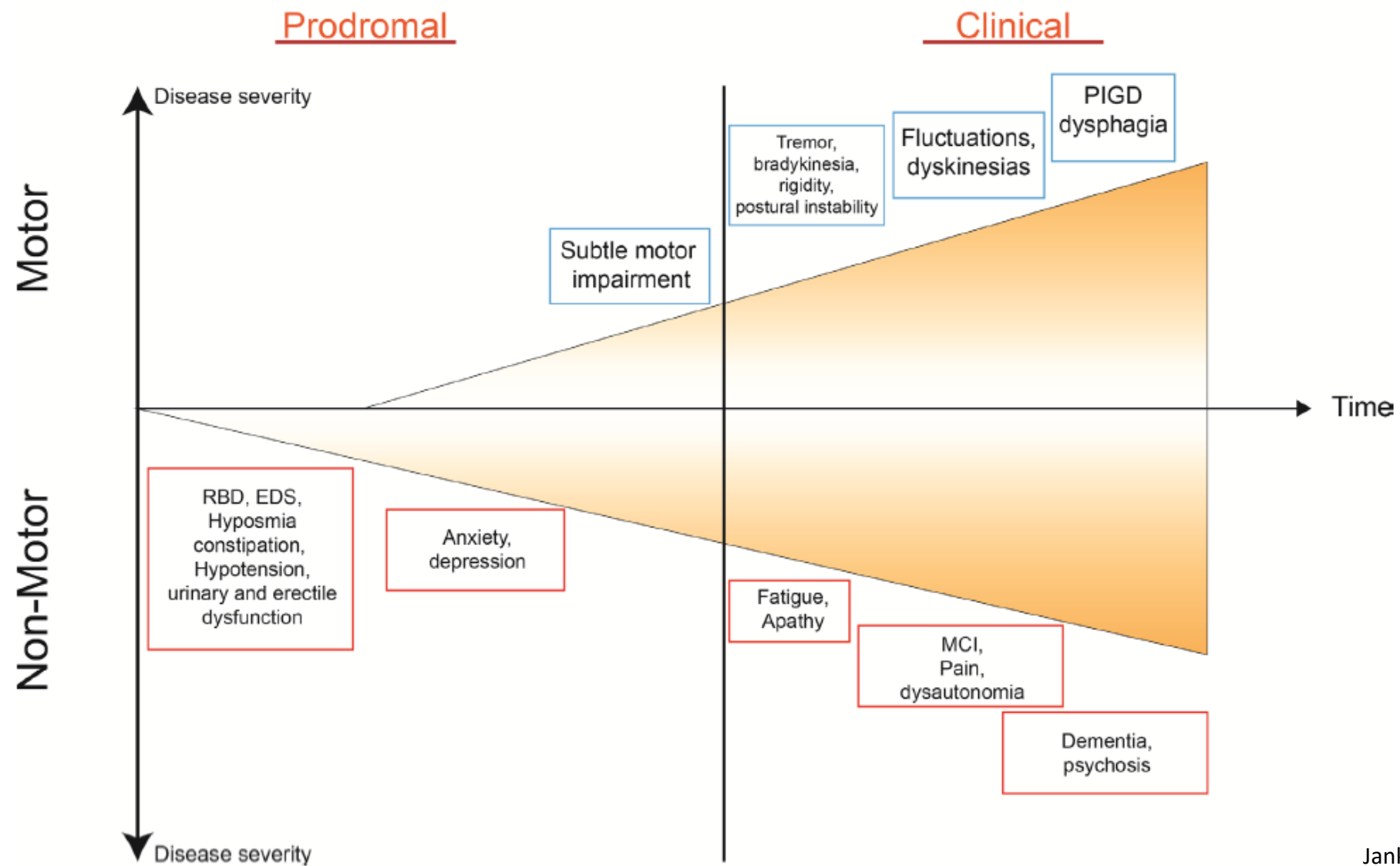


		1990	2021	2030	2040	2050		
No 1	China	662 000	5 091 000	6 702 000	8 854 000	10 516 000	China	No 1
No 2	USA	295 000	1 033 000	1 376 000	1 961 000	2 765 000	India	No 2
No 3	India	252 000	690 000	716 000	852 000	893 000	USA	No 3
No 4	Russian Federation	153 000	414 000	446 000	526 000	574 000	Germany	No 4
No 5	Italy	151 000	241 000	302 000	413 000	524 000	Brazil	No 5
No 6	Germany	124 000	226 000	284 000	341 000	465 000	Indonesia	No 6
No 7	UK	124 000	224 000	252 000	335 000	356 000	France	No 7
No 8	Japan	111 000	202 000	230 000	294 000	351 000	Spain	No 8
No 9	France	97 000	200 000	230 000	286 000	338 000	Mexico	No 9
No 10	Spain	82 000	199 000	228 000	272 000	307 000	UK	No 10
No 12	Brazil	56 000	190 000	212 000	248 000	304 000	Russian Federation	No 11
No 13	Indonesia	50 000	164 000	179 000	216 000	219 000	Japan	No 21
No 20	Mexico	27 000	125 000	172 000	177 000	170 000	Italy	No 23
Global		3 144 000	11 894 000	15 213 000	20 192 000	25 224 000		



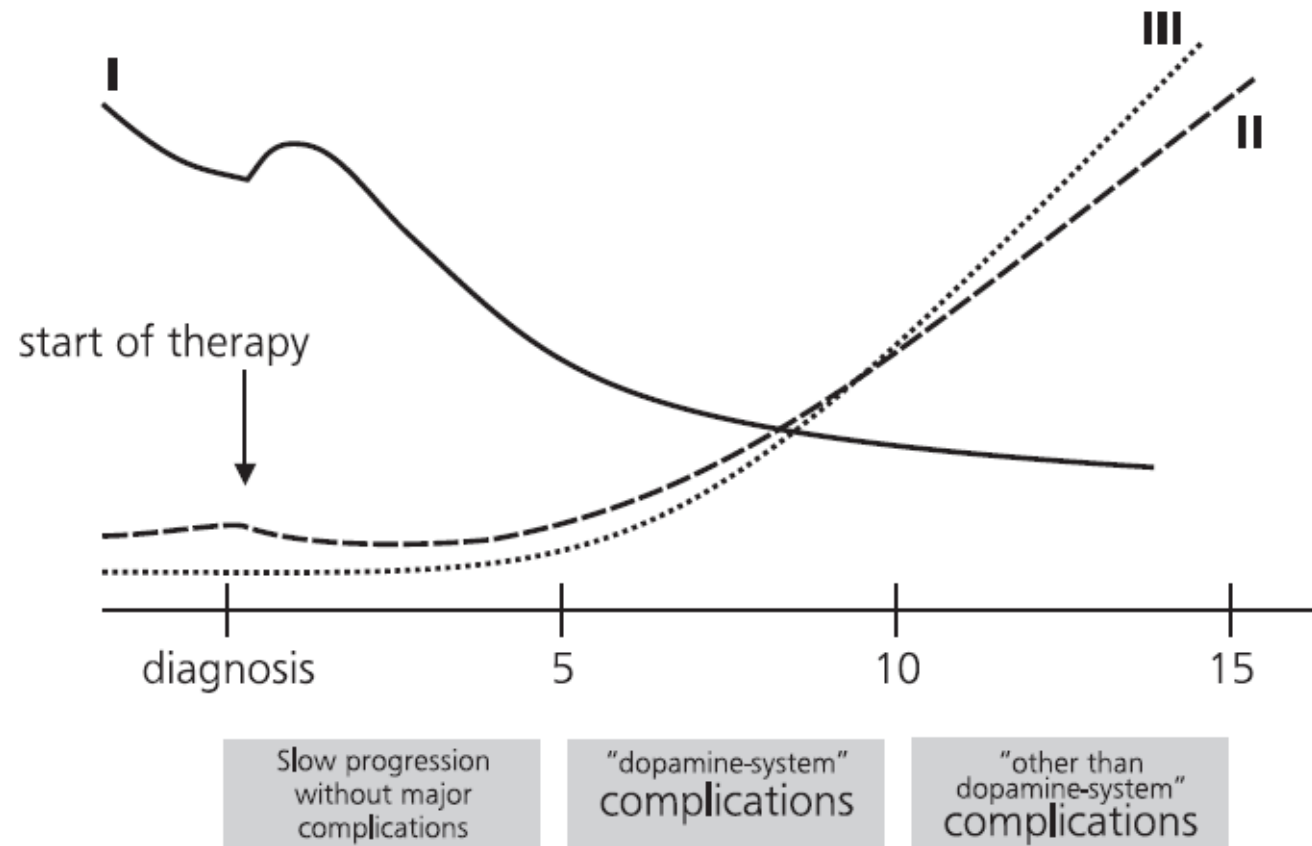


Bloem. Lancet, 2021

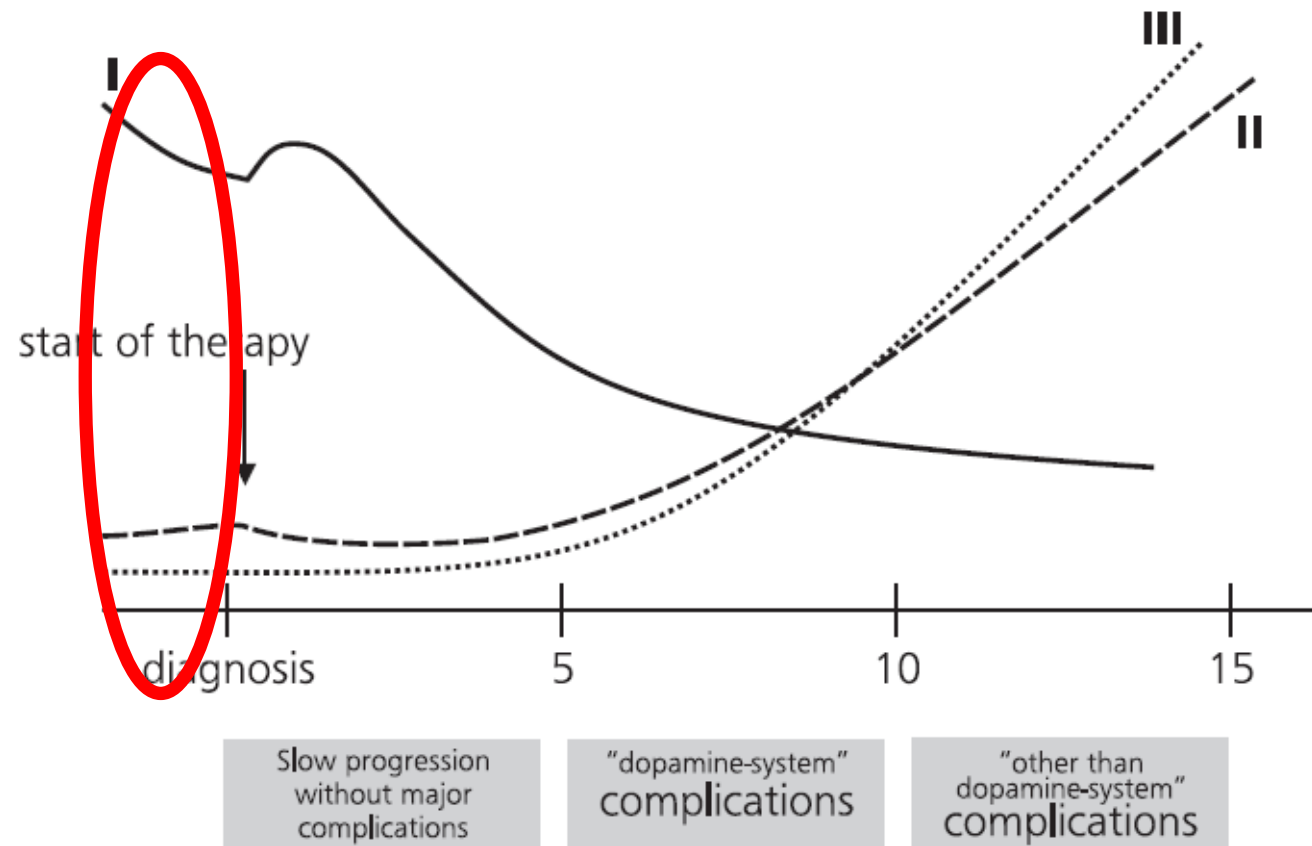


Jankovic. JNNP, 2020

Basis model ZvP



Basis model ZvP

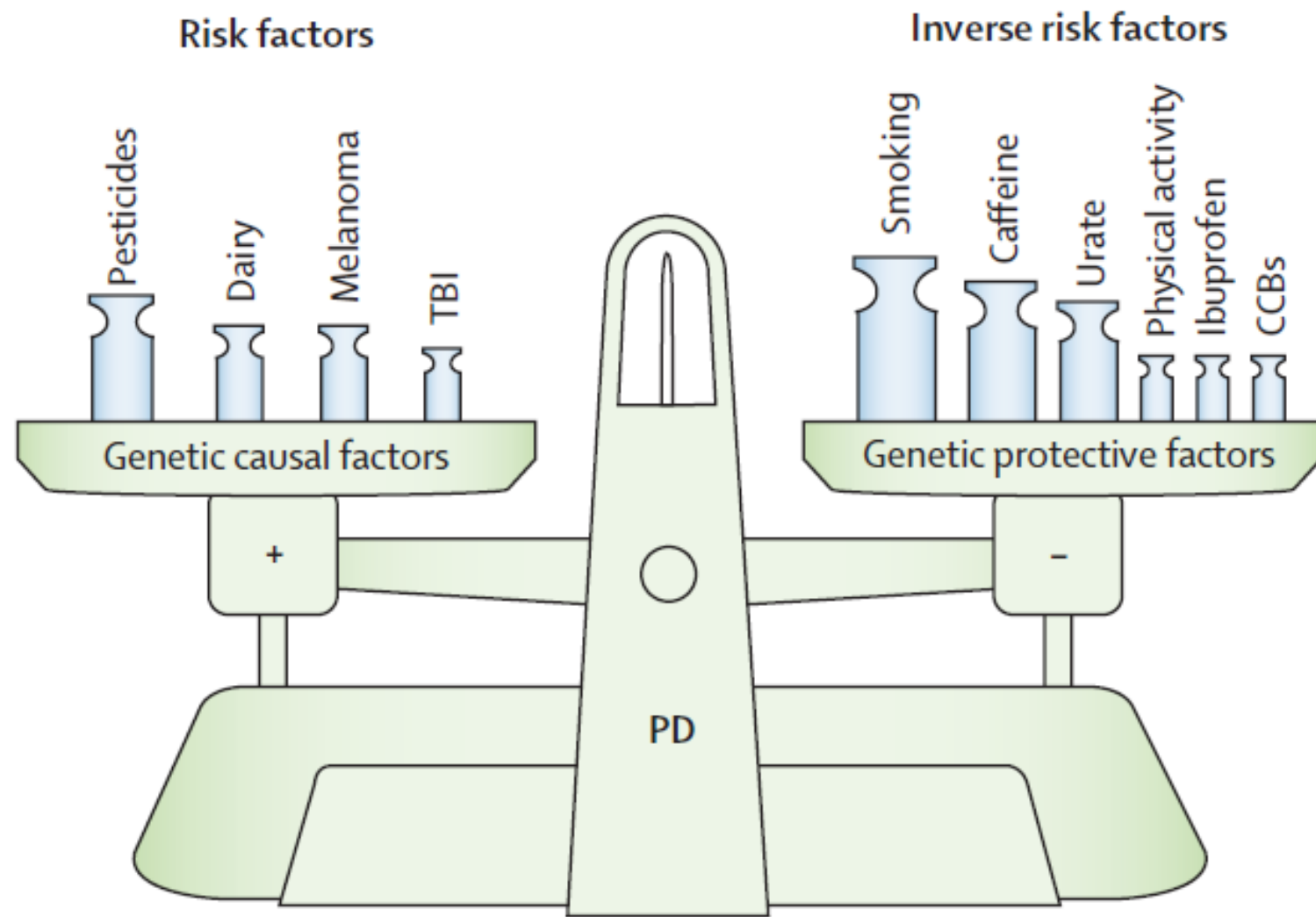


Belangrijke vragen voor deze fase

- Wat is de oorzaak van de ZvP?
- Hoe kunnen we de ZvP remmen?

Belangrijke vragen voor deze fase

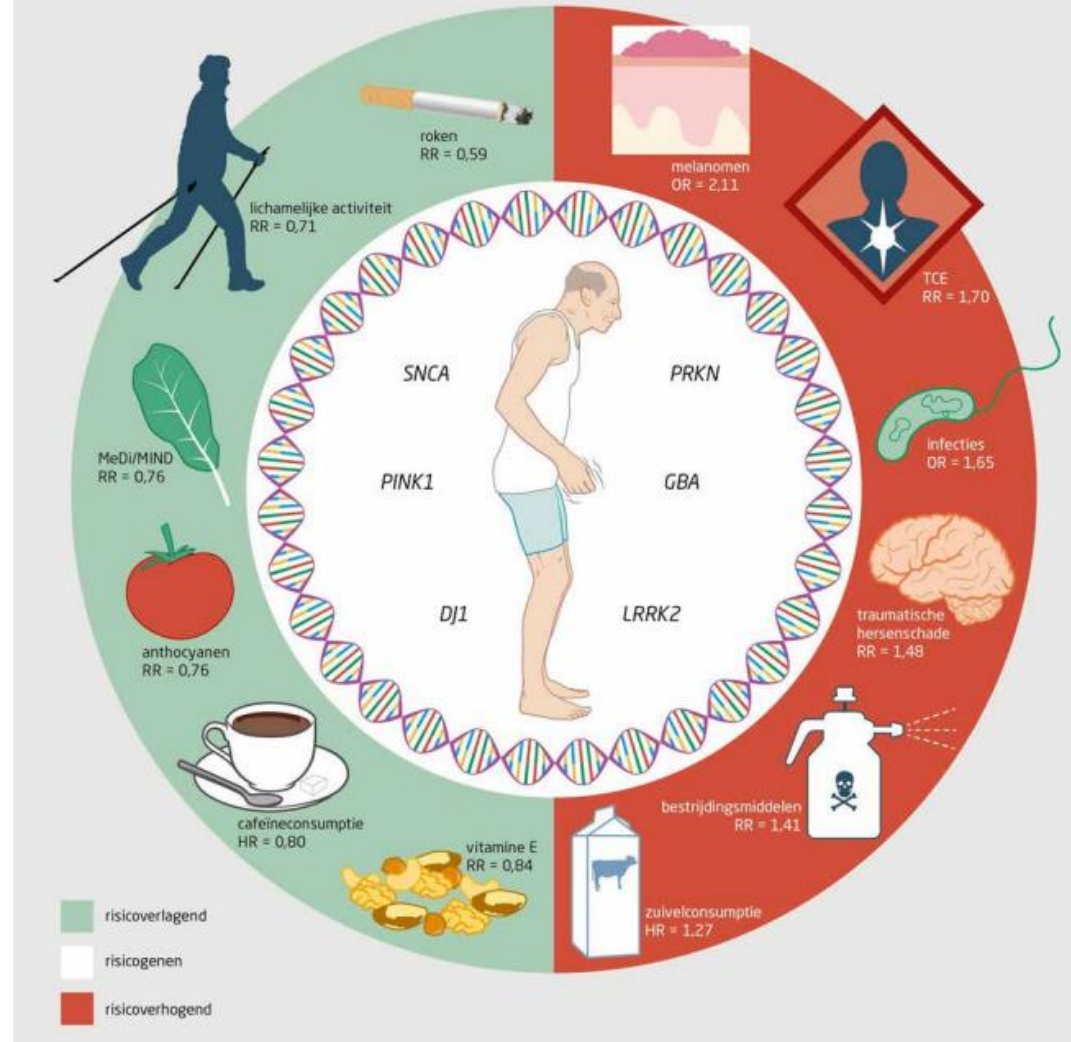
- Wat is de oorzaak van de ZvP?
- Hoe kunnen we de ziekte remmen?



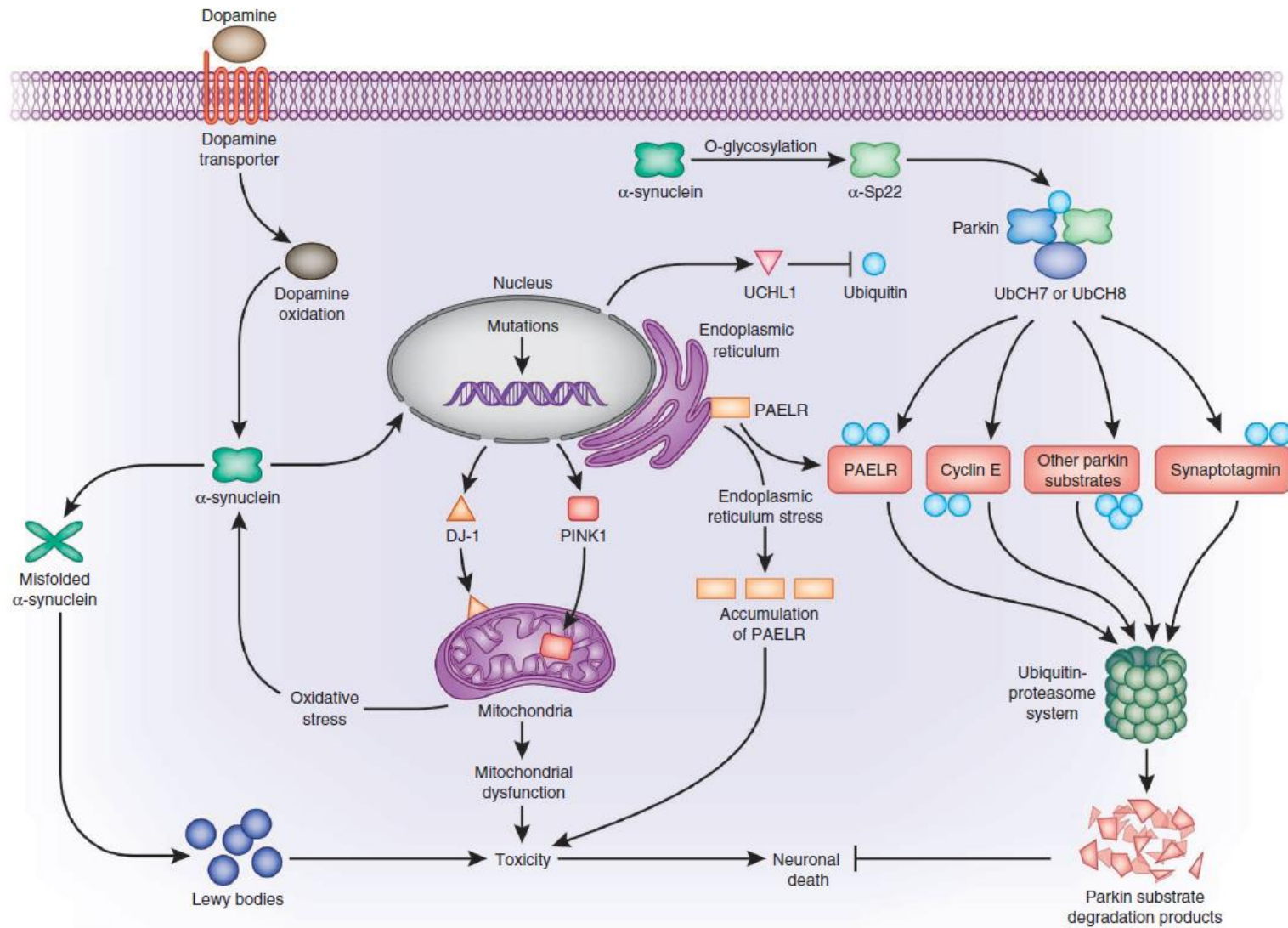
Ascherio, Lancet Neurology, 2016

FIGUUR 2

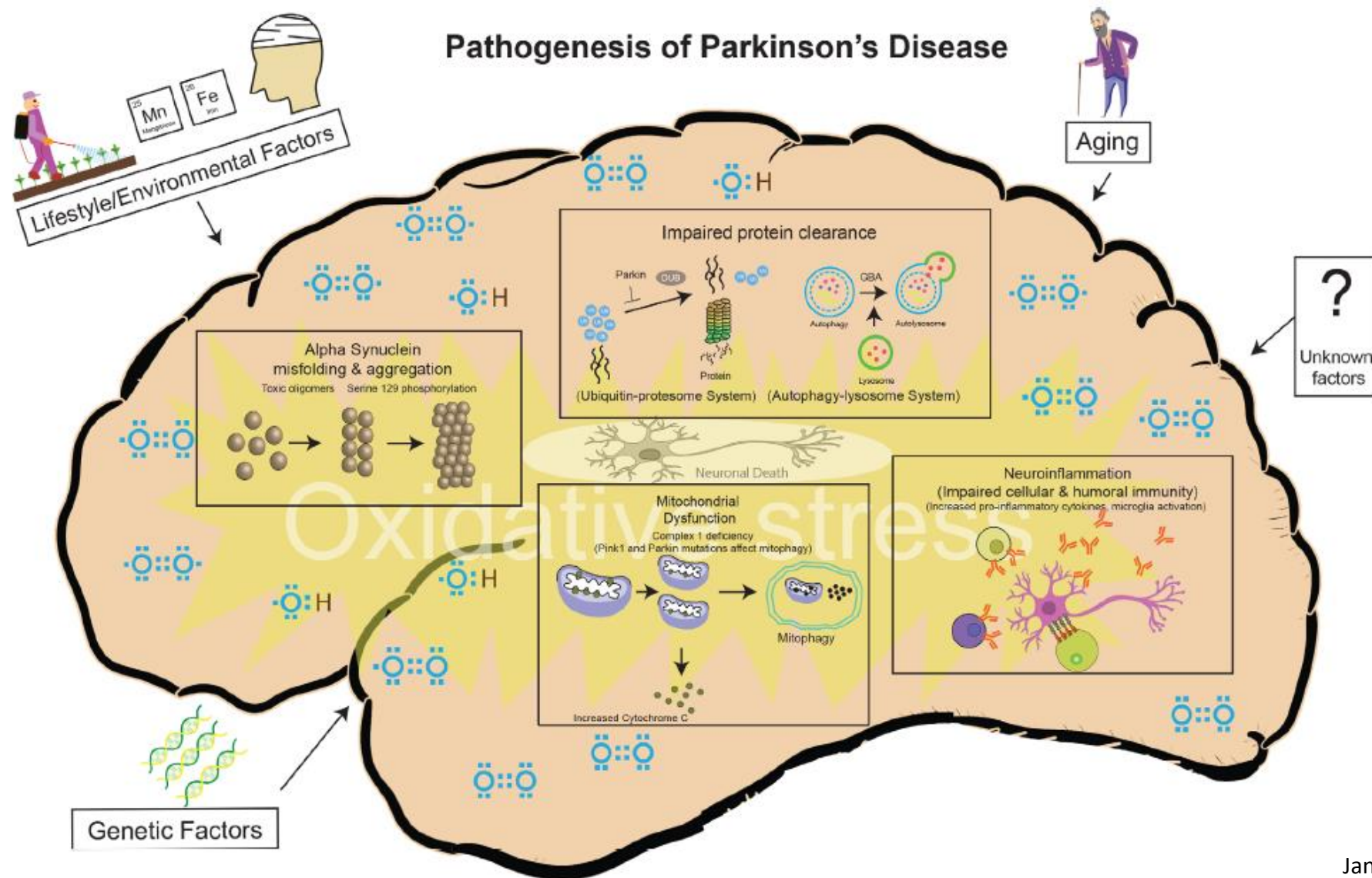
Risicofactoren en beschermende factoren



Gaag, NTVG, 2023



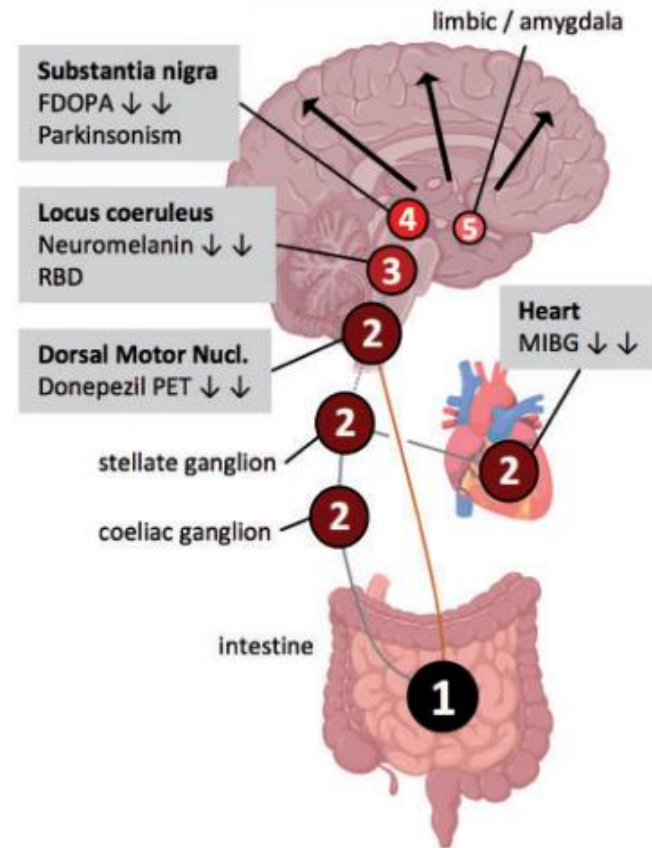
Obeso, Nature Medicine, 2010



Jankovic. JNNP, 2020

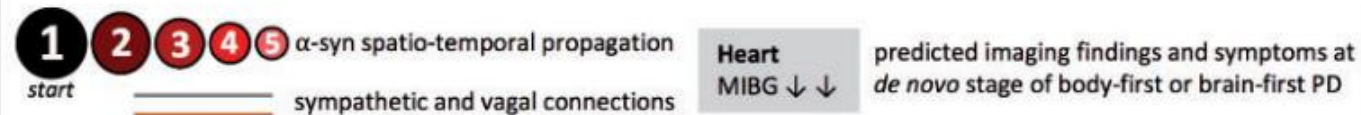
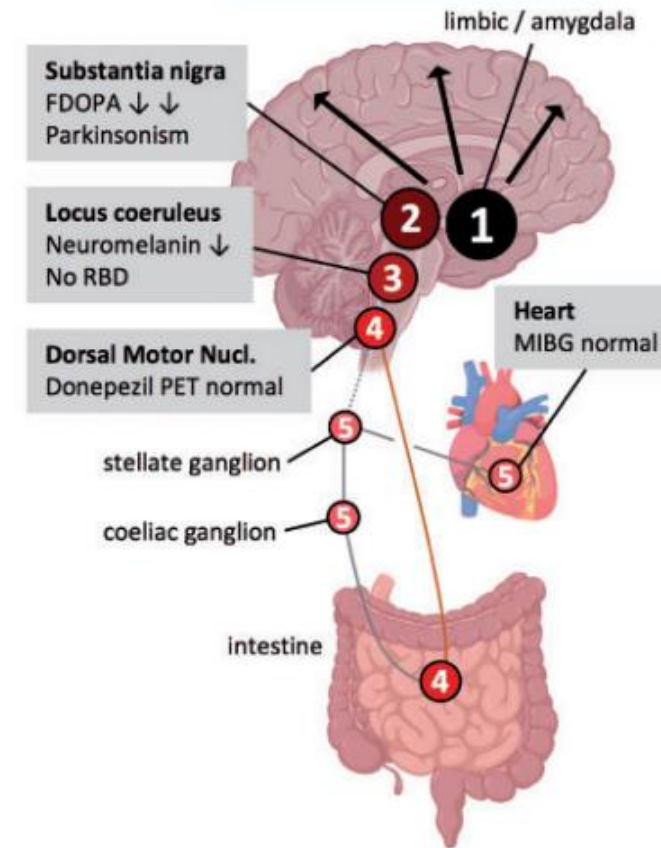
A

BODY-FIRST PD



B

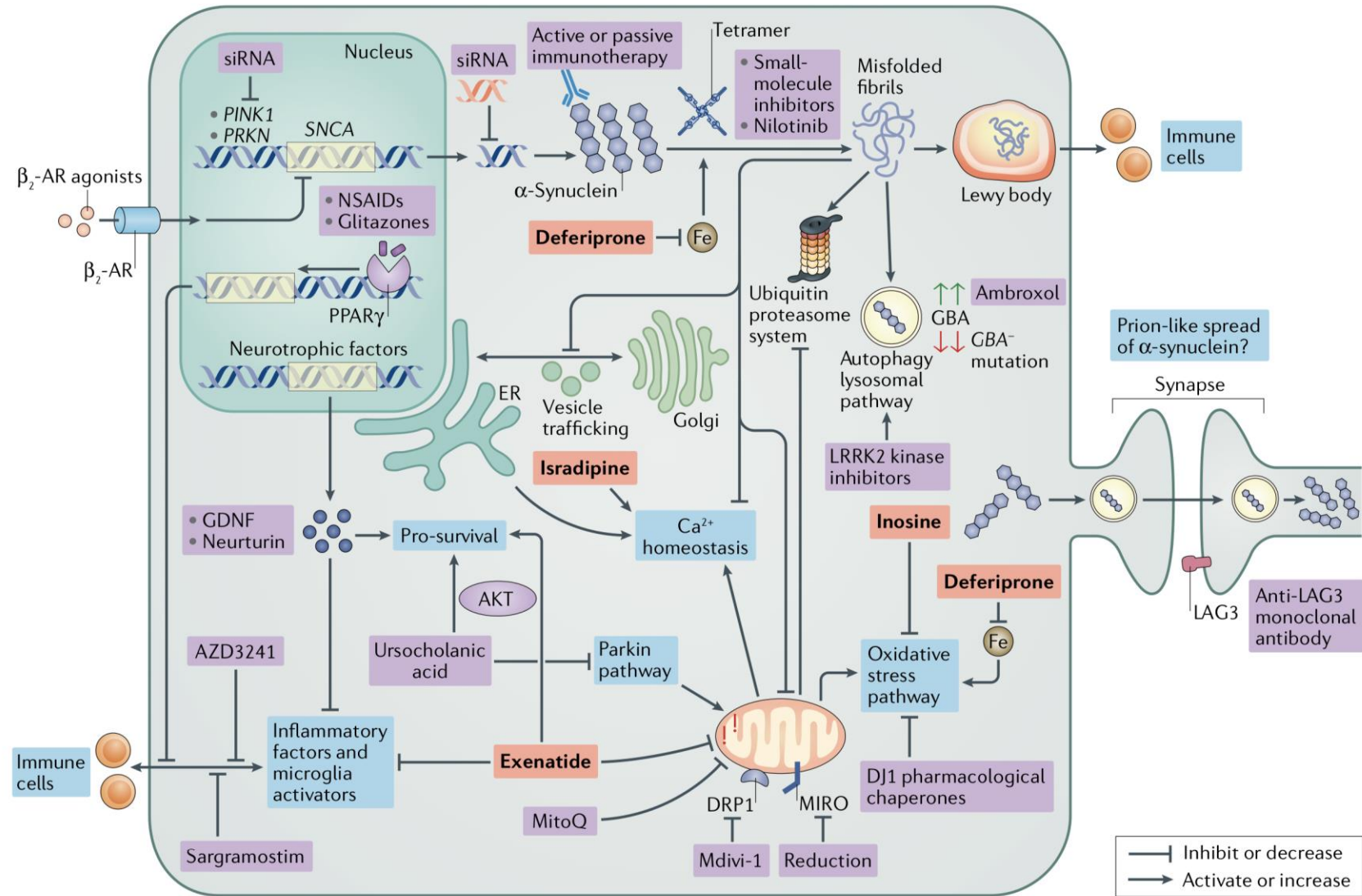
BRAIN-FIRST PD



Horsager. Brain, 2020

Belangrijke vragen voor deze fase

- Wat is de oorzaak van de ZvP?
- Hoe kunnen we de ZvP remmen?



Elkouzi, NRN, 2019

Verbeeldingskr8





KEVIN MCFARTHING

Diagnose: 2012

Nationaliteit: British

Hoehn en Yahr-schaal: 2

Korte levensloop: Dr. Kevin McFarthing was oorspronkelijk een biochemicus en bracht het grootste deel van zijn carrière door met het leiden van R & D-groepen in de levenswetenschappen (Amersham), diagnostiek (Serono) en consumentengezondheid (Reckitt Benckiser). Hij runt nu het adviesbureau *Innovation Fixer*. Bij hem werd in 2012 op 55-jarige leeftijd de diagnose 'Ziekte van Parkinson' gesteld.

Activisme: Kevin onderhoudt de zogeheten 'Parkinson's Hope List', is auteur/editor van de "Clinical trial highlights" in het *Journal of Parkinson's Disease*, presenteert geregeld over zijn inzichten en heeft recent een artikel geschreven met een aantal mede-auteurs: 'Parkinson's disease drug therapies in the clinical trial pipeline: 2020' (McFarthing et al, 2020).

Meeste last van: Traagheid, minder uitdrukking in het gezicht, gedwongen rechts schrijven terwijl je links bent en vroege tekenen van problemen met de stem.

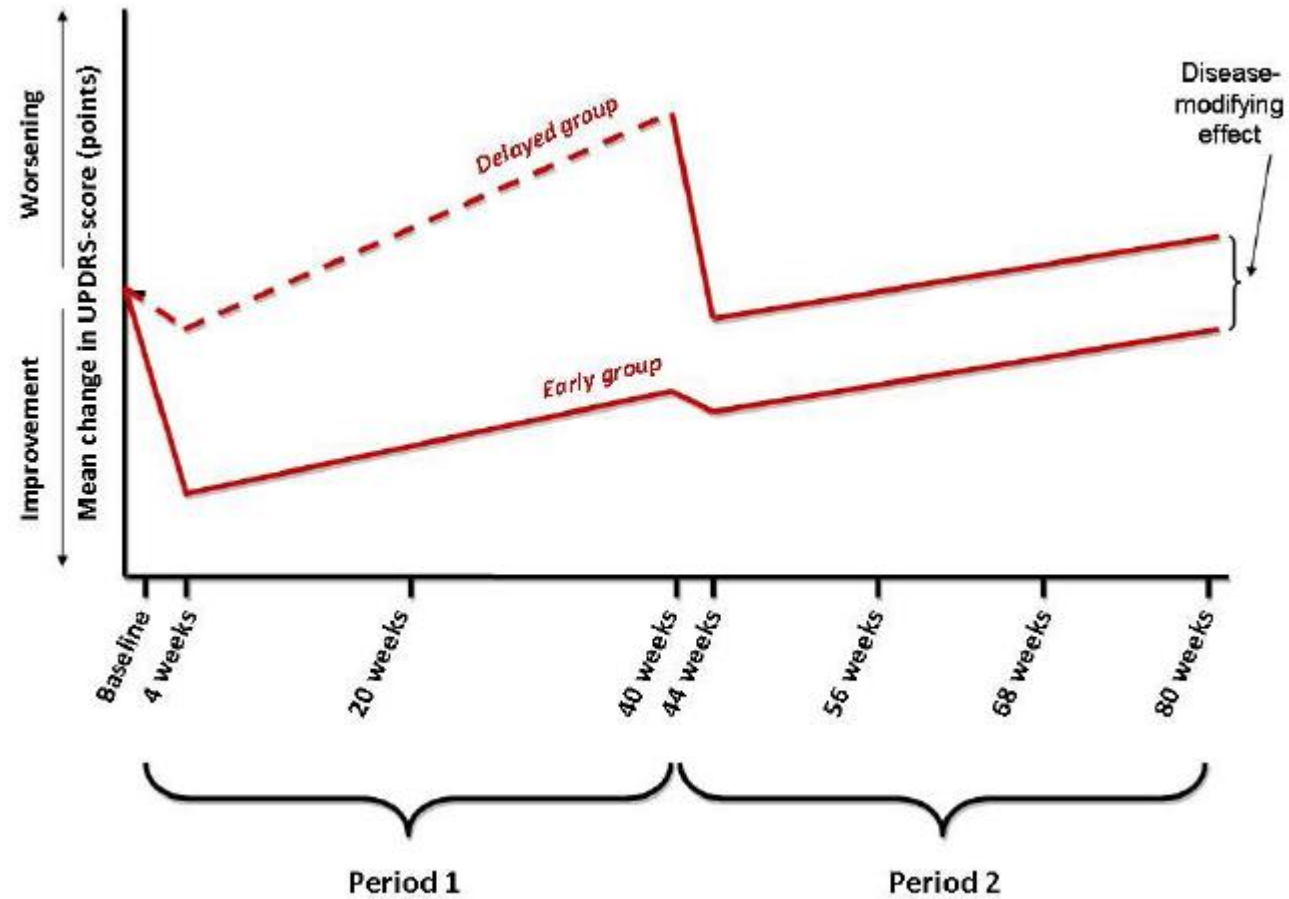


ZonMw



Internationaal
Parkinson Fonds

Appendix — Figure 2. Current study design



The NEW ENGLAND
JOURNAL *of* MEDICINE

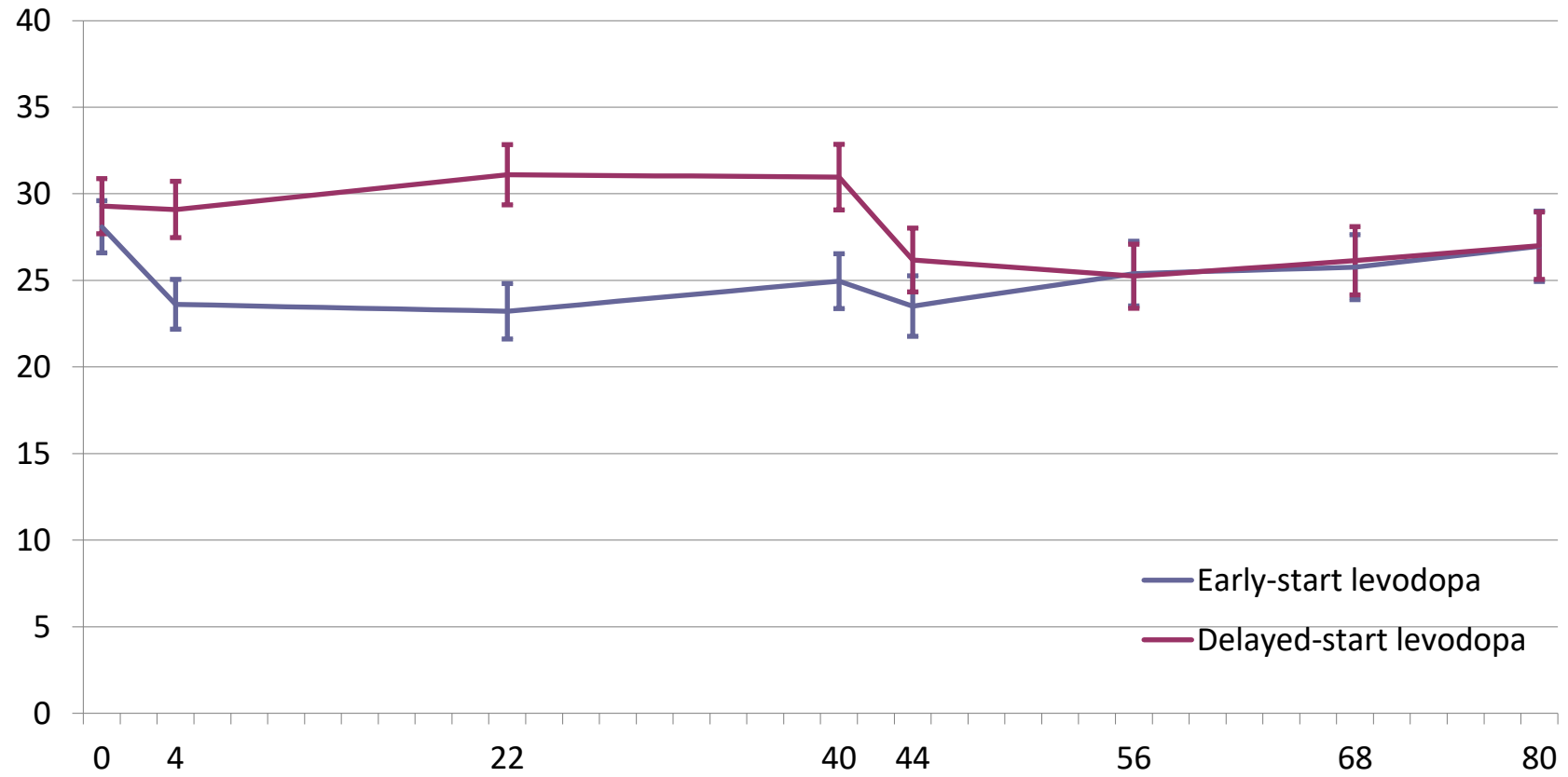
ESTABLISHED IN 1812

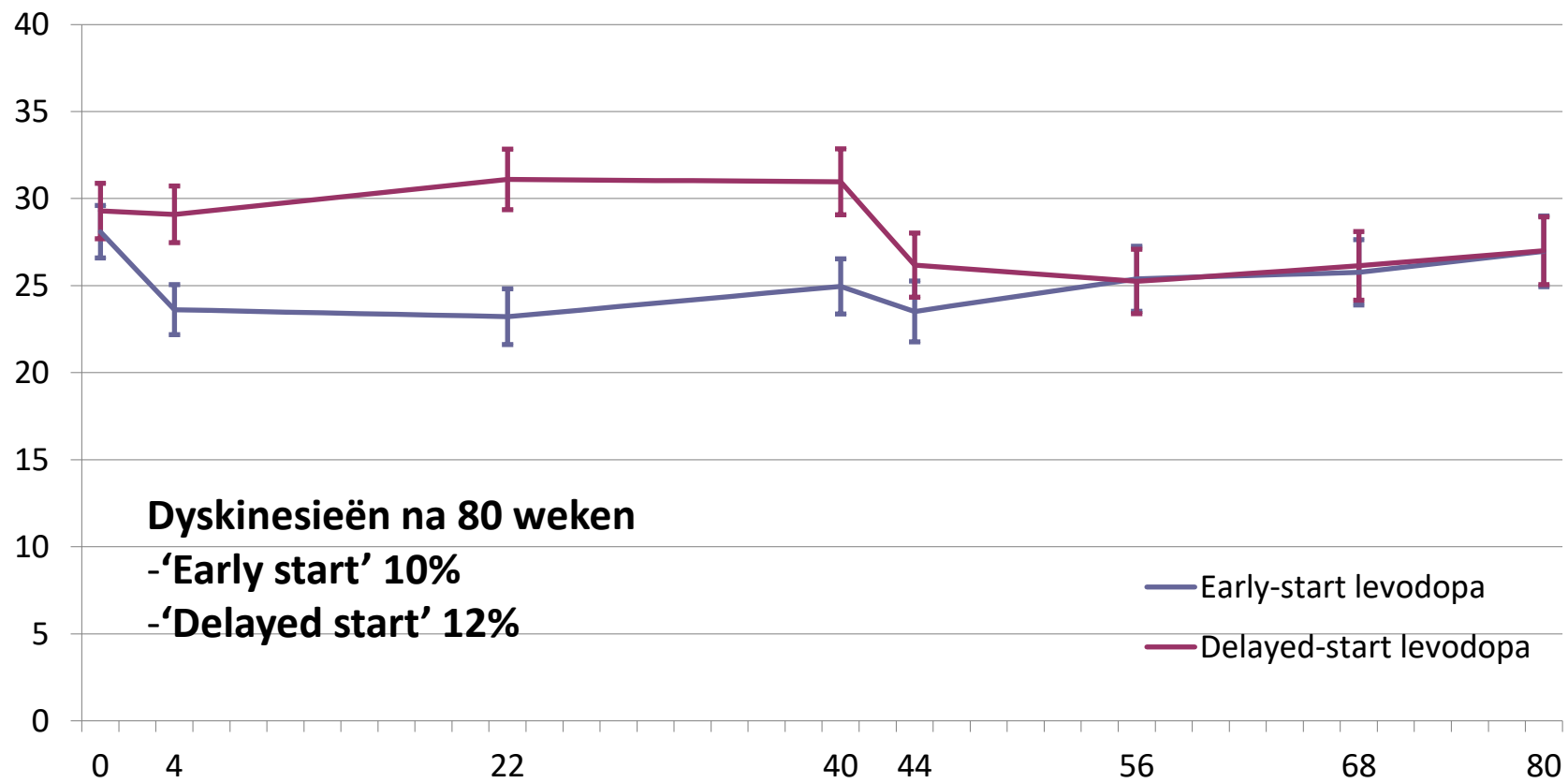
JANUARY 24, 2019

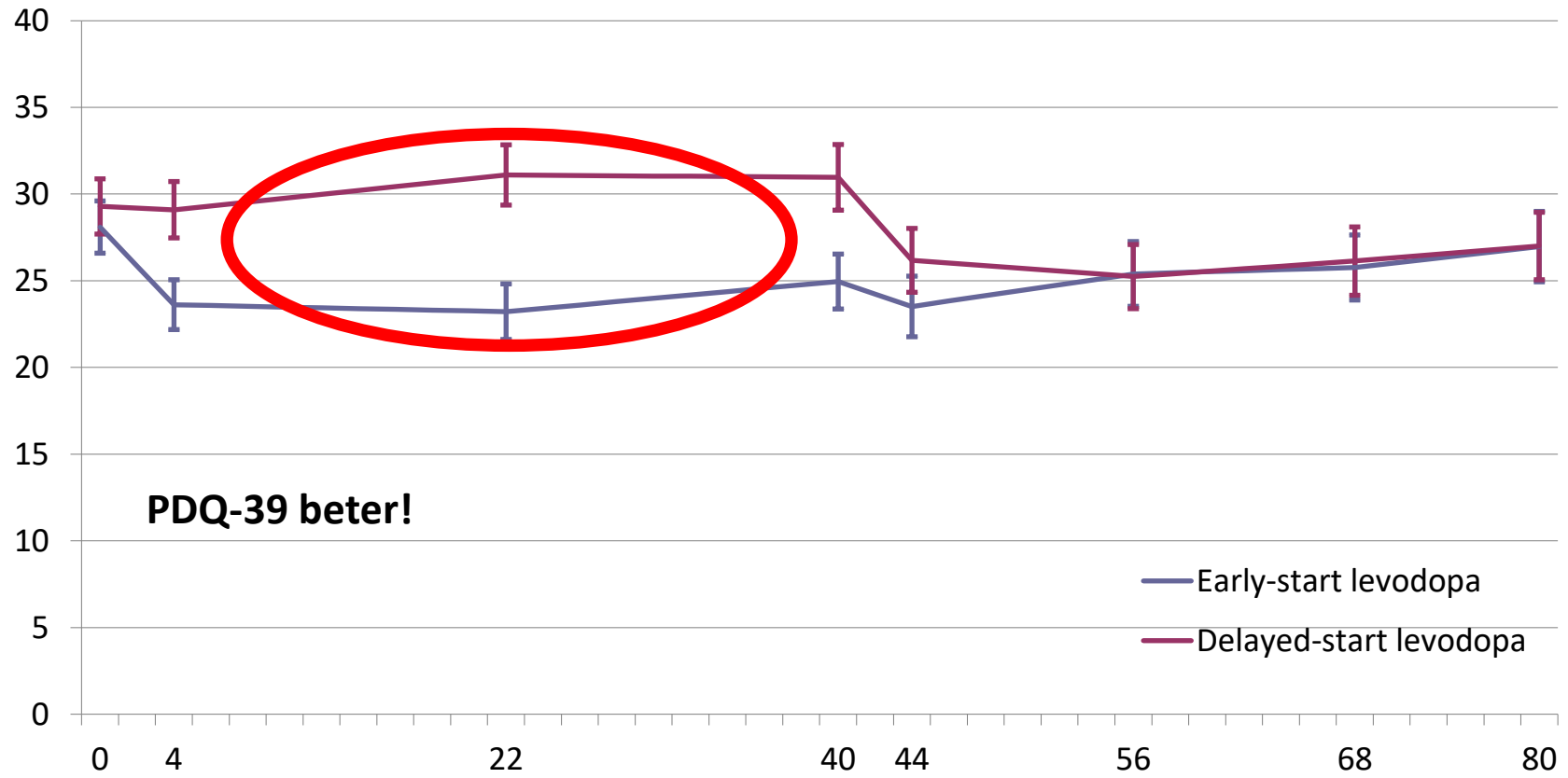
VOL. 380 NO. 4

Randomized Delayed-Start Trial of Levodopa
in Parkinson's Disease

C.V.M. Verschuur, S.R. Suwijn, J.A. Boel, B. Post, B.R. Bloem, J.J. van Hilten, T. van Laar, G. Tissingh, A.G. Munts,
G. Deuschl, A.E. Lang, M.G.W. Dijkgraaf, R.J. de Haan, and R.M.A. de Bie, for the LEAP Study Group*







Vaccinatie en de ZvP

Journal of
Neurochemistry



● JOURNAL OF NEUROCHEMISTRY | 2017

doi: 10.1111/jnc.14207

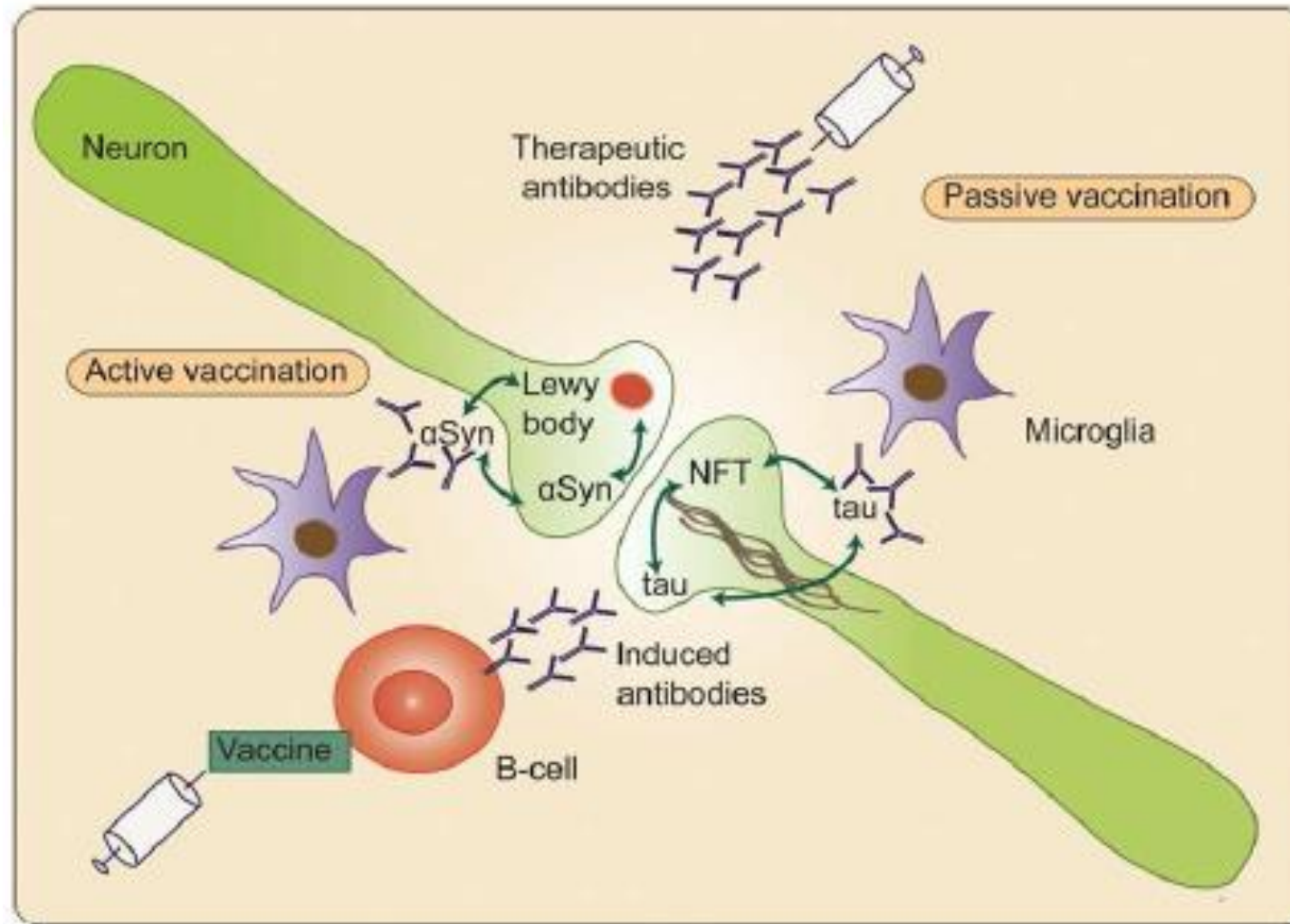
REVIEW

Vaccination strategies in tauopathies and synucleinopathies

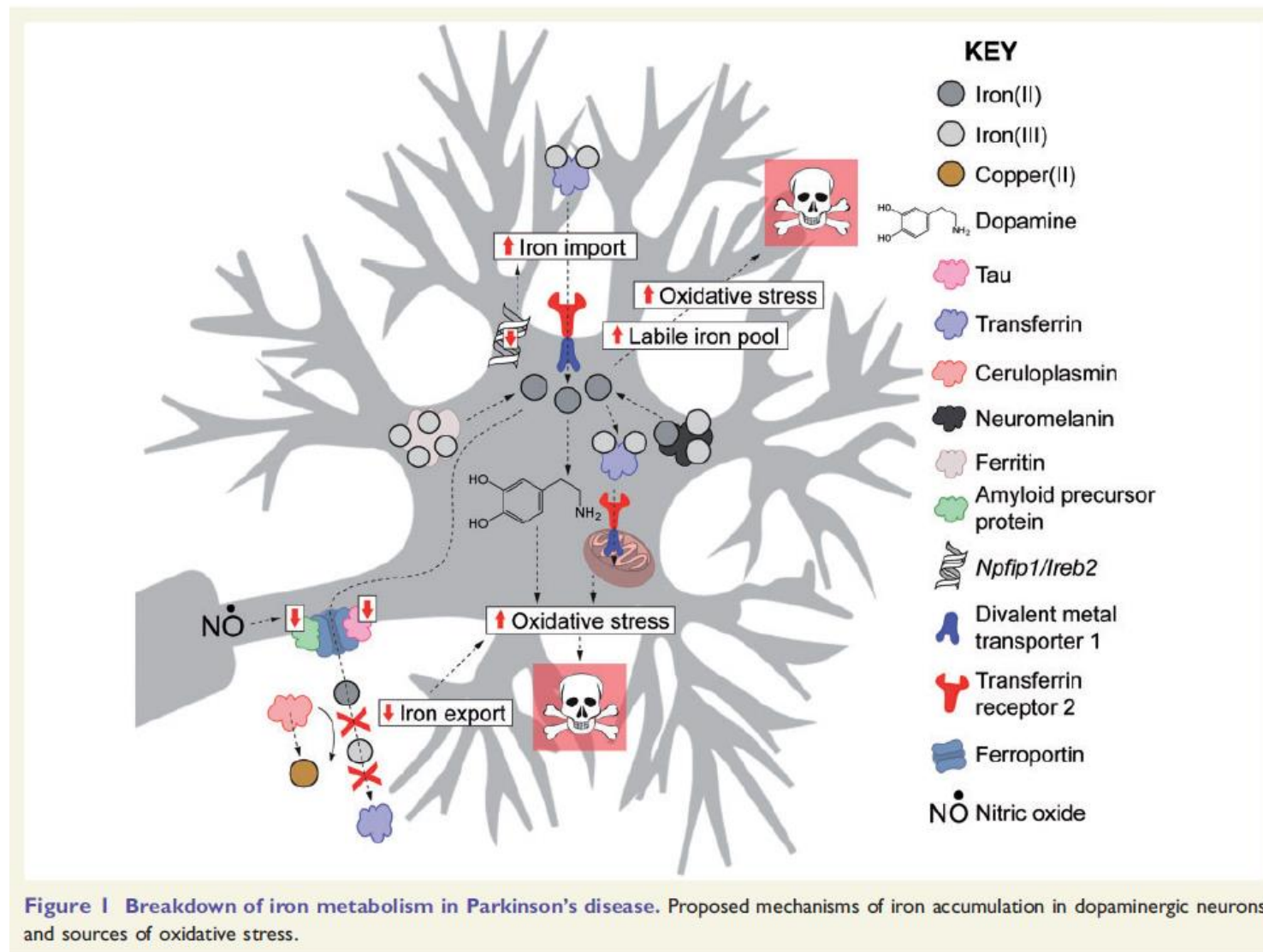
Anne K. Braczynski,*  Jörg B. Schulz*†  and Jan-Philipp Bach*

**Department of Neurology, RWTH Aachen University Hospital, Aachen, Germany*

†Jülich Aachen Research Alliance (JARA) – JARA-Institute Molecular Neuroscience and Neuroimaging, FZ Jülich and RWTH University, Aachen, Germany



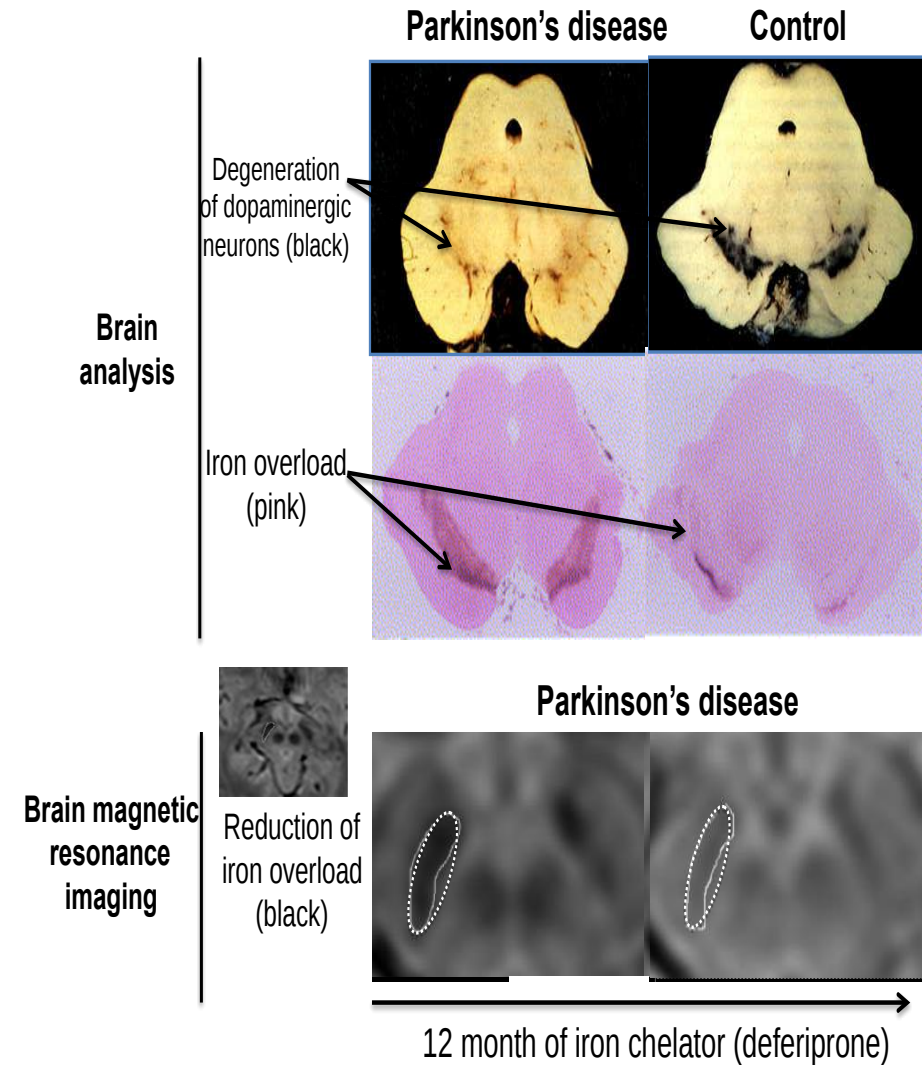
Braczynski, Neurochemistry, 2017



Hare, 2016

David Devos

Confirmation:
European trial in progress
<http://www.fairpark2.eu>



ORIGINAL ARTICLE

Trial of Deferiprone in Parkinson's Disease

D. Devos, J. Labreuche, O. Rascol, J.-C. Corvol, A. Duhamel, P. Guyon Delannoy, W. Poewe, Y. Compta, N. Pavese, E. Růžička, P. Dušek, B. Post, B.R. Bloem, D. Berg, W. Maetzler, M. Otto, M.-O. Habert, S. Lehericy, J. Ferreira, R. Dodel, C. Tranchant, A. Eusebio, S. Thobois, A.-R. Marques, W.G. Meissner, F. Ory-Magne, U. Walter, R.M.A. de Bie, M. Gago, D. Vilas, J. Kulisevsky, C. Januario, M.V.S. Coelho, S. Behnke, P. Worth, K. Seppi, T. Ouk, C. Potey, C. Leclercq, R. Viard, G. Kuchcinski, R. Lopes, J.-P. Pruvo, P. Pigny, G. Garçon, O. Simonin, J. Carpentier, A.-S. Rolland, D. Nyholm, C. Scherfler, J.-F. Mangin, M. Chupin, R. Bordet, D.T. Dexter, C. Fradette, M. Spino, F. Tricta, S. Ayton, A.I. Bush, J.-C. Devedjian, J.A. Duce, I. Cabantchik, L. Defebvre, D. Deplanque, and C. Moreau, for the FAIRPARK-II Study Group*

Table 2. Primary, Secondary, and Exploratory Clinical Outcomes (Intention-to-Treat Population).*

Outcome	Deferiprone (N=186)	Placebo (N=186)	Mean Adjusted Difference (95% CI)†
Primary outcome			
MDS-UPDRS total score			
Value at wk 36	50.7±23.4	39.6±17.7	
Change from baseline (95% CI)	15.6 (13.5 to 17.6)†	6.3 (4.2 to 8.4)†	9.3 (6.3 to 12.2)‡
Secondary outcomes§			
Score on MDS-UPDRS part III			
Value at wk 36	31.8±14.0	25.9±11.7	
Change from baseline (95% CI)	9.8 (8.2 to 11.3)†	4.0 (2.7 to 5.3)†	5.8 (3.8 to 7.7)
Score on MDS-UPDRS part II			
Value at wk 36	10.2±7.7	7.1±5.4	
Change from baseline (95% CI)	4.2 (3.4 to 5.1)†	1.8 (1.0 to 2.6)†	2.5 (1.3 to 3.6)
Sum of scores on MDS-UPDRS parts II and III			
Value at wk 36	42.2±18.8	33.1±15.0	
Change from baseline (95% CI)	14.2 (12.2 to 16.1)†	5.9 (4.1 to 7.6)†	8.3 (5.7 to 10.8)
Exploratory clinical outcome§			
Score on MDS-UPDRS part I			
Value at wk 36	8.2±5.9	6.2±4.6	
Change from baseline (95% CI)	2.0 (1.3 to 2.7)†	0.2 (−0.4 to 0.9)†	1.8 (0.8 to 2.8)

Exenatide once a week versus placebo as a potential disease-modifying treatment for people with Parkinson's disease in the UK: a phase 3, multicentre, double-blind, parallel-group, randomised, placebo-controlled trial



Nirosen Vijiaratnam, Christine Girges, Grace Auld, Rachel McComish, Alexa King, Simon S Skene, Steve Hibbert, Alan Wong, Sabina Melander, Rachel Gibson, Helen Matthews, John Dickson, Camille Carroll, Abigail Patrick, Jemma Inches, Monty Silverdale, Bethan Blackledge, Jessica Whiston, Michele Hu, Jessica Welch, Gordon Duncan, Katie Power, Sarah Gallen, Jacqueline Kerr, K Ray Chaudhuri, Lucia Batzu, Silvia Rota, Edwin Jabbari, Huw Morris, Patricia Limousin, Nigel Greig, Yazhou Li, Vincenzo Libri, Sonia Gandhi, Dilan Athauda, Kashfia Chowdhury, Tom Foltynie



www.thelancet.com Vol 405 February 22, 2025

	Exenatide group (n=97)	Placebo group (n=97)	Total (n=194)
Age, years	61.02 (9.05)	60.35 (9.26)	60.68 (9.14)
Age at diagnosis, years	56.37 (9.60)	56.30 (9.53)	56.33 (9.54)
Weight, kg	79.57 (14.73)	78.39 (13.55)	78.98 (14.13)
Sex			
Female	28 (29%)	28 (29%)	56 (29%)
Male	69 (71%)	69 (71%)	138 (71%)
Ethnicity			
White	92 (95%)	88 (91%)	180 (93%)
Mixed	1 (1%)	1 (1%)	2 (1%)
Black or Black British	1 (1%)	0	1 (1%)
Asian or Asian British	3 (3%)	5 (5%)	8 (4%)
Other or prefer not to say	0	3 (3%)	3 (2%)
Hoehn and Yahr stage at randomisation			
≤2.0	83 (86%)	82 (85%)	165 (85%)
2.5	14 (14%)	15 (15%)	29 (15%)
BMI, kg/m ²	25.80 (23.50–28.60)	25.20 (23.10–28.00)	25.60 (23.40–28.10)
Levodopa equivalent daily dose	475 (340–615)	475 (300–700)	475 (300–90)

Data are mean (SD), n (%), or median (IQR). All 194 randomly assigned participants were on Parkinson's disease medication at baseline.

Table 1: Baseline characteristics

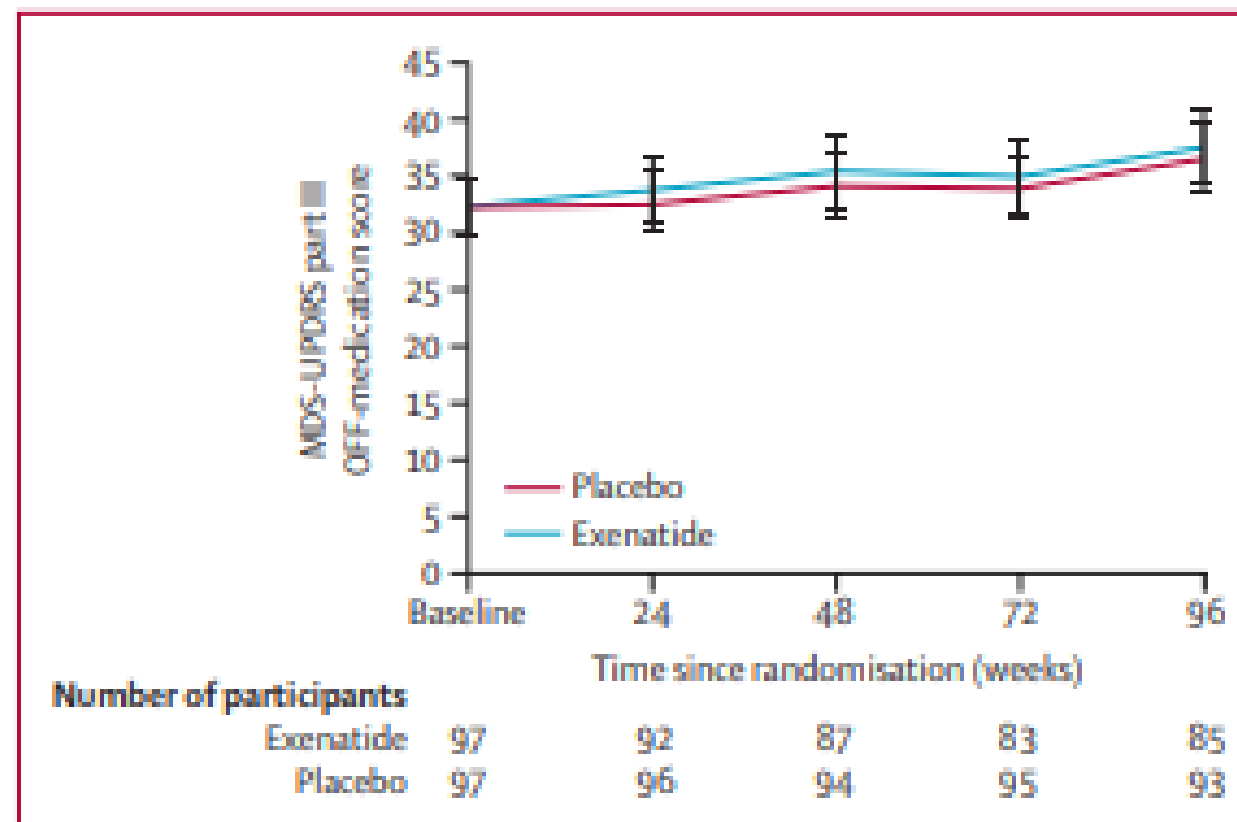
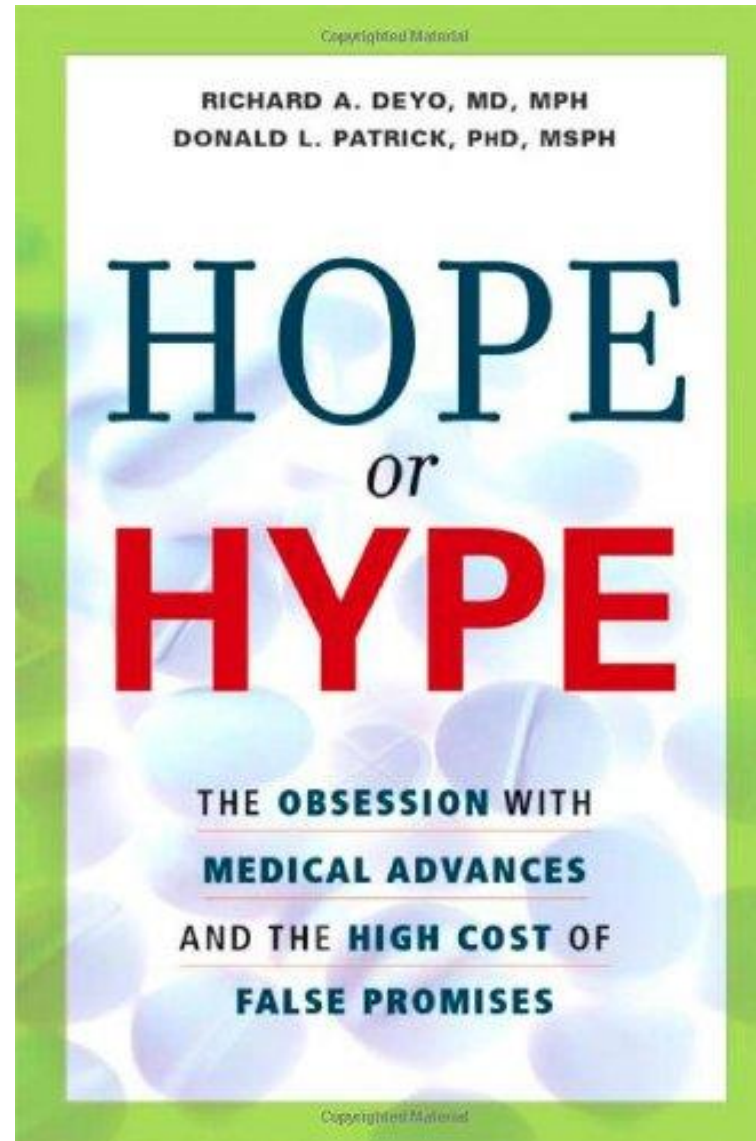


Figure 2: Mean MDS-UPDRS part III OFF-medication score by group over 96 weeks

MDS-UPDRS=Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale.

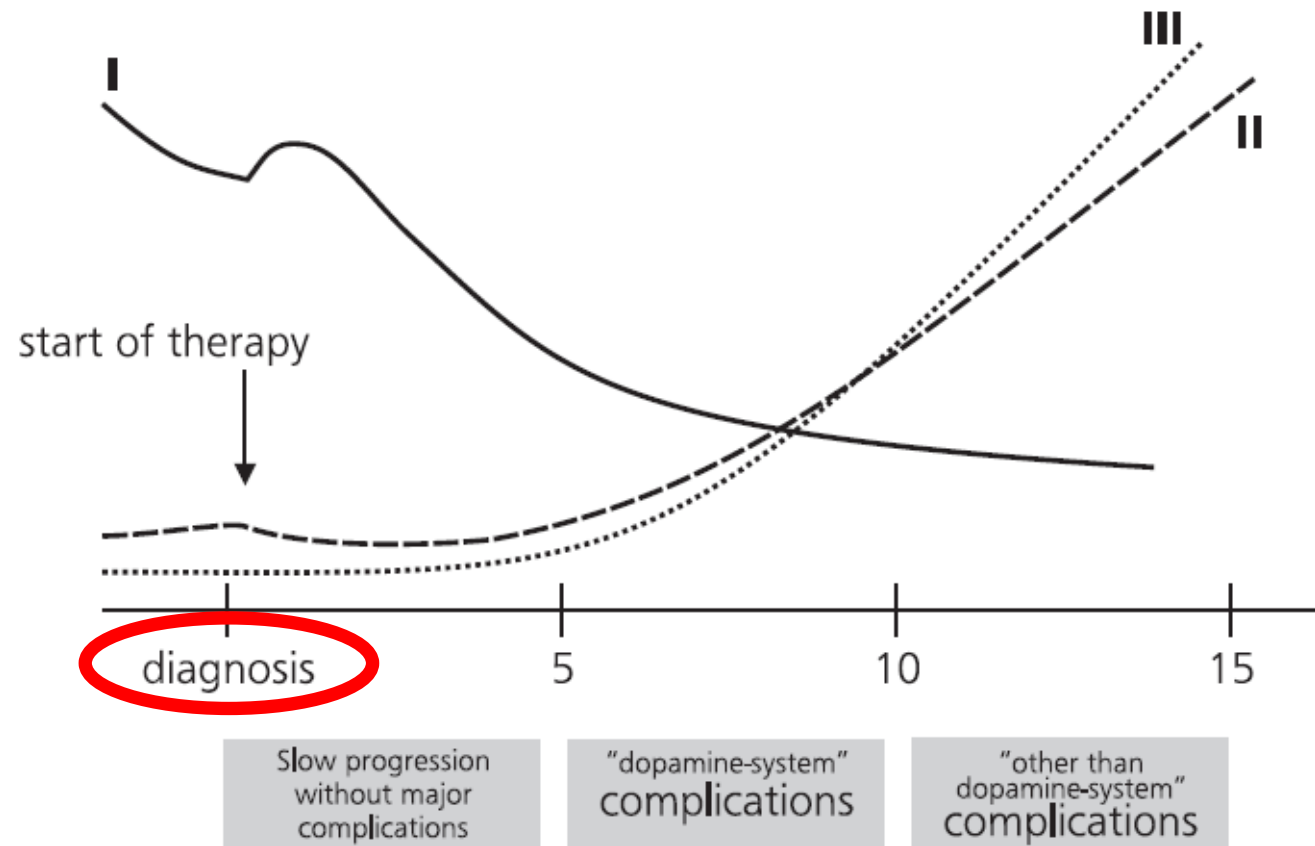


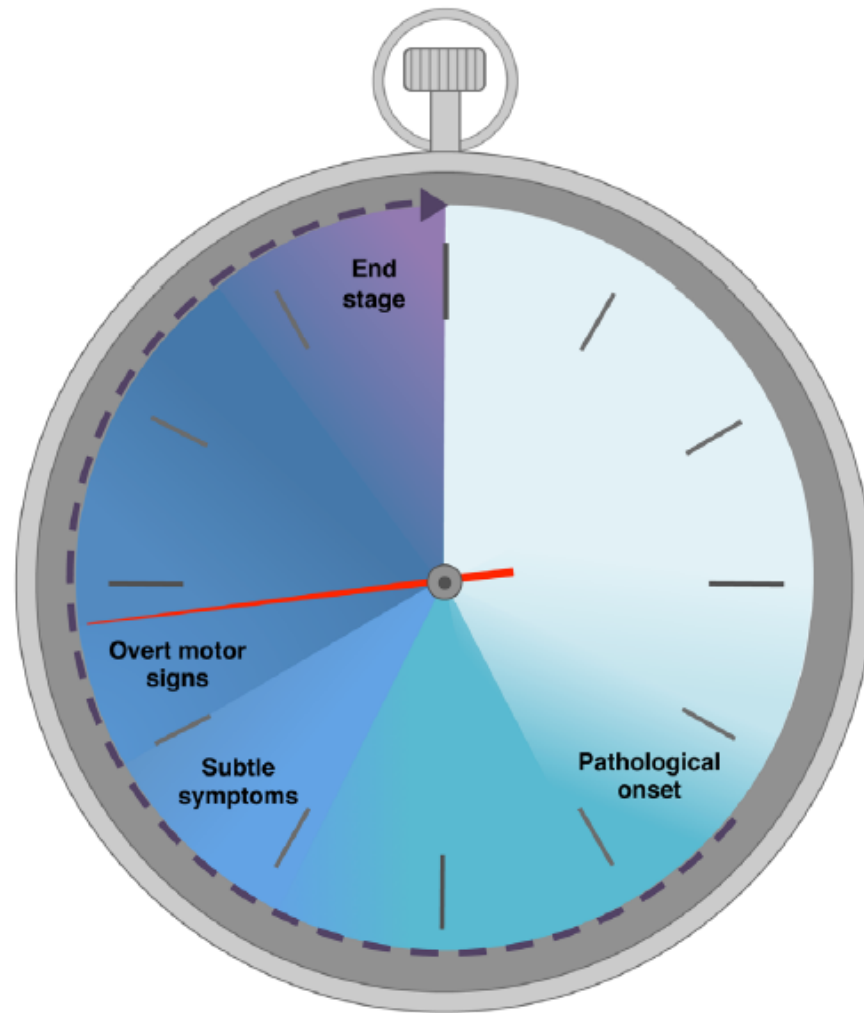
Tom Isaacs: “This is a time
of cautious hope instead of
conservative paternalism”





Basis model ZvP





When is it **timely** to know?



In the **early** and **asymptomatic** periods, some people will want to know their risk, whether or not there are neuroprotective strategies. For them, **timely** constitutes the earlier the better.



Others will only want to know if something can be done to alter their **risk** or **asymptomatic** disease. For them, **timely** depends on the availability of neuroprotective strategies.



Many will only want to know when they are **symptomatic** (either early prodromal features or overt motor signs) and treatment will offer relief. For them, **timeliness** relates to symptom relief in the absence of neuroprotective/disease-modifying strategies.



Finally there are a minority of people who would rather **never** know that they are at risk or even when they have the disease. For them, there is no point at which the disclosure is **timely**.

Rees, F1000 research, 2018

Wanneer 'EOPD'

- Early onset parkinsonisme
 - <21 jr **juveniel parkinsonisme**
 - 21-40 / 50 jr **young-onset ziekte van Parkinson (YOPD)**
- Voorkomen op basis van leeftijd
 - Schrag 2006 3-5% onder 40 in USA
 10% onder 40 in Japan
 - Wickremaratchi 5,4% onder de 50 in Cardiff
 31,2% onder de 65

Fenotype YOPD

TABLE 1. Clinical and treatment characteristics of the study cohort by onset group

Onset group	All N = 358	<45 yr N = 70	45–54 yr N = 103	55–64 yr N = 88	≥ 65 yr N = 97	P-value*
Men:Women	1:0.6	1:0.7	1:0.6	1:0.6	1:0.6	0.945
Mean age at onset (range)	56 (8–85)	38 (8–44.9)	51 (45–54.9)	59 (55–64.9)	72 (65–85)	<0.0001
Mean current age (range)	65 (28–88)	51 (28–64)	61 (47–79)	67 (58–82)	77 (67–88)	<0.0001
Mean disease duration (range)	9 (1–39)	13 (1–39)	10 (1–28)	8 (1–24)	6 (1–27)	<0.0001
Mean motor UPDRS score (95% CI)	27 (26–28)	23 (21–26)	27 (24–29)	27 (24–30)	31 (29–33)	0.0013
L-DOPA treatment duration, yrs (range)	4.9 (0.2–26)	7.2 (0.20–20)	5.3 (0.02–26)	4.8 (0.02–22)	3.5 (0.03–12)	0.0024
L-DOPA treatment dose, mg (range)	428 (40–1450)	470 (50–1100)	473 (100–1450)	420 (100–1450)	363 (50–900)	0.0153

*Chi-squared test for heterogeneity.

Fenotype YOPD

TABLE 2. Presentations at onset in PD patients by onset group

Onset group	All n (%)	<45 yr n (%)	45–54 yr n (%)	55–64 yr n (%)	≥ 65 yr n (%)	P value	P value for trend
Presentation							
Tremor	175 (49)	21 (31)	41 (40)	53 (61)	66 (62)	<0.001	<0.0001
Akinetic-rigid	156 (44)	46 (68)	58 (56)	26 (30)	26 (27)	<0.001	<0.0001
Gait	24 (7)	1 (1)	4 (4)	8 (9)	11 (11)	0.04	0.004

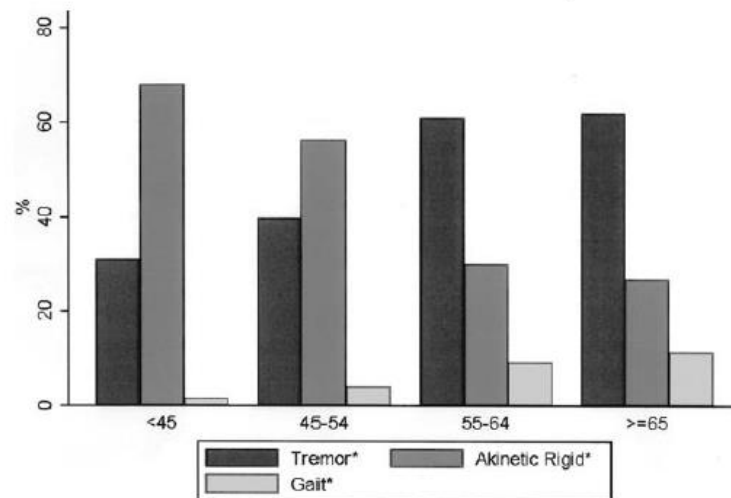


FIG. 1. Prevalence of presenting symptom in each PD age at onset group [*Significant *P*-value for trend and heterogeneity (*P*-values < 0.005 trend, each onset symptom)].

Wickremaratchi, jnp, 2011

Fenotype YOPD

TABLE 3. Characteristics of dystonia by onset group

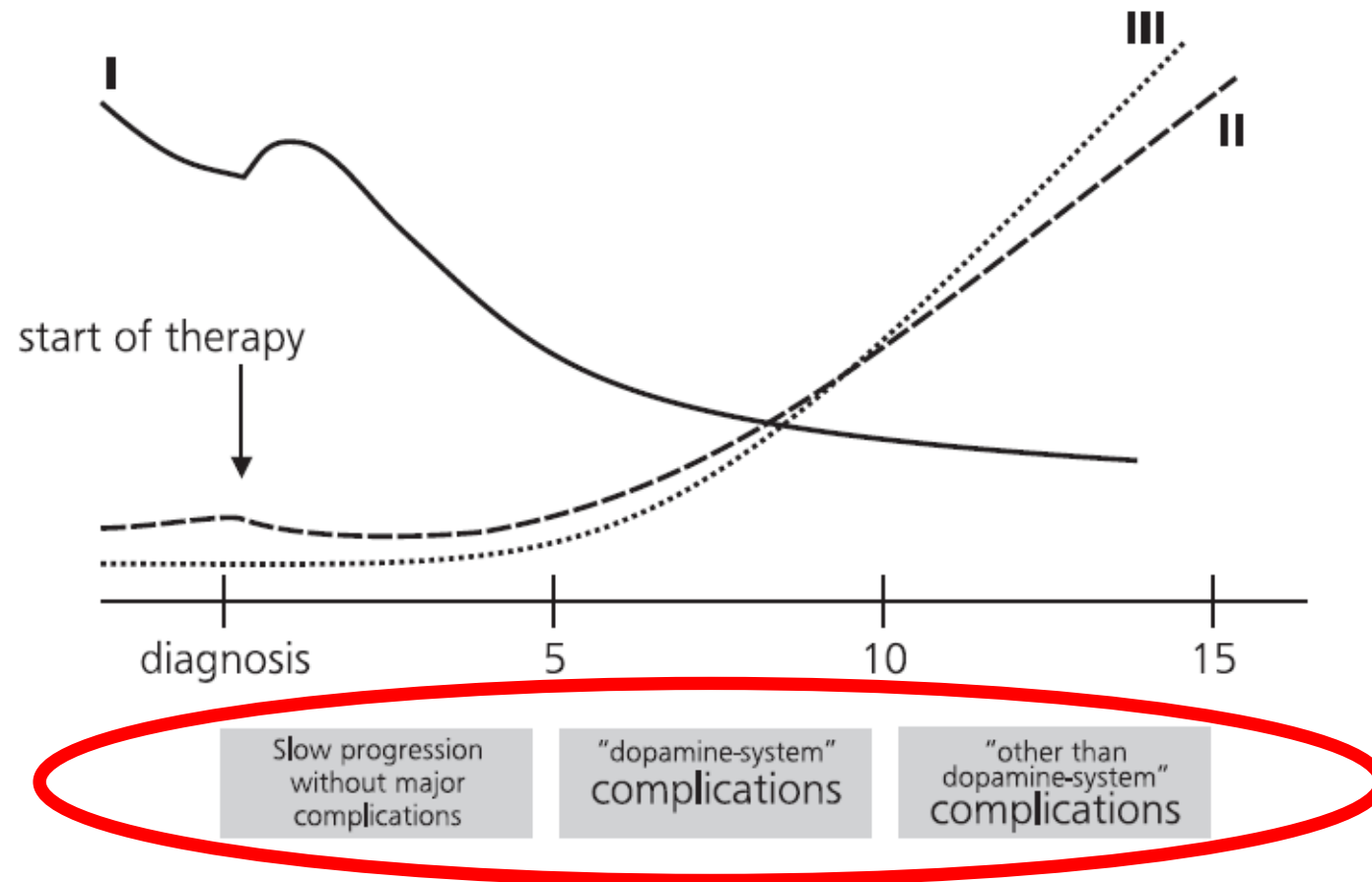
<i>Onset group</i>	<i>All n (%)</i>	<i><45 yr n (%)</i>	<i>45–54 yr n (%)</i>	<i>55–64 yr n (%)</i>	<i>≥ 65 yr n (%)</i>	<i>P value</i>	<i>P value for trend</i>
Presence of Dystonia	125 (39)	37 (59)	52 (58)	26 (30)	10 (12)	<0.001	<0.0001 ^a
Dystonia:							
At Onset	41 (12)	13 (20)	20 (20)	5 (6)	3 (3)	<0.001	<0.0001 ^a
In first 2 years	21 (6)	7 (11)	9 (10)	4 (5)	1 (1)	0.02	0.0025
Exercise induced	33 (9)	12 (18)	15 (15)	5 (6)	1 (1)	<0.001	<0.0001 ^a
Pre-treatment morning	2 (1)	1 (2)	0	0	1 (1)	0.47	0.87
Off period dystonia	44 (13)	19 (30)	21(20)	4 (5)	0	<0.001	<0.0001 ^a
Peak dose dystonia	15 (4)	7 (11)	4 (4)	2 (2)	2 (2)	0.03	0.0118 ^b
Treatment related	26 (8)	13 (21)	7 (7)	4 (5)	2 (2)	<0.001	0.0001
Non-dose related	34 (12)	4 (9)	19 (15)	14 (17)	6 (7)	0.22	0.65

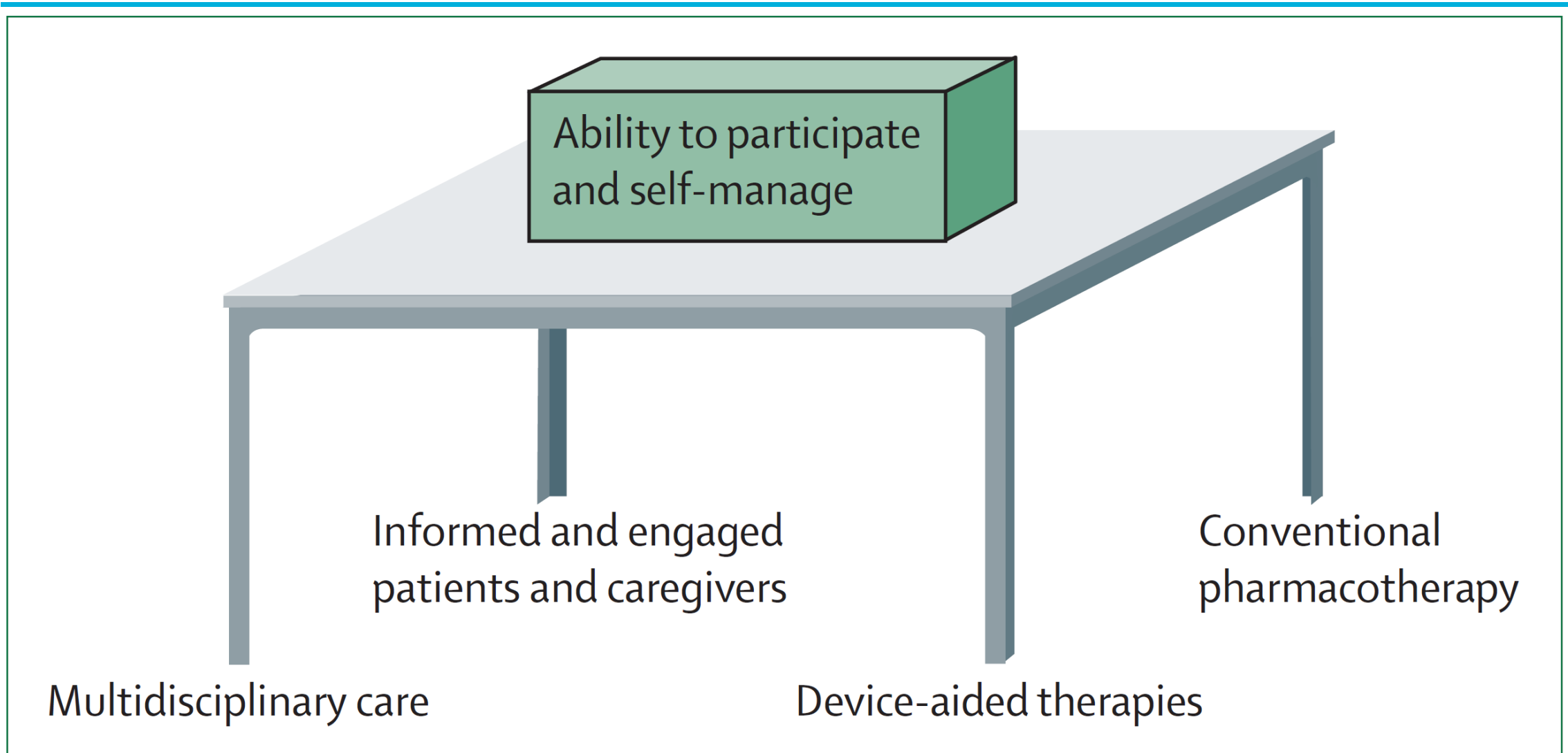
Chi-squared tests for heterogeneity and trend.

^a<55 vs. ≥55 heterogeneity test *P* value (Dystonia < 0.001, At Onset < 0.001 Exercise induced < 0.001, Off-period < 0.0001).

^b<45 vs. ≥45 heterogeneity test *P* value (Peak dose = 0.004)

Basis model ZvP



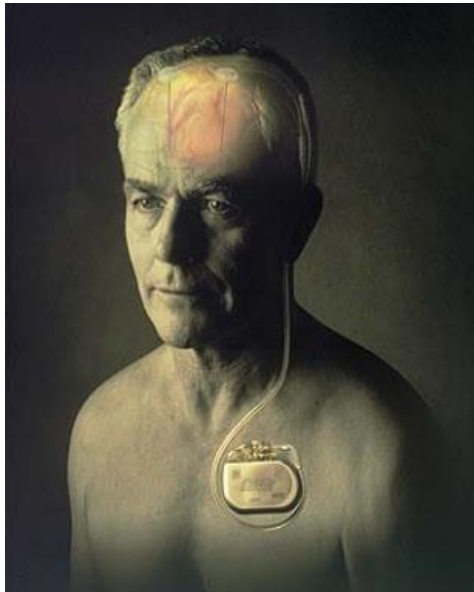


Bloem. Lancet, 2021

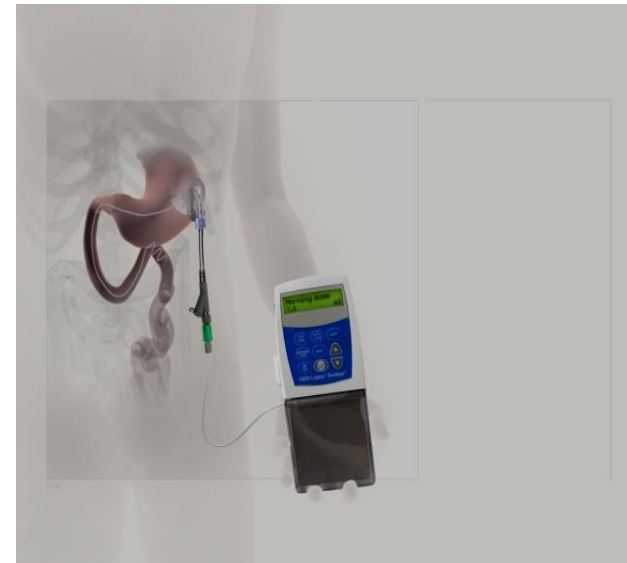
Wat kan je zelf doen?

- Goede kennis over de ziekte van Parkinson
- Bewust zijn van je eigen coping strategie
- Leefstijl interventies
 - Inspanning / Training
 - Stress management
 - Voeding

Geavanceerde therapie



Geen vergelijkende studies!



Focused ultrasound subthalamotomy in patients with asymmetric Parkinson's disease: a pilot study

Raul Martínez-Fernández, Rafael Rodríguez-Rojas, Marta del Álamo, Frida Hernández-Fernández, Jose A Pineda-Pardo, Michele Dileone, Fernando Alonso-Frech, Guglielmo Foffani, Ignacio Obeso, Carmen Gasca-Salas, Esther de Luis-Pastor, Lydia Vela, José A Obeso

ARTICLE

CLASS OF EVIDENCE

Lancet Neurol 2018; 17: 54–63

Focused ultrasound thalamotomy in Parkinson disease

Nonmotor outcomes and quality of life

Scott A. Sperling, PsyD, Binit B. Shah, MD, Matthew J. Barrett, MD, MSc, Aaron E. Bond, MD, PhD, Diane S. Huss, DPT, Jorge A. Gonzalez Mejia, BA, and W. Jeffrey Elias, MD

Neurology® 2018;91:e1275–e1284. doi:10.1212/WNL.0000000000006279

Correspondence

Dr. Sperling
sas7yr@virginia.edu

Apomorphine subcutaneous infusion in patients with Parkinson's disease with persistent motor fluctuations (TOLEDO): a multicentre, double-blind, randomised, placebo-controlled trial

Regina Katzenschlager, Werner Poewe, Olivier Rascol, Claudia Trenkwalder, Günther Deuschl, K Ray Chaudhuri, Tove Henriksen, Teus van Laar, Kevin Spivey, Senthil Vel, Harry Staines, Andrew Lees

Lancet Neurol 2018

RCT: General Anesthesia vs Local Anesthesia in Micoelectrode Recording-Guided Deep-Brain Stimulation for Parkinson Disease

POPULATION

78 Men, 32 Women



Patients with advanced Parkinson disease and motor response fluctuations
Mean (SD), 60.6 (7.7) y

SETTINGS / LOCATIONS



1 University hospital in Amsterdam, the Netherlands

INTERVENTION

110 Patients randomized



56 Surgery under local anesthesia

Electrode implantation in the subthalamic nuclei with microelectrode recordings and clinical tests

54 Surgery under general anesthesia

Electrode implantation in the subthalamic nuclei with microelectrode recordings only

PRIMARY OUTCOME

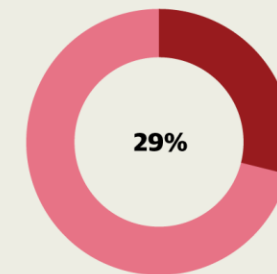
Composite score of adverse effects after 6 mo based on 4 areas:

- (1) Cognitive deterioration
- (2) Period of psychosis, anxiety, or depression
- (3) Loss of professional activity
- (4) Delirium after surgery

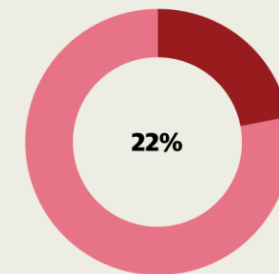
FINDINGS

There was no difference in the composite score of adverse events between the 2 treatment groups

Local anesthesia



General anesthesia



Adverse effects

Local Anesthesia: 15 of 52 (29%)

General anesthesia: 11 of 51 (22%)

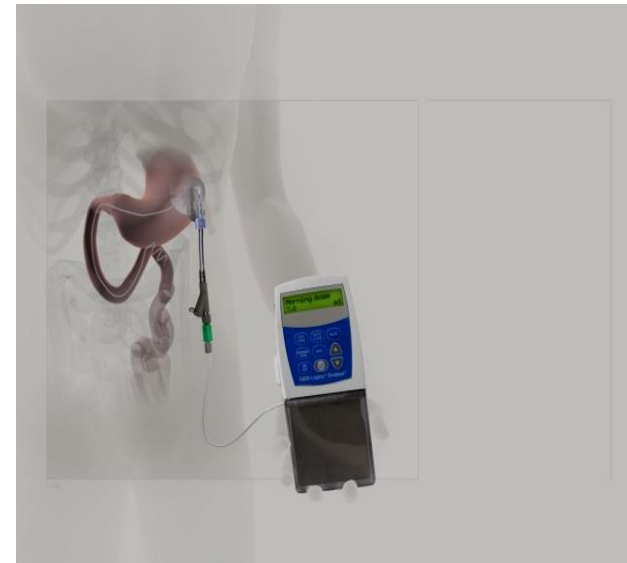
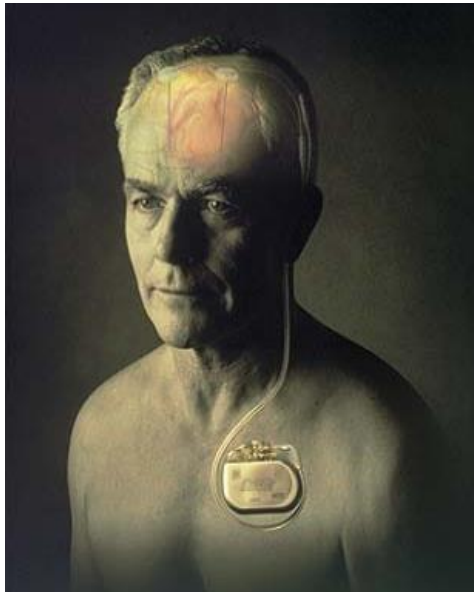
Odds ratio, 0.7; 95% CI, 0.3-1.7; $P = .40$

Holewijn RA, Verbaan D, van den Munckhof PM, et al. General Anesthesia vs Local Anesthesia in Micoelectrode Recording-Guided Deep-Brain Stimulation for Parkinson Disease: A Randomized Clinical Trial. *JAMA Neurol*. Published online September 7, 2021. doi:10.1001/jamaneurol.2021.2979

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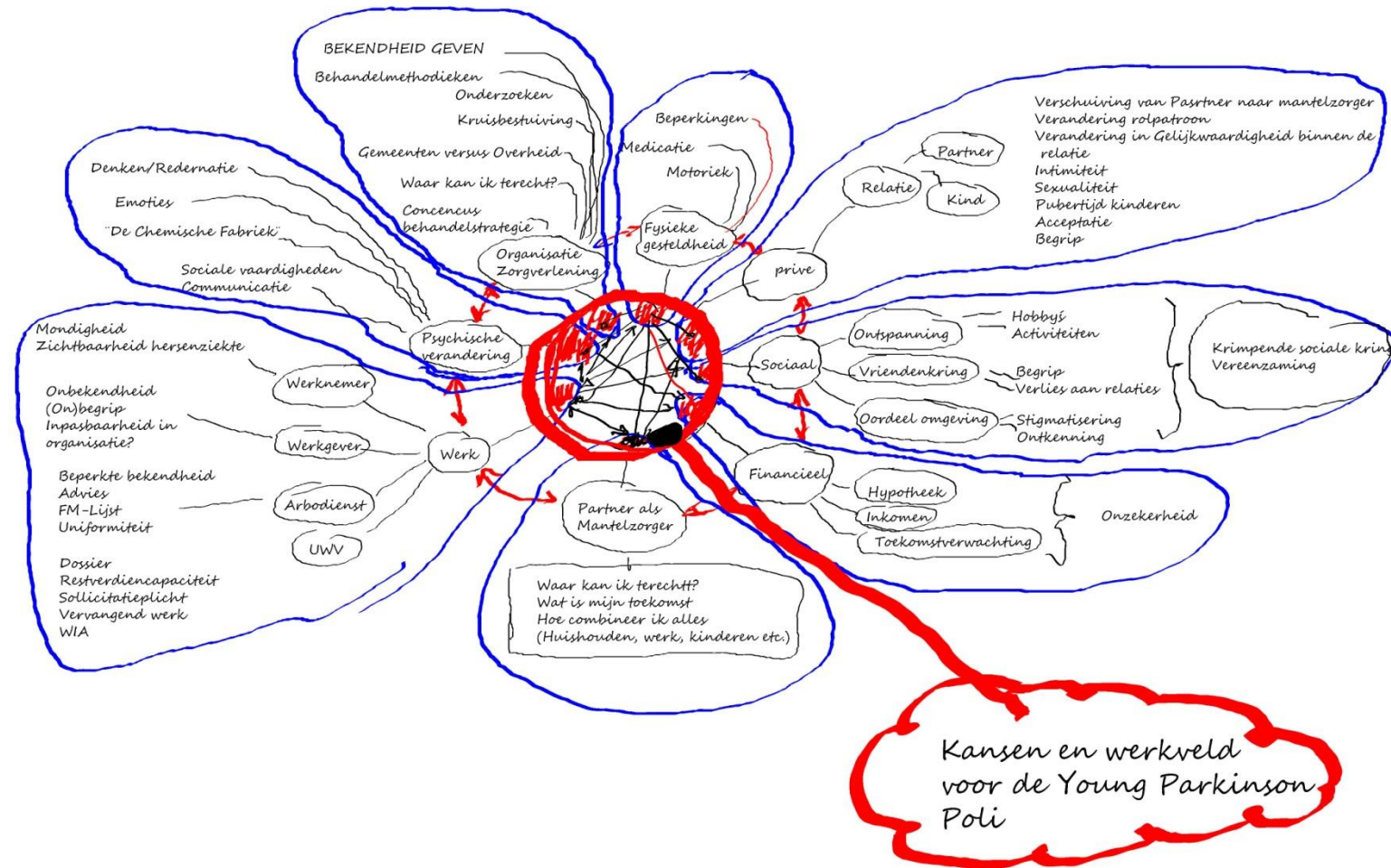
Geavanceerde therapie



Shared decision making

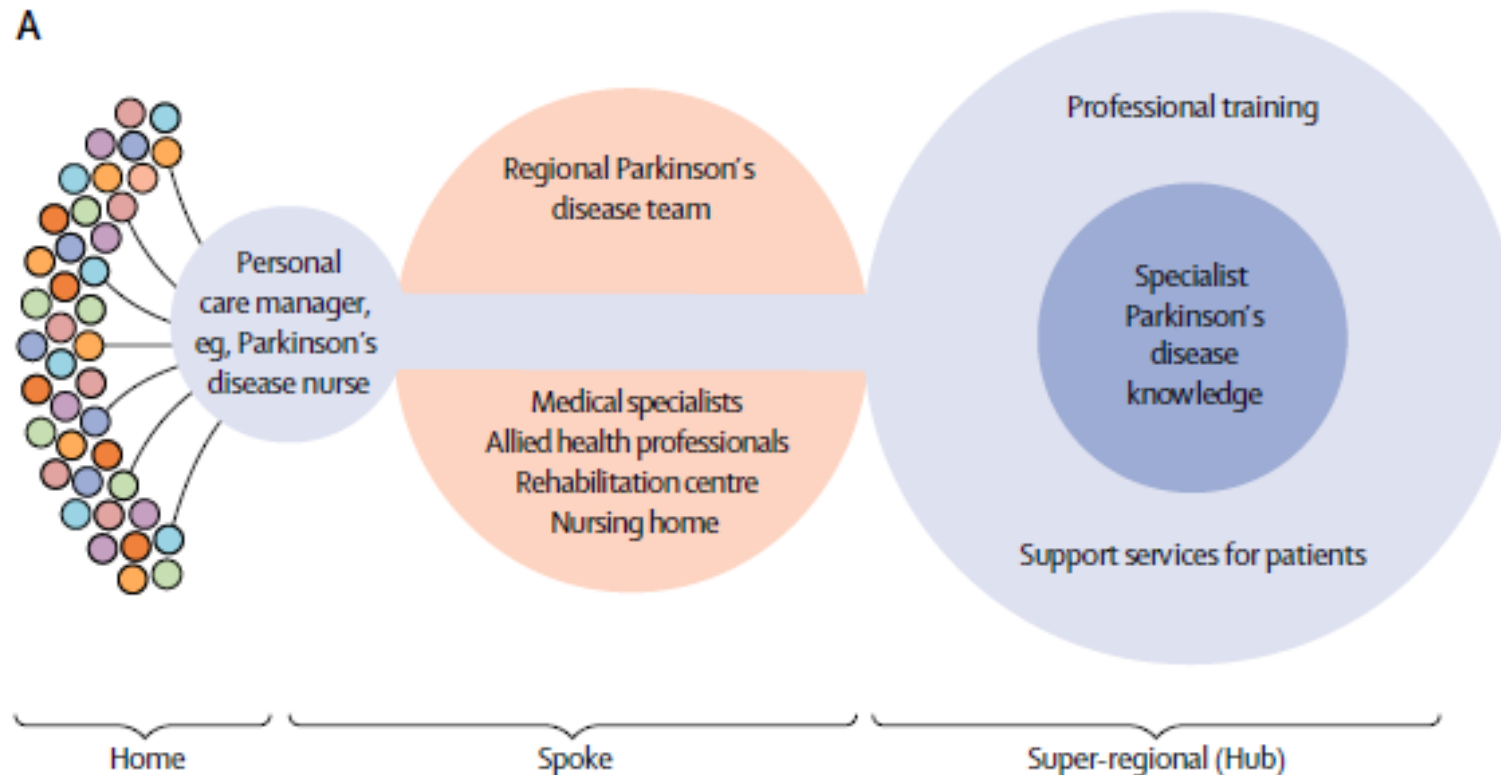
Tweet Bas Bloem

‘Patients do not know best,
they know different.
Together we know best.’



© Dorien Wissink & Xander van Ruissen

Wat willen we?

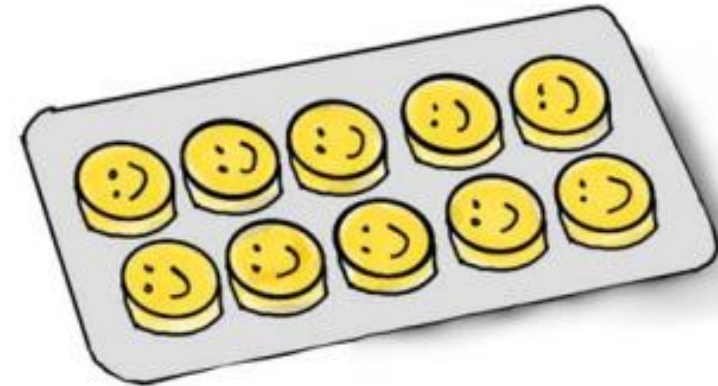
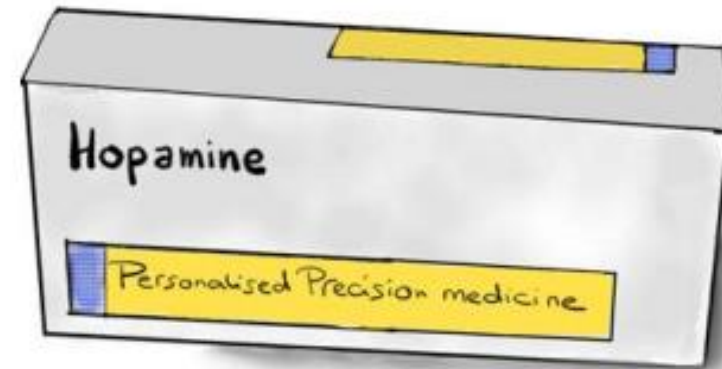


Hopamine as Personalized Medicine for Persons with Parkinson's Disease

Marina A. Noordegraaf^{a,1}, Sanne W. van den Berg^b and Bastiaan R. Bloem^{b,*}

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^b*Radboud University Medical Centre; Donders Institute for Brain, Cognition and Behaviour; Department of Neurology; Centre of Expertise for Parkinson & Movement Disorders, Nijmegen, The Netherlands*



Noordegraaf, JPD, 2023

Tom Isaacs: “This is a time
of cautious hope instead of
conservative paternalism”

