IRLAB

Transforming life for people with Parkinson´s disease

– and other disorders of the brain

Capital Markets Day, March 22, 2022

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Welcome and Introduction

Moderator Mats Thoren

20 years in life science banking and investing, board member in four listed Nordic healthcare companies

A world-leading developer of **innovative drugs** for the treatment of **Parkinson's disease** and other disorders of the brain

Validation of strategy towards vision

Science → Published in high ranked publications
Recognition by independent well established scientists (2017 and onward)

Translation with high success rate → Successful clinical proof of concept for both mesdopetam and pirepemat (2019)

Innovation/Novelty → New drug classes with unique INN stems for both mesdopetam and pirepemat (2020)

Commercial value → Global licensing deal for mesdopetam (2021)

Well positioned to deliver

- Two “first in class” programs in late-stage **clinical Phase IIb**
- Addressing **large global markets**
- Partnership with **Ipsen** – a leading global neuroscience company
- Preclinical development **candidates towards** clinical Phase I
- Highly efficient **discovery platform** for **“first in class”**

Strong momentum in operations

- **Well ahead** of competition
- Mesdopetam **fully financed through Phase III** and marketing
- Strong **cash position**
- **Strong newsflow** 2022-2024

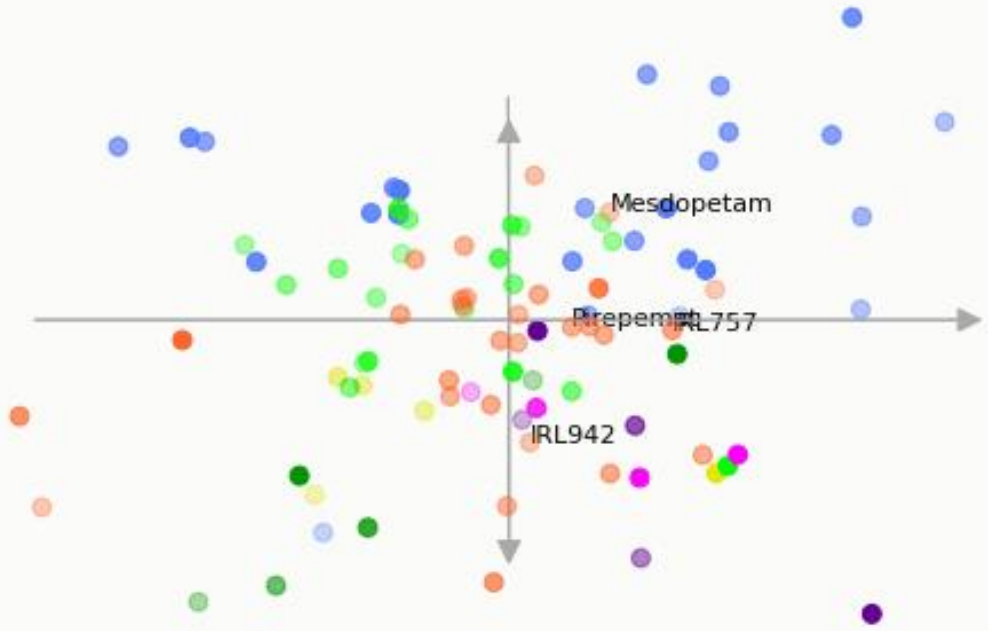
Pipeline generated by our unique proprietary technology platform: ISP

ISP – next level drug discovery

- Advanced systems biology interlinked with drug design and machine learning (ML, AI) techniques

Results in

- Discovery of novel “first in class” compounds
- Strong IPR
- Predictive science for use indication
- Improvement in probability of success



ISP – Effect spectrum of CNS classes

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Reference: In Vivo Systems Response Profiling and Multivariate Classification of CNS Active Compounds: A Structured Tool for CNS Drug Discovery. ACS Chemical Neuroscience 2017;8(4):785-97.

ISP: improvement in probability of success

Based on use of ISP, 2000 to date

Performance statistics	CD to PhI	PhI to PhII	PhII to PhIII	Estimated overall transition CD to Phase III
ISP – percentage*	50 %	80 %	50 %	20 %
Industry – percentage**	35 %	63 %	30 %	7 %

* Based on ISP-generated “first in class” candidate drugs from 2000. NB, small sample size.

** Based on Paul et al, Nat. Rev. Drug Discov. 2010

Portfolio transforming treatment of patients with Parkinson's

Mesdopetam *

PARKINSON – LEVODOPA-INDUCED DYSKINESIAS (LIDS)

PARKINSON – PSYCHOSIS

Pirepemat

PARKINSON – IMPAIRED BALANCE AND FALLS

PARKINSON – DEMENTIA

IRL942

NEUROLOGY– COGNITIVE IMPAIRMENT

IRL757

NEUROLOGY– APATHY

P003

PARKINSON – DOPAMINE SUBSTITUTION

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* Currently in development with partner Ipsen who holds an exclusive global license to develop and commercialize mesdopetam

Path to deliver strong growth

Foundation
for transformative treatments

2020 – 2023

Mesdopetam

Successful completion of Phase IIb/III study

Pirepemat

Successful completion of Phase IIb study

Pipeline

Initiate Phase I studies with IRL942 and IRL757

Initiate preclin development of CD from P003

Deepen AI in the ISP methodology

Business development

Licensing agreement for the mesdopetam project

Continued work toward new revenue-generating collaborations

Building
for the future

2023 – 2025

Mesdopetam

Phase III studies initiated with partner Ipsen

Pirepemat

Initiating Phase III studies

Pipeline

Development of new drug candidates toward clinical proof-of-concept in phase Ib and phase II – IRL942, IRL757, CD from P003

Continued ISP development

Business development

Pirepemat partnering &

Continued work toward new revenue-generating collaborations

Delivering
first-in-class treatments

2025 – 2027

Mesdopetam

Finalizing Phase III and apply for marketing authorization

Pirepemat

Finalizing Phase III and apply for marketing authorization

Pipeline

Development of new drug candidates: Phase II PoC and initiation of Phase III (IRL 942, IRL757 and CD from P003)

Upcoming newsflow 2022-2024

2022

- Mesdopetam Phase IIb LIDs TLR**
- Pirepemat IIb FPFV*
- IRL942 through preclin dev
- IRL757 through preclin dev
- P003 first CD

2023

- Pirepemat Phase IIb Top Line Res
- IRL942 Phase I FPFV
  - IRL942 phase 1 TLR
- IRL757 Phase I FPFV
  - IRL757 phase I TLR
- P003 CD Phase I FPFV
- Mesdopetam Phase III LIDs
- Mesdopetam Phase II PD-P

2024

- Pirepemat Phase III FPFV
- IRL942 Phase IIa FPFV
- IRL757 Phase IIa FPFV
- P003 CD Phase I TLR
- Mesdopetam market preparations
- Mesdopetam Phase II PD-P

- IPSEN led activity & decision

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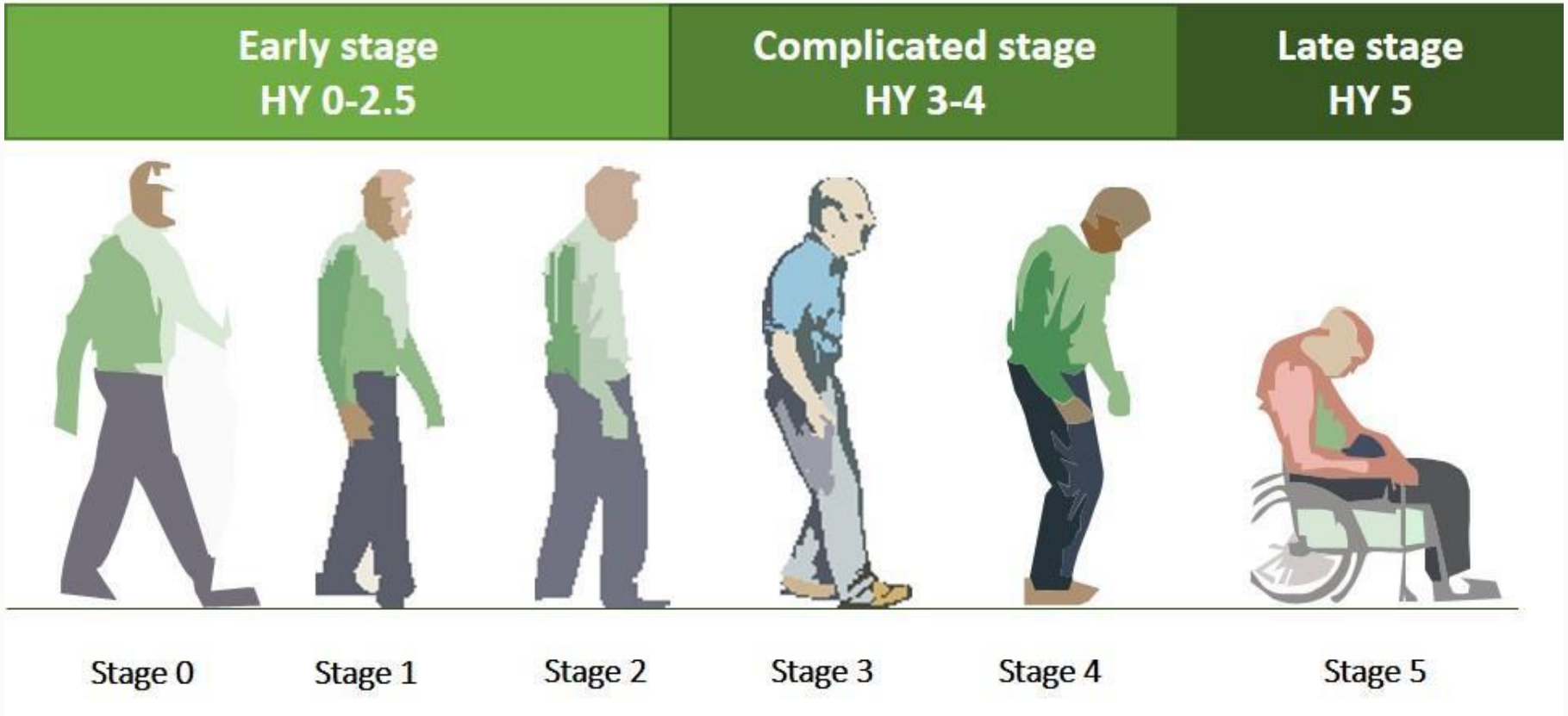
* FPFV: First Patient First Visit
** TLR: Top Line Results

Parkinson’s disease stages



	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Prevalence		**13%**	**29%**	**34%**	**17%**	**7%**

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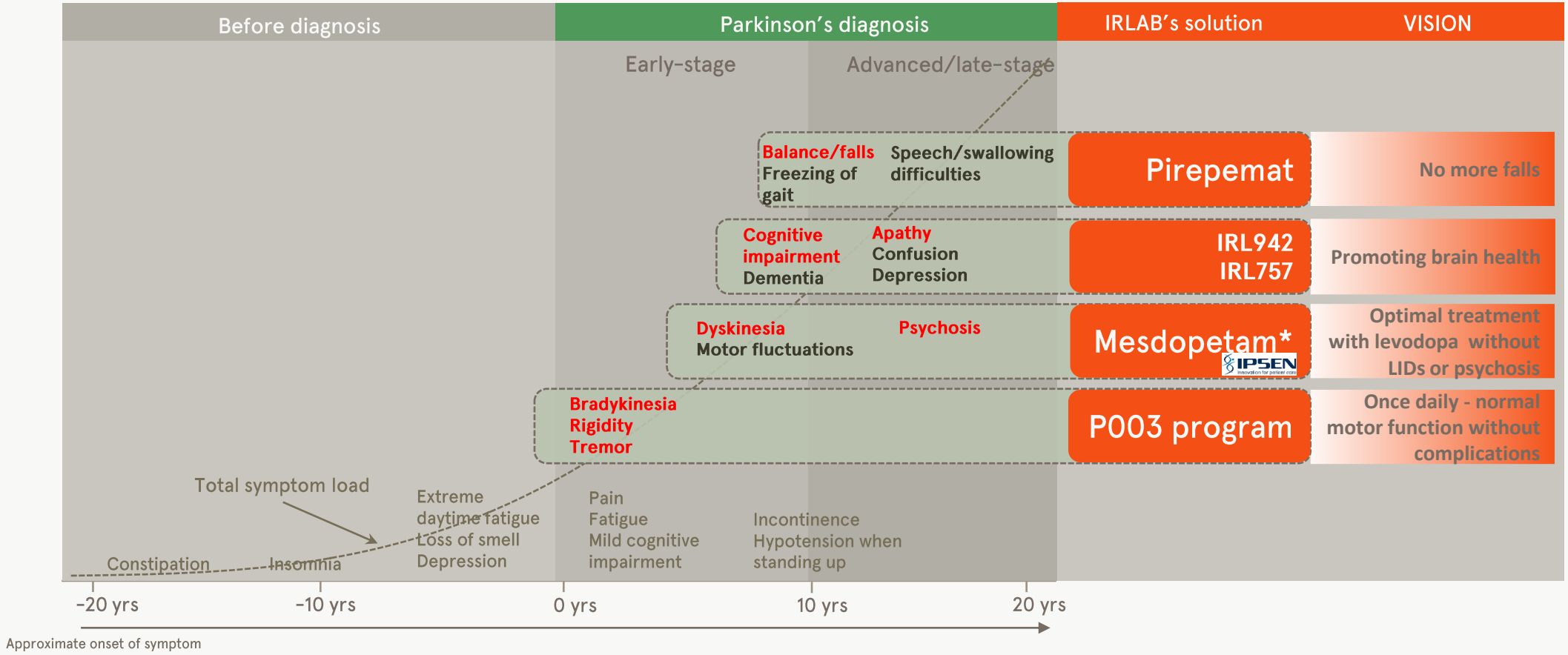
- Adapted from Claesson I, Better Balance with Somatosensory Exercises-a Parkinson Perspective Thesis · January 2018
- Prevalence: Enders et al, 2017

Living with Parkinson's:
IRLAB transforms the treatment algorithm



References: Based on Kalia, LV. and Lang, AE. Lancet 2015;386-912.

* Currently in development with partner Ipsen who holds an exclusive global license to develop and commercialize mesdopetam

Q&A

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Partnering with IRLAB

Stephen Glyman Senior Vice President and
Head of Neuroscience Therapeutic area at Ipsen

- Currently in development with partner Ipsen who holds an exclusive global license to develop and commercialize mesdopetam
- (https://www.irlab.se/press-releases/ipsen-and-irlab-enter-exclusive-worldwide-licensing-agreement-aimed-to-improve-the-lives-of-people-living-with-parkinsons-disease//)

IPSEN
Innovation for patient care

Ipsen-IRLAB

March 2022

About Ipsen

Our mission

We are dedicated to prolonging and improving patients' lives and health outcomes.

Our vision

To be a leading global, mid-sized biopharmaceutical company with a focus on transformative medicines in Oncology, Rare Disease & Neuroscience.

Our key figures

€2.9bn

2021 Group sales
up by +12.3%[1]

In 2021, Ipsen invested

€428.4m

in R&D, equivalent to
14.9% of sales

25+	Medicines in over 100 countries
5,700+	Colleagues worldwide
7	Manufacturing facilities
4	Global R&D hubs: Paris-Saclay, France; Oxford, U.K.; Cambridge, U.S.; Shanghai, China
30+	Countries with a direct presence

(1) At constant exchange rates and consolidation scope

Bolstering an innovative pipeline

Our pipeline is driven by external innovation. We encourage open innovation through trusted partnerships with biotech and academic institutions.

Our pipeline includes innovative new molecules, including small molecules and neurotoxins as well as lifecycle management (LCM) of our well-established products.

Partnerships focused on our 3 key pillars

Accelerated external innovation efforts to build a high-value sustainable pipeline: Focus on assets across all stages of development

Oncology

- Solid & hematological tumors
- Niche tumors or biomarker segments in broad tumors
- Lifecycle management (LCM) potential

Rare Disease

- Disease areas with unmet needs beyond endocrinology & bone disease
- Established & innovative technologies including gene-based modalities

Neuroscience

- Focus on in-house recombinant long-acting toxins & TSIs
- Rare neurological disorders

TSI: Targeted secretion inhibitorDon't need this as it is spelt out aboves.

Why mesdopetam for Ipsen?

Matt & Suzanne
Scientific Intelligence dpt.
& Communication dpt.
Milton Park, UK

IRLAB's mesdopetam: Fit with Ipsen's Neuro Strategy

- **Novel mechanism of action with strong scientific rationale**
  - Dopamine D3 receptor has been demonstrated in preclinical studies (e.g., knock-out studies) to be involved in the development of levodopa-induced dyskinesia (LID). The results of the Phase 1 and Phase 2 trials further support the involvement of D3 in LID.
- **Promising clinical data**
  - Phase 1b: Good safety and tolerability and improvement in Unified Dyskinesia Rating Scale (UDysRS) score
  - Phase 2a: Good safety and tolerability and dose-dependent increase in "good ON-time" by ≈ 4.5 hours and corresponding decrease in "bad ON-time"
  - Phase 2b: Ongoing, study design incorporates guidance from highly experienced advisors, FDA, and selection of expert sites
- **Entry into an indication with substantial unmet medical need**
  - An estimated 117k and 120k patients in the US and EU respectively suffer from bothersome LID and could be eligible for a novel pharmacological treatment
  - LID limits the optimization of levodopa and ultimately leads to suboptimal control of PD symptoms
- **LCM potential beyond PD-LID**
  - Phase 2-ready for PD psychosis
  - Tardive dyskinesia also provides an additional possible LCM opportunity

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Innovation for patient care

ALL-ALL-004381

Q&A

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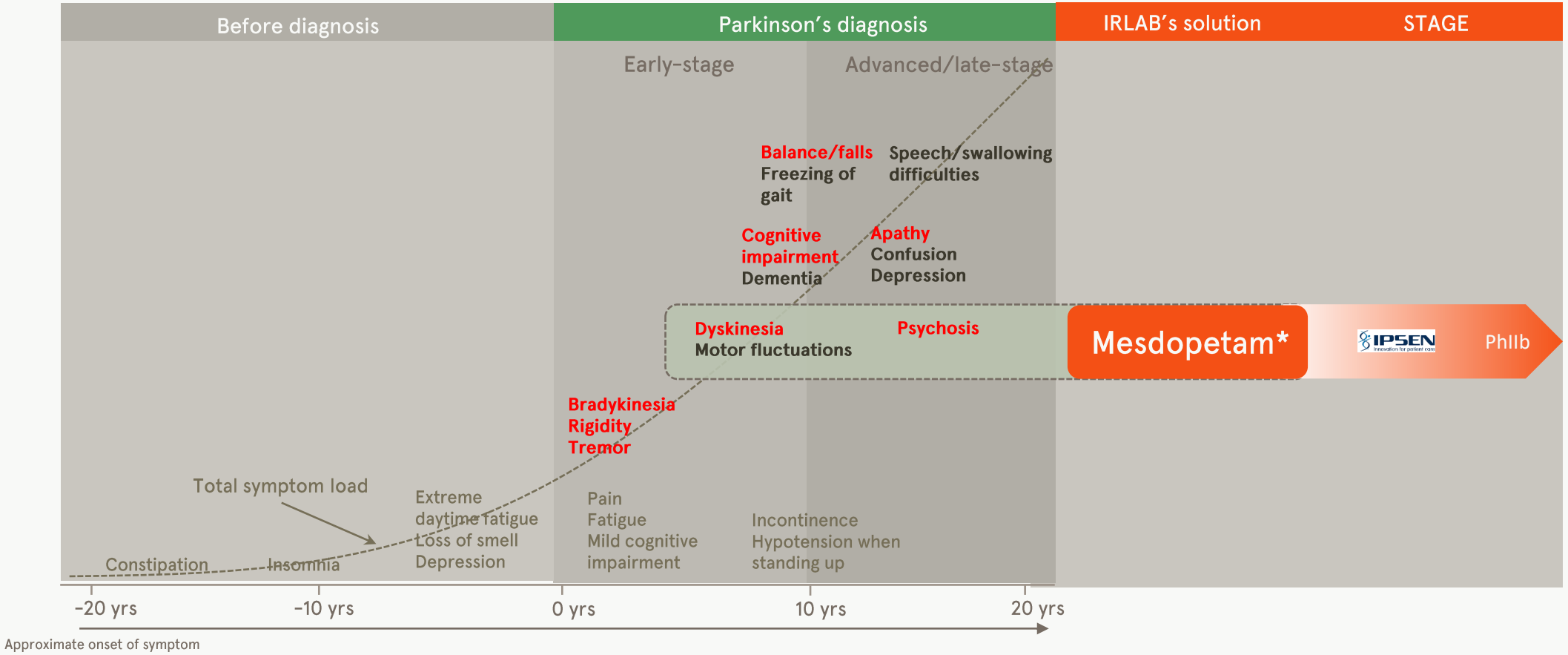
Mesdopetam (IRL790)

- Improve motor function through prevention and reduction of dyskinesias (LIDs)
- Treatment and prevention of psychosis in Parkinson’s (PD-P)
- Potential opportunity in TD

- Currently in development with partner Ipsen who holds an exclusive global license to develop and commercialize mesdopetam
- (https://www.irlab.se/press-releases/ipsen-and-irlab-enter-exclusive-worldwide-licensing-agreement-aimed-to-improve-the-lives-of-people-living-with-parkinsons-disease//)

Living with Parkinson's: IRLAB transforms the treatment algorithm



References: Based on Kalia, LV. and Lang, AE. Lancet 2015;386-912.

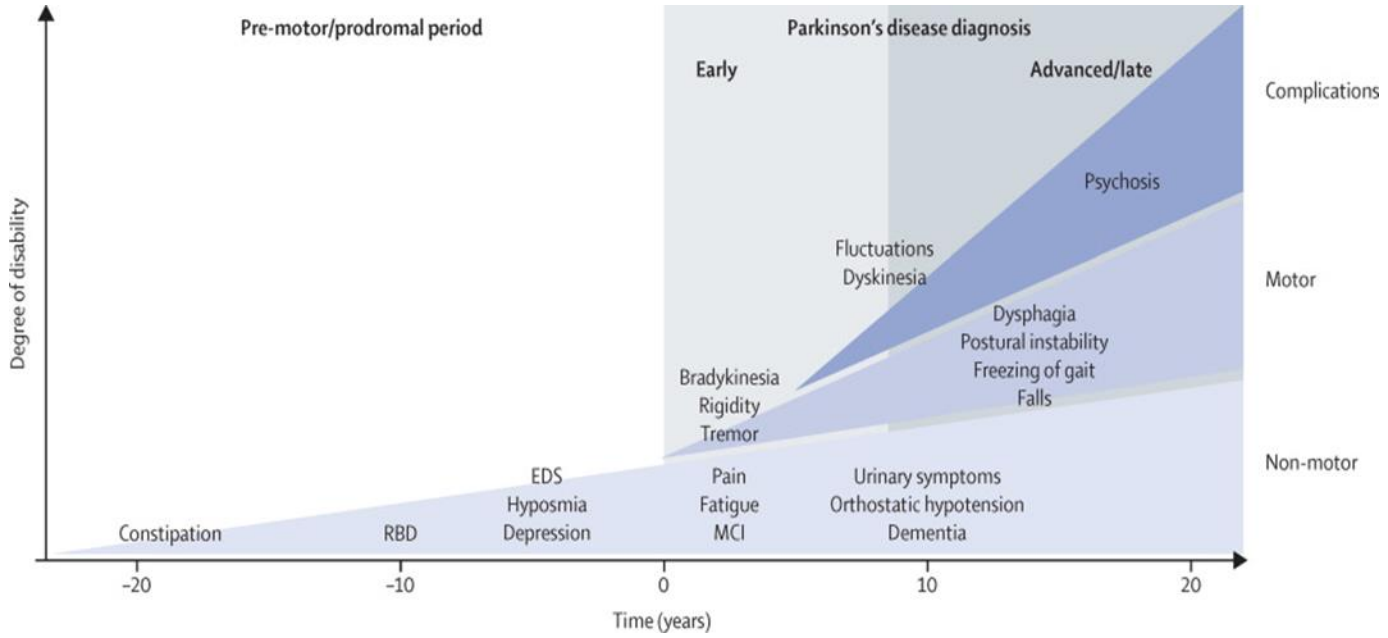
* Currently in development with partner Ipsen who holds an exclusive global license to develop and commercialize mesdopetam

Important motor and non-motor outcomes in PD

Karl Kieburtz MD MPH
Professor of Neurology
University of Rochester School of Medicine

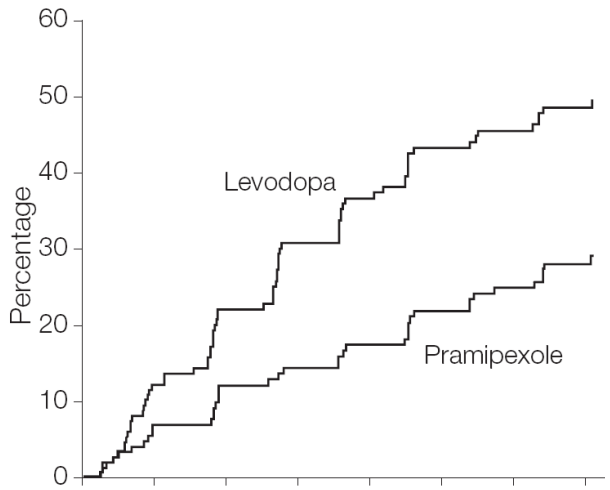
President, Clintrex LLC

Major PD disability occurs late in the clinical course: Motor fluctuations and Hallucinations are common, and are worsened (or unaided) by current therapies

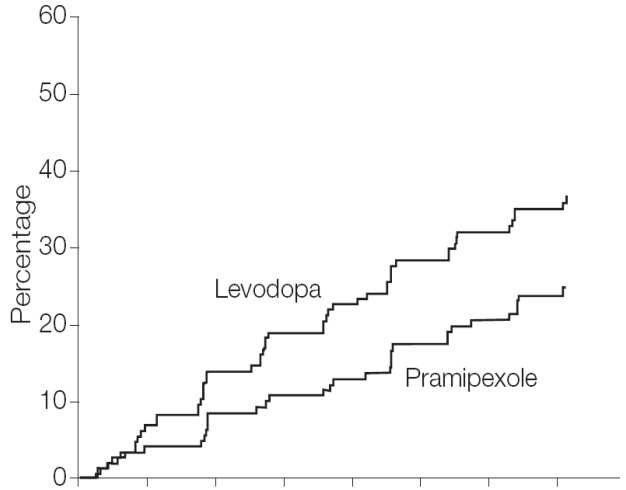


CALM PD:Pramipexole vs. Levodopa as Initial Treatment for PD Demonstrated that 50% of treated PD have motor complications by 2 years

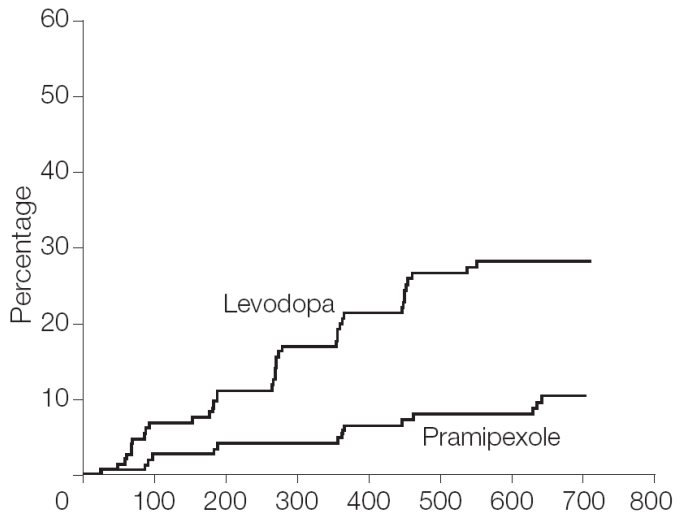
first dopaminergic complication



wearing-off



dykinesias



PSG JAMA 2000; 284:1931-1938

Eventually, most of the day is 'Bad time'- 'off' or 'on' with troublesome dyskinesias:
DBS helps (medication does not), but invasive with significant morbidities

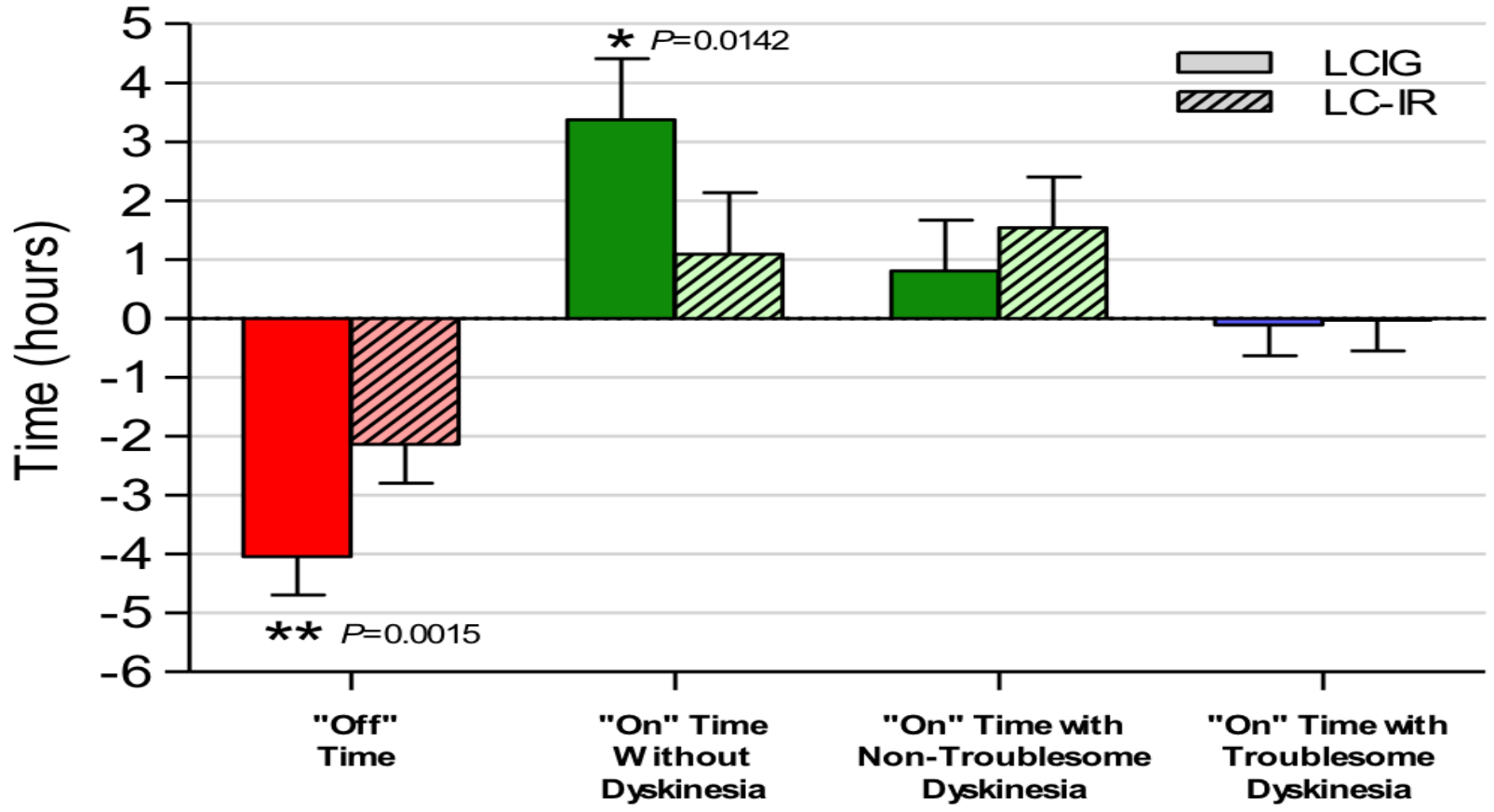
Table 2. Patient Motor Diary Outcomes

Time	Best Medical Therapy (n = 134)			Deep Brain Stimulation (n = 121)			Best Medical Therapy Minus Deep Brain Stimulation	
	Baseline, Mean (SD)	6 mo, Mean (SD)	Mean Difference (95% CI)	Baseline, Mean (SD)	6 mo, Mean (SD)	Mean Difference (95% CI)	Mean Difference (95% CI)	*P* Value[a]
On, h/d[b]								
Without troublesome dyskinesia	7.0 (2.9)	7.1 (3.3)	0 (–0.5 to 0.5)	6.4 (2.7)	10.9 (4.2)	4.6 (3.8 to 5.3)	–4.5 (–5.4 to –3.7)	<.001
With troublesome dyskinesia	4.2 (3.1)	3.9 (3.3)	–0.3 (–0.8 to 0.3)	4.4 (3.1)	1.8 (3.0)	–2.6 (–3.3 to –2.0)	2.3 (1.5 to 3.2)	<.001
Off, h/d[b]	5.6 (2.9)	5.7 (2.8)	0 (–0.4 to 0.5)	5.9 (2.6)	3.4 (3.1)	–2.4 (–3.1 to –1.8)	2.5 (1.7 to 3.2)	<.001
Asleep, h/d	7.1 (1.7)	7.3 (2.0)	0.3 (0 to 0.6)	7.3 (1.8)	7.7 (2.0)	0.4 (0 to 0.7)	–0.1 (–0.6 to 0.4)	.66

Abbreviation: CI, confidence interval.
[a] Test for the change scores from baseline to 6 months between the best medical therapy group and the deep brain stimulation group.
[b] "On" and "off" time are described in the "Study Procedures" section of the "Methods."

JAMA. 2009;301(1):63-73. doi:10.1001/jama.2008.929

Intestinal infusion (perhaps SQ now) helps fluctuations, but still invasive
Unlike DBS, little observed impact on troublesome dyskinesias

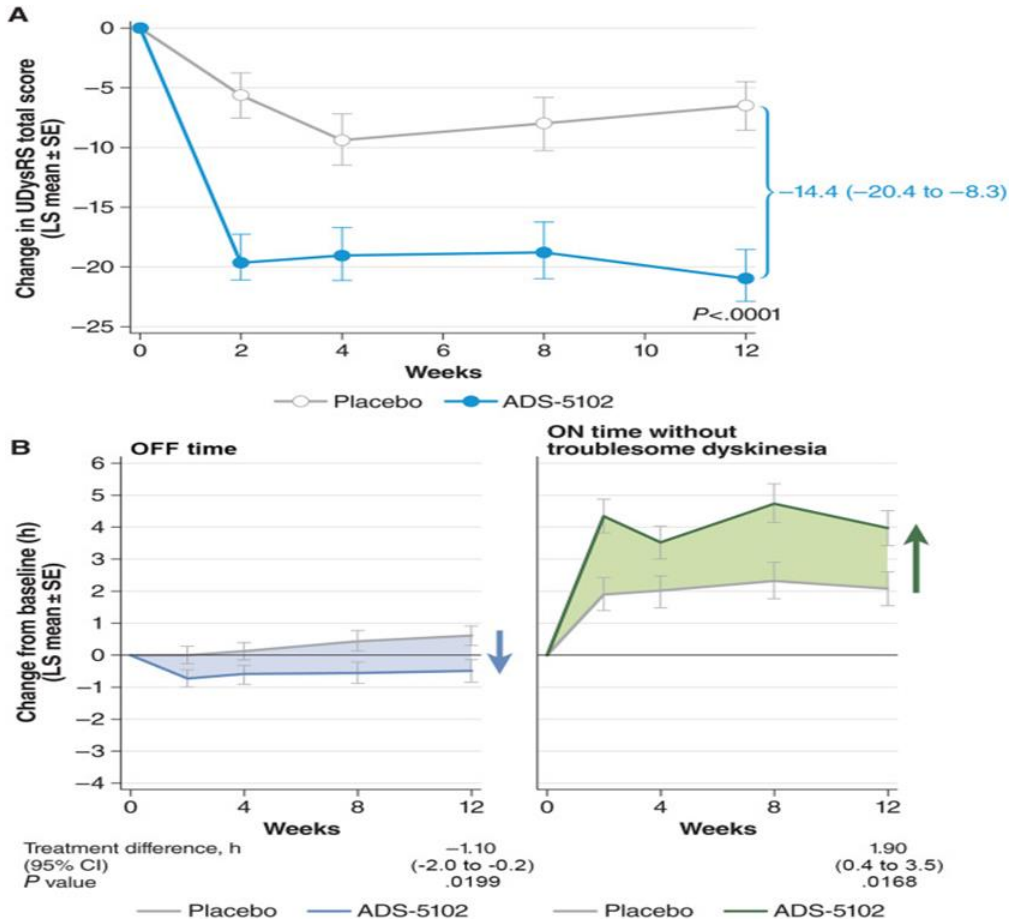


OFF time Reduction Approximately an Hour with available oral Adjunctive Treatment- modest effects

Drug	Duration	Active	Placebo	Treatment Effect
pramipexole	32 week	31%* (1.8 h)	7% (0.2 h)	24% (1.6 h)
pramipexole	40 week	15%*	3%	12%
ropinirole	12 week	23%*	4%	19%
ropinirole	26 week	11.7%*	5%	6.7%
ODT selegiline	12 week	32% (2.2 h)*	9% (0.6 h)	23% (1.6 h)
rasagiline (0.5mg)	26 week	23% (1.4h)*	15% (0.9 h)	8% (0.5 h)
rasagiline (1.0mg)	26 week	29% (1.8h)*	15% (0.9 h)	14% (0.9 h)
rasagiline	18 week	21% (1.2 hr)*	7% (0.4 h)	14% (0.8 h)
tolcapone (100mg tid)	12 week	32% (2.3 h)	20% (1.4 h)	12% (0.9 h)
tolcapone (200mg tid)	12 week	48% (3.2 h)*	20% (1.4 h)	28% (1.8 h)
tolcapone (100mg tid)	12 week	31.5%*	11%	20.5%
entacapone	18 week	21% (1.2 h)*	7% (0.4 h)	14% (0.8 h)
entacapone	24 week	25.8% (1.6 h)*	13.4% (0.9 h)	12.4% (0.7 h)
entacapone	24 week	23.6% (1.3 h)*	1.9% (0.1 h)	21.7% (1.2 h)

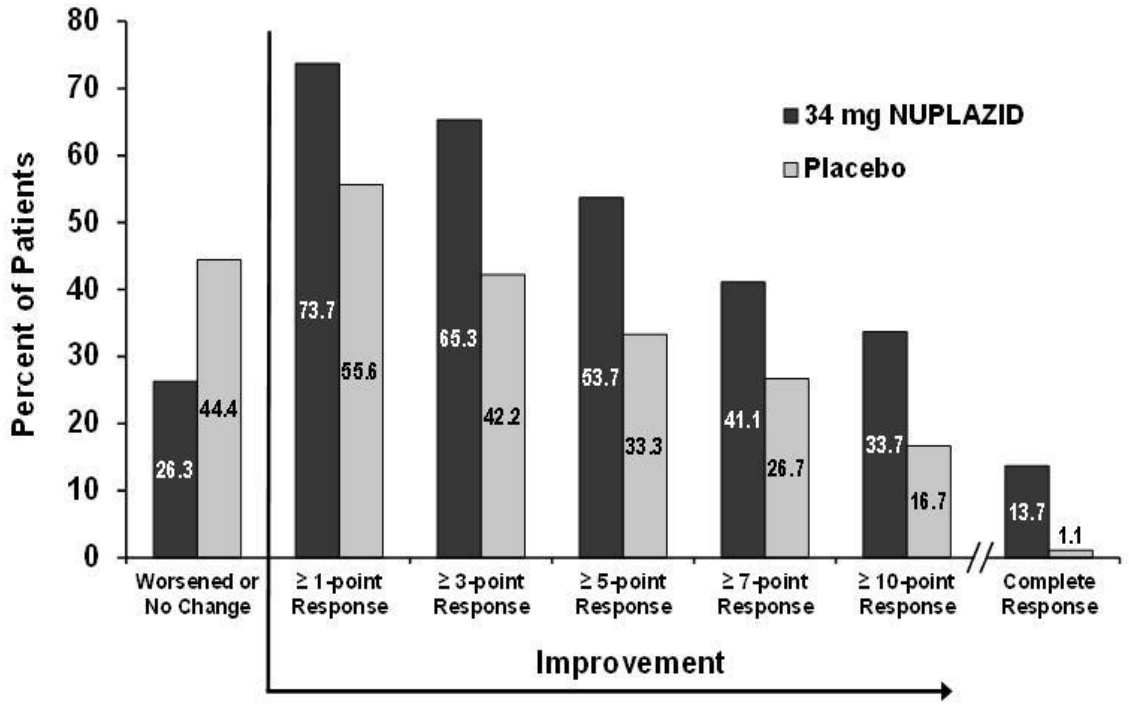
Pahwa, R., et al., Neurology 2006;66:983–995 Appendix E-1

Amantadine can decrease dyskinesias, and thereby increase ‘good on time’- on without troublesome dyskinesias- but many PD patients do not tolerate an adequate dosage, in part due to mental side effects



Movement Disorders, Volume: 32, Issue: 12, Pages: 1701-1709, First published: 21 August 2017, DOI: (10.1002/mds.27131)

Hallucinations are a dosage limiting problem in PD treatment
The only available treatment can work well, in a subset of PD



PD Patients Continue to Have Persistent Motor Fluctuations and Hallucinations Despite Current Medical Options Representing Significant Unmet Needs

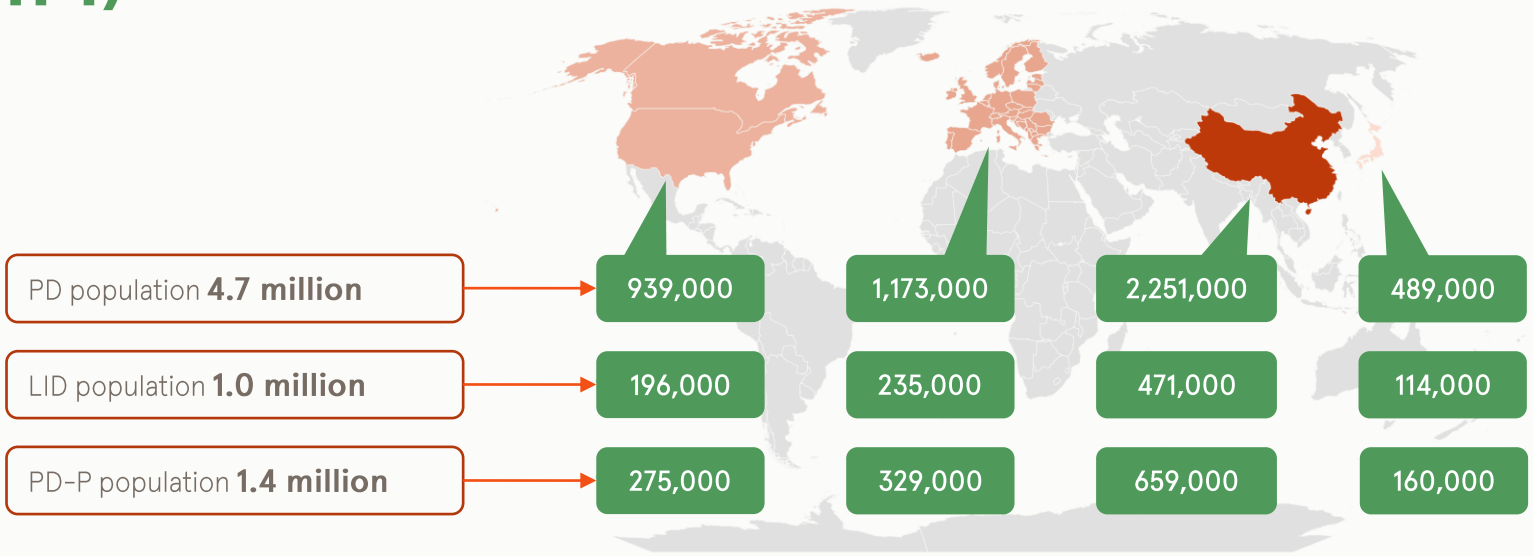
- Off time persists despite available treatments
  - 2.3 hours OFF time at 12 weeks despite double-dummy optimal titration of duopa
  - Rytary end of study: 3.9 hours OFF time
- **Persistent OFF episodes represents a significant unmet medical need**
- **Dyskinesias lack a well tolerated oral treatment**
- **An intervention that decreases troublesome dyskinesias can increase the 'good time' in PD- on time without troublesome dyskinesias**

- **A broadly effective treatment for hallucinations that does not worsen underlying PD features is urgently needed**

Q&A

Mesdopetam – Market opportunity in the largest markets (8MM)

(US, DE, UK, FR, ES, IT, CH, JP)



Total population eligible for mesdopetam within PD

2.4 million patients

There might be an overlap between patients with LID and patients with PD-P which would decrease the total population.

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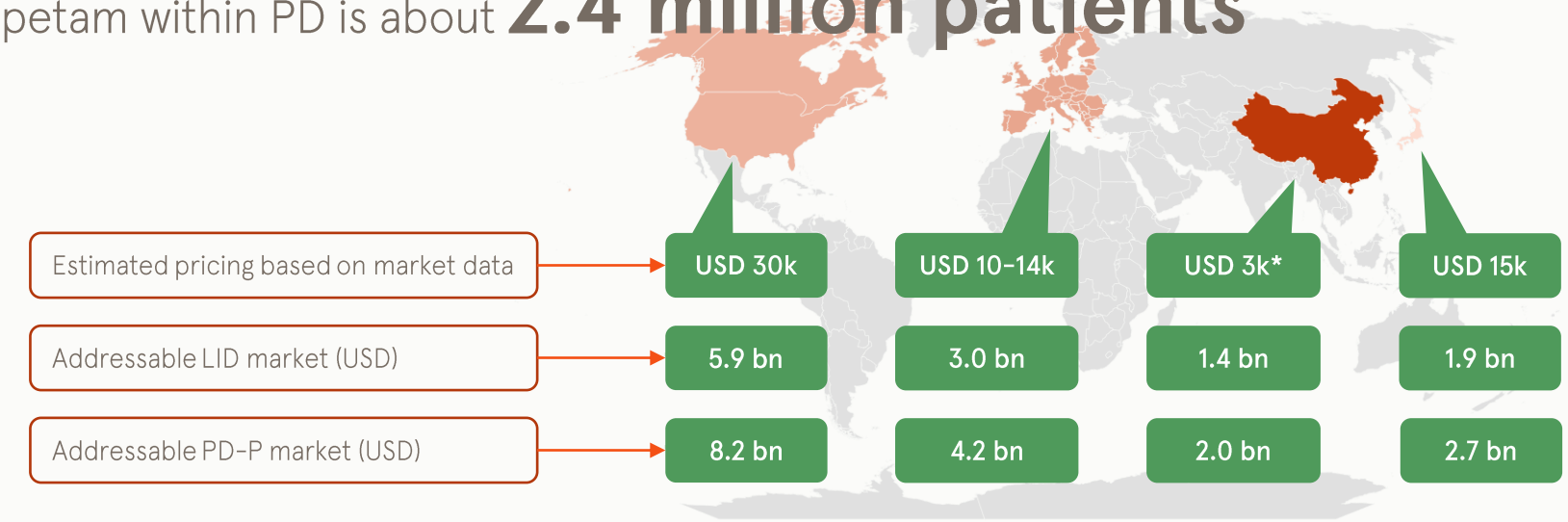
Source: Global Data 2020. Europe represented by "EU5" (DE, FR, IT, SP and UK)

Mesdopetam – Market opportunity

Total population eligible for mesdopetam within PD is about **2.4 million patients**

Peer prices 2021 are about
USD 30,000 per year
in the US in both LIDs and PD-P
(Amantadin for PD-LIDs and Pimavanserin for PD-P)



Total addressable market in LIDs is about **USD 12.3 bn**

Total addressable market in PD-P is about **USD 17.2 bn**

Total addressable market LIDs and PD-P
USD 29.5 bn

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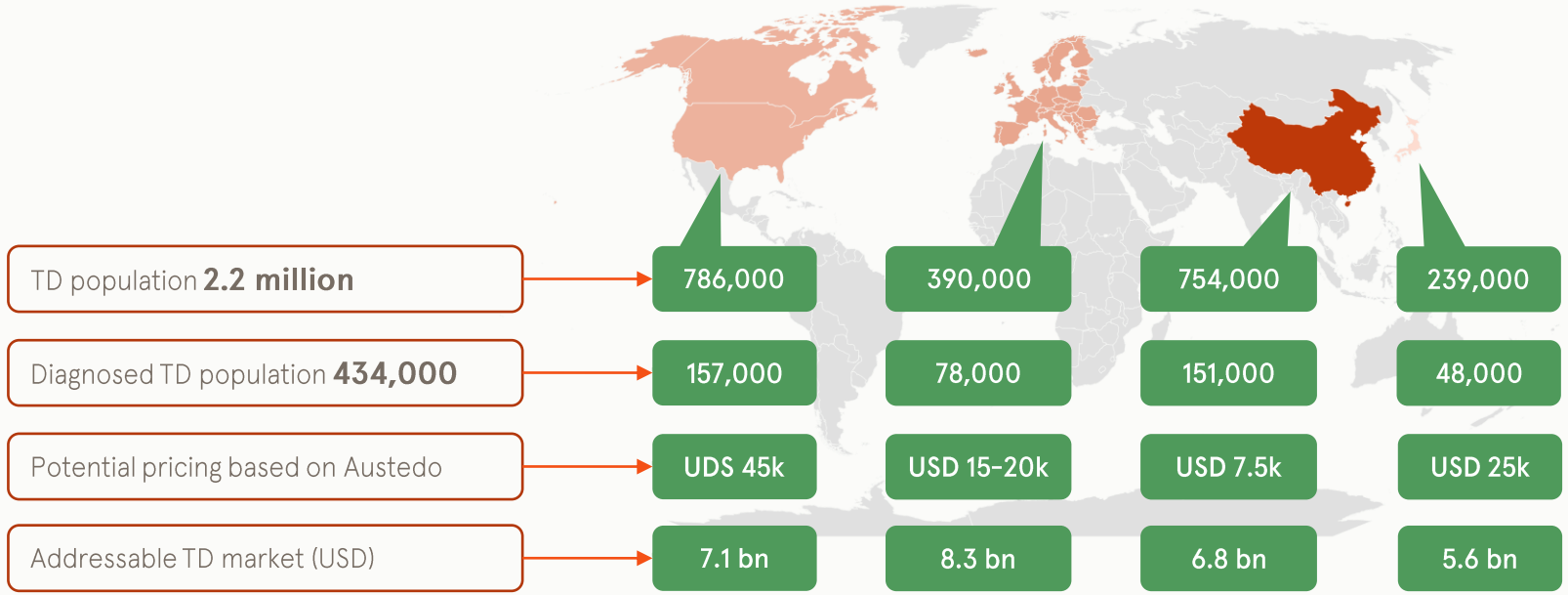
Source: Global Data 2020. Europe represented by "EU5" (DE, FR, IT, SP and UK)

Mesdopetam – Market opportunity

Peer prices 2021 are about **USD 45,000** per year in the US

(Using data for Austedo with Ingrezza being even higher)



Total addressable market for mesdopetam within TD is about **USD 11 bn**

Source: Global Data 2020. Europe represented by "EU5" (DE, FR, IT, SP and UK)

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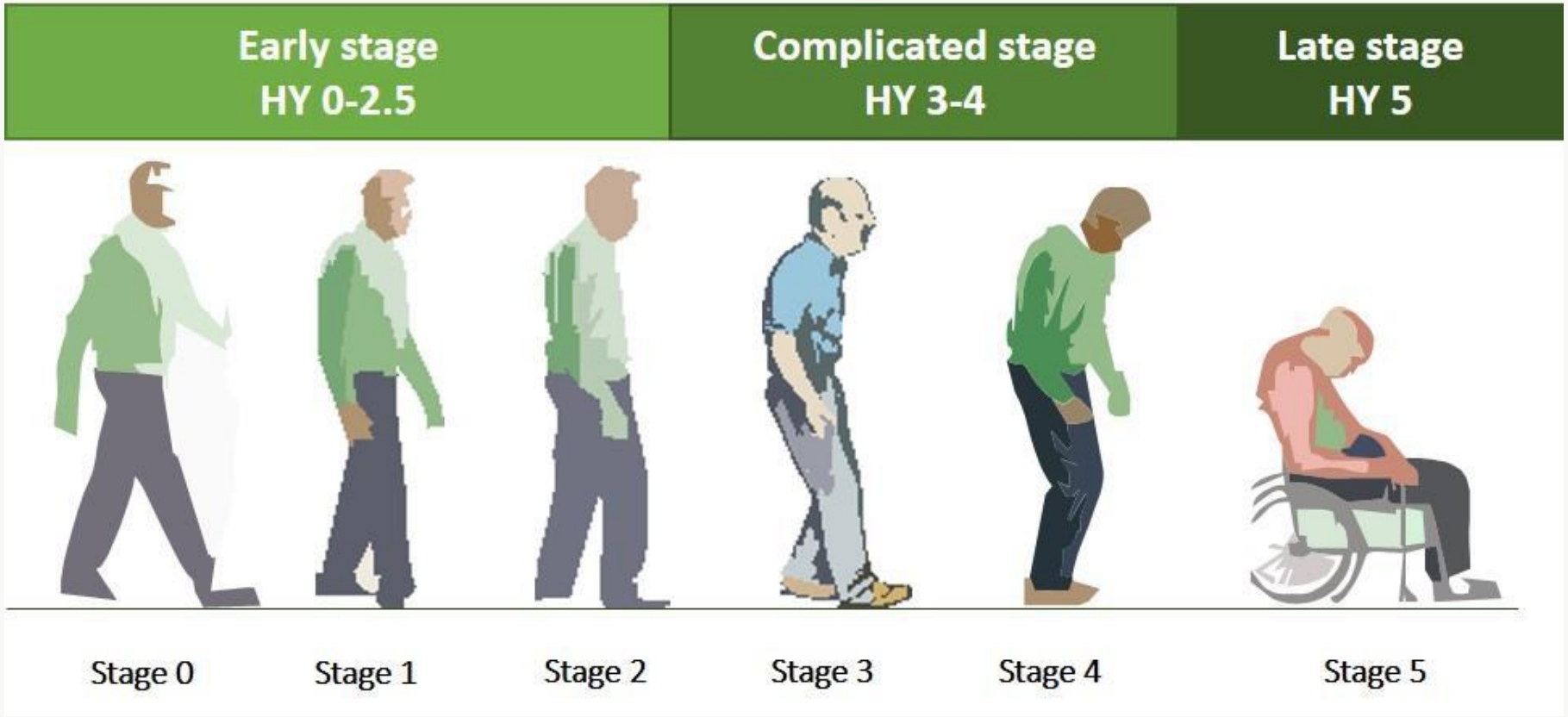
Pirepemat (IRL752)

Improve balance and reduce falls in Parkinson’s (PD-Falls)

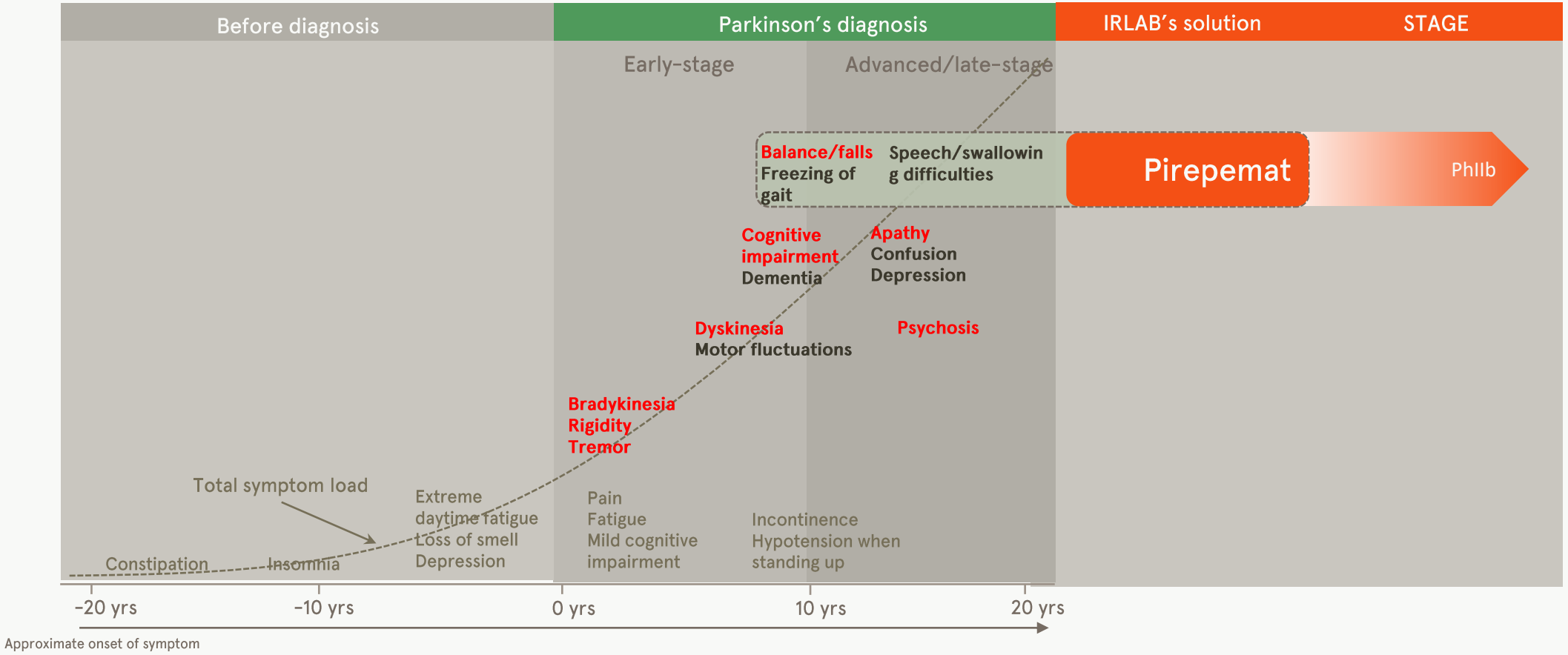
Parkinson’s disease stages



	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4	Stage 5
Prevalence		**13%**	**29%**	**34%**	**17%**	**7%**

- Adapted from Claesson I, Better Balance with Somatosensory Exercises-a Parkinson Perspective Thesis · January 2018
- Prevalence: Enders et al, 2017

Living with Parkinson's: IRLAB transforms the treatment algorithm



References: Based on Kalia, LV. and Lang, AE. Lancet 2015;386-912.

Balance and falls in Parkinson's disease

Professor Bas Bloem

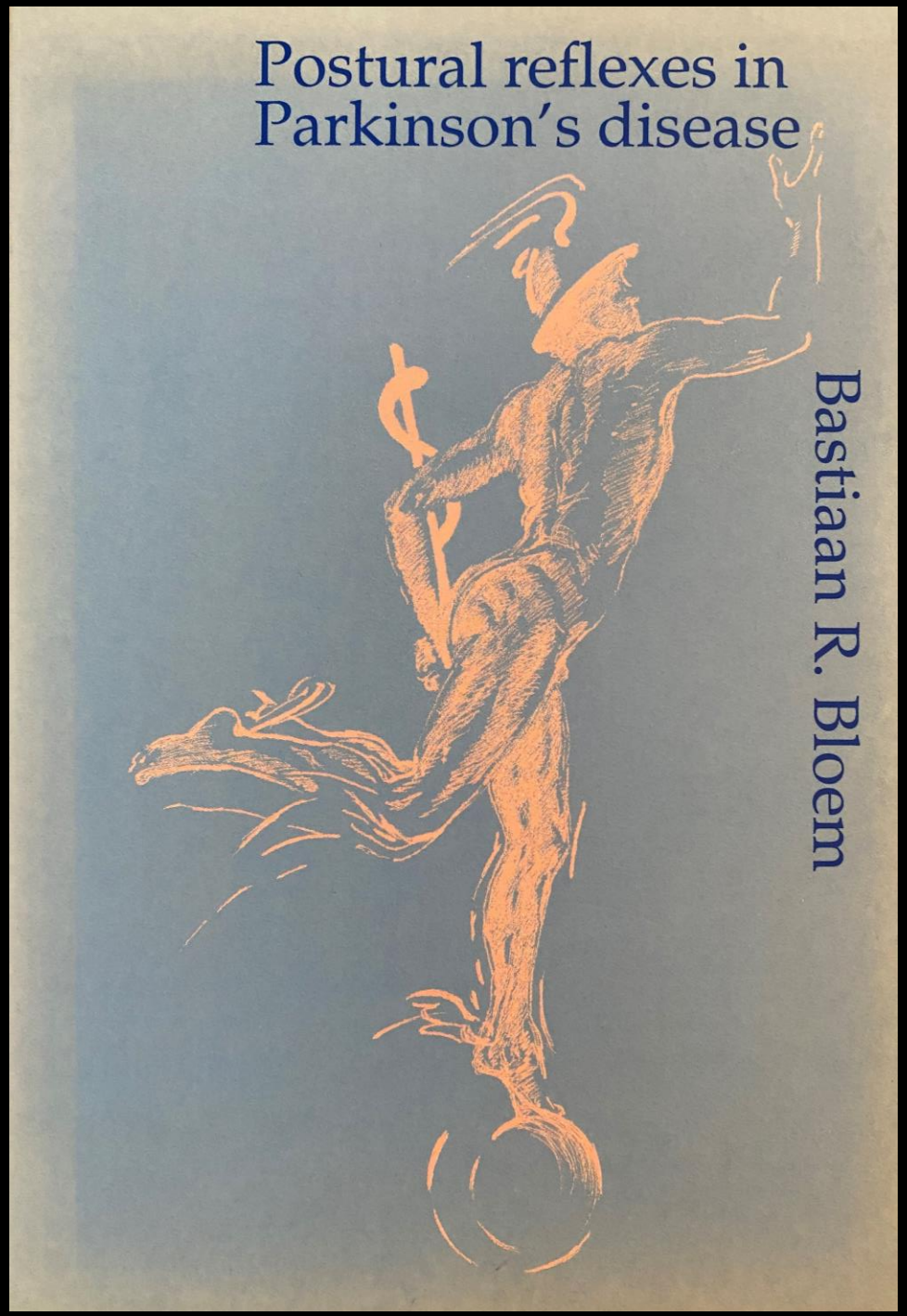
Centre of Expertise for Parkinson & Movement Disorders

Radboud University Medical Centre

@BasBloem

Radboudumc

Parkinson's Foundation
CENTER OF EXCELLENCE



1994 (!)

March 21, 2022 (!)

Acceptance of Interventions for preventing falls in Parkinson's disease from Cochrane Evidence Production & Methods Directorate - [EMID:731cab2a8a7ddd5b]

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Aan Bloem, Bas

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CC: tlasserson@cochrane.org, covelman@cochrane.org, "Natalie Allen" natalie.allen@sydney.edu.au, "Lorena Rosa Almeida" lorenasantos@gmail.com, "Bastiaan Bloem" bas.bloem@radboudumc.nl, "Samyra Keus" s.h.j.keus@olvg.nl, "Niklas Löfgren" niklas.lofgren@neuro.uu.se, "Alice Nieuwboer" alice.nieuwboer@faber.kuleuven.be, "Catherine Sherrington" cathie.sherrington@sydney.edu.au, "Geert Verheyden" geert.verheyden@faber.kuleuven.be, "Tiê Yamato" tiparma@gmail.com

21 Mar 2022

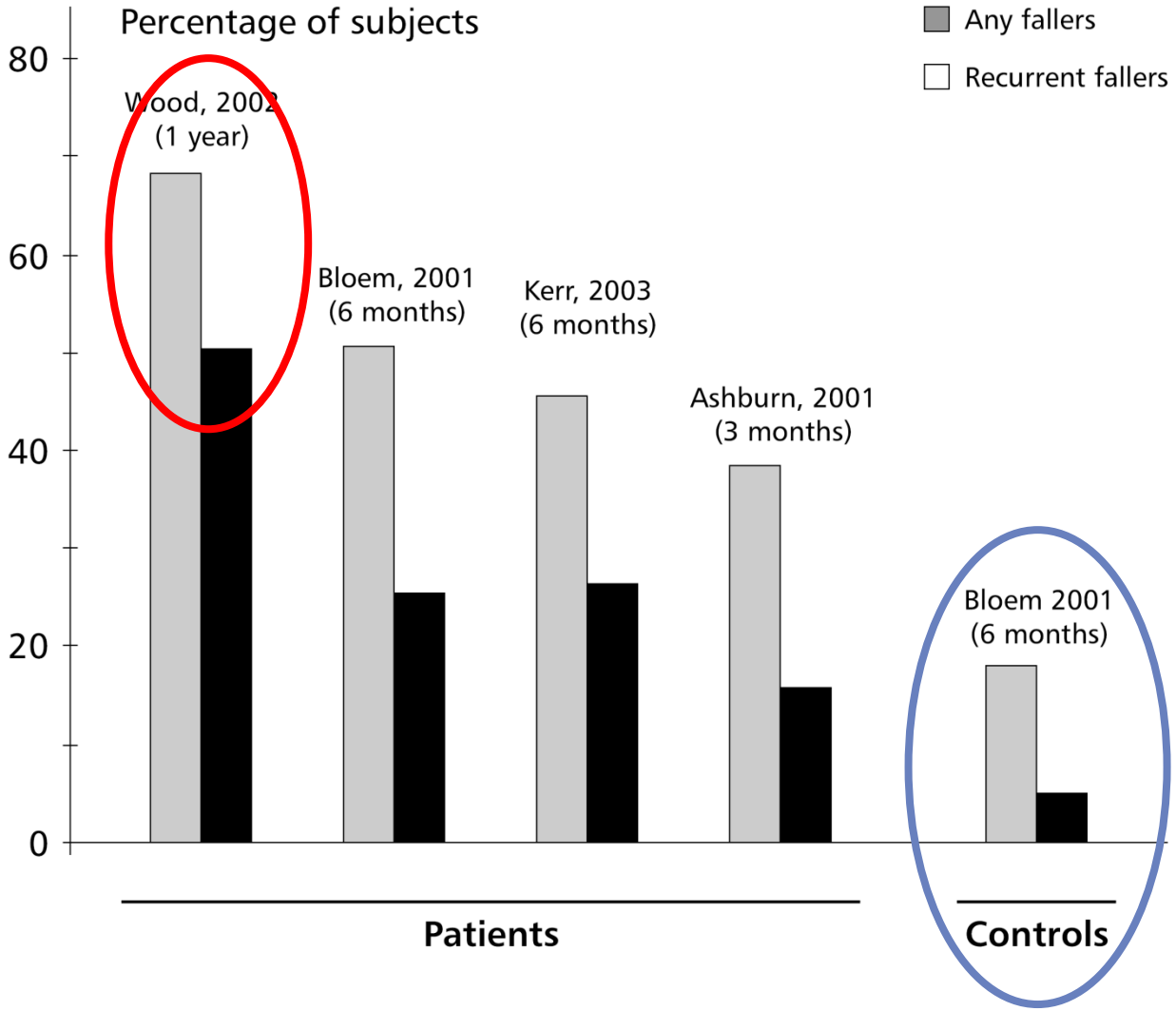
RE: Interventions for preventing falls in Parkinson's disease (MS# COCHRANEEMD-2021-00069R1), Colleen G Canning; Natalie Allen; Lorena Rosa Almeida; Bastiaan Bloem; Samyra Keus; Niklas Löfgren; Alice Nieuwboer; Catherine Sherrington; Geert Verheyden; Tiê Yamato (Evidence Production & Methods Directorate)

Dear Dr Colleen Canning,

We are very pleased to accept your draft Interventions for preventing falls in Parkinson's disease for publication in the Cochrane Database of Systematic Reviews (CDSR) in the Cochrane Library. Your article will now be sent for copy editing, and you will receive the copy-edited article to review.

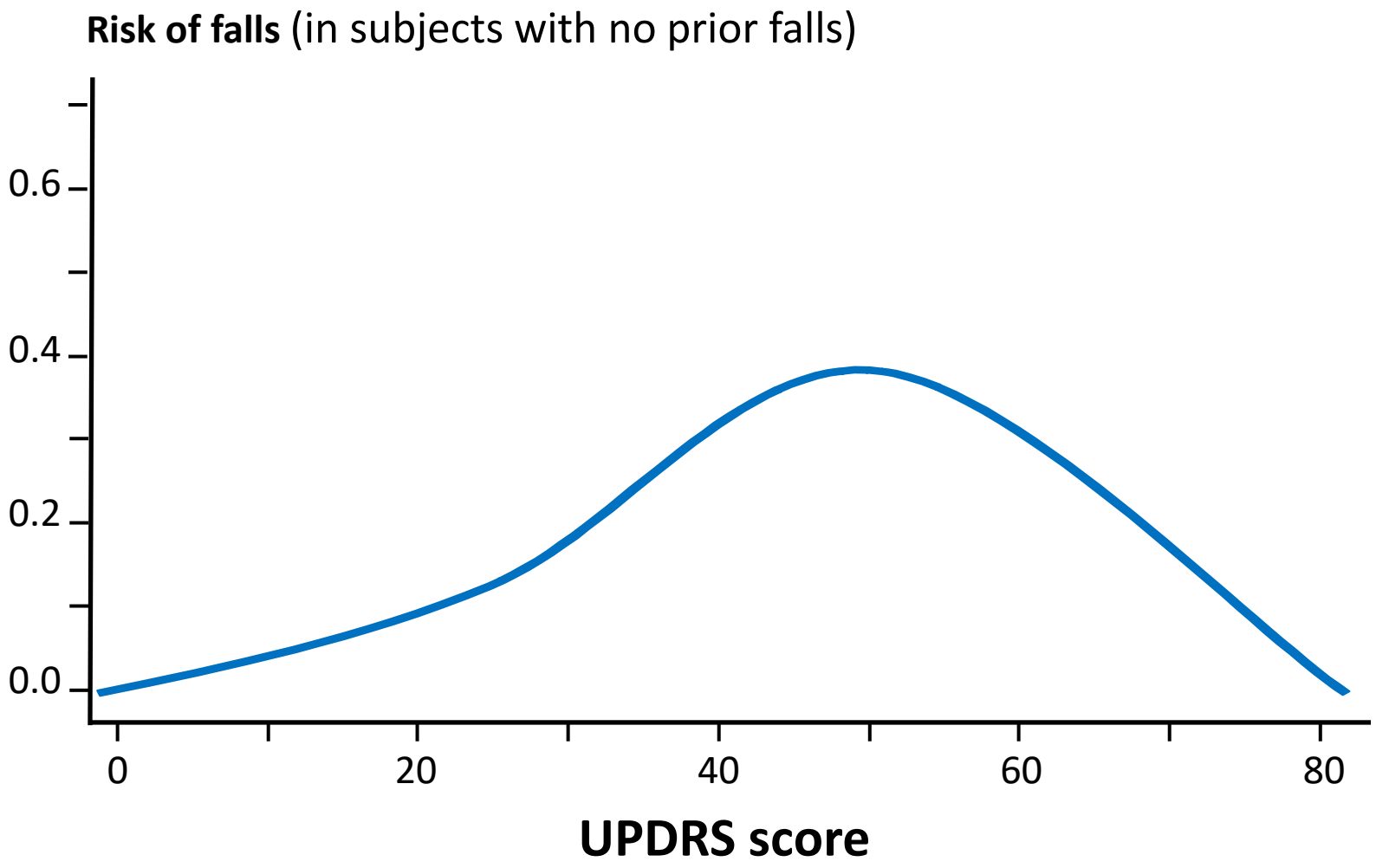
Impact of falls

Is falling an issue in Parkinson disease?



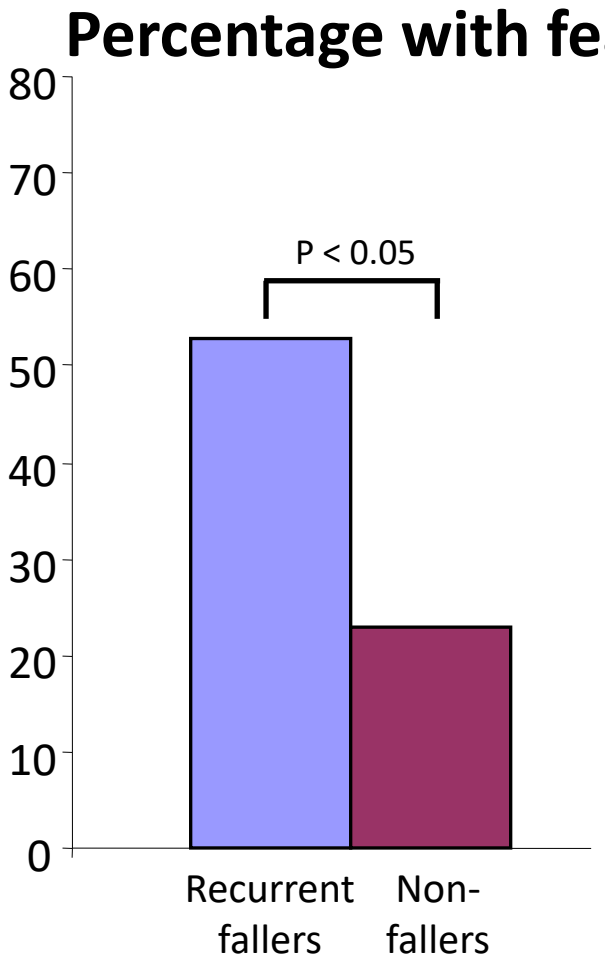
Bloem et al., Mov Disord 2004;19:871-884

Falls are a “late” feature in Parkinson’s



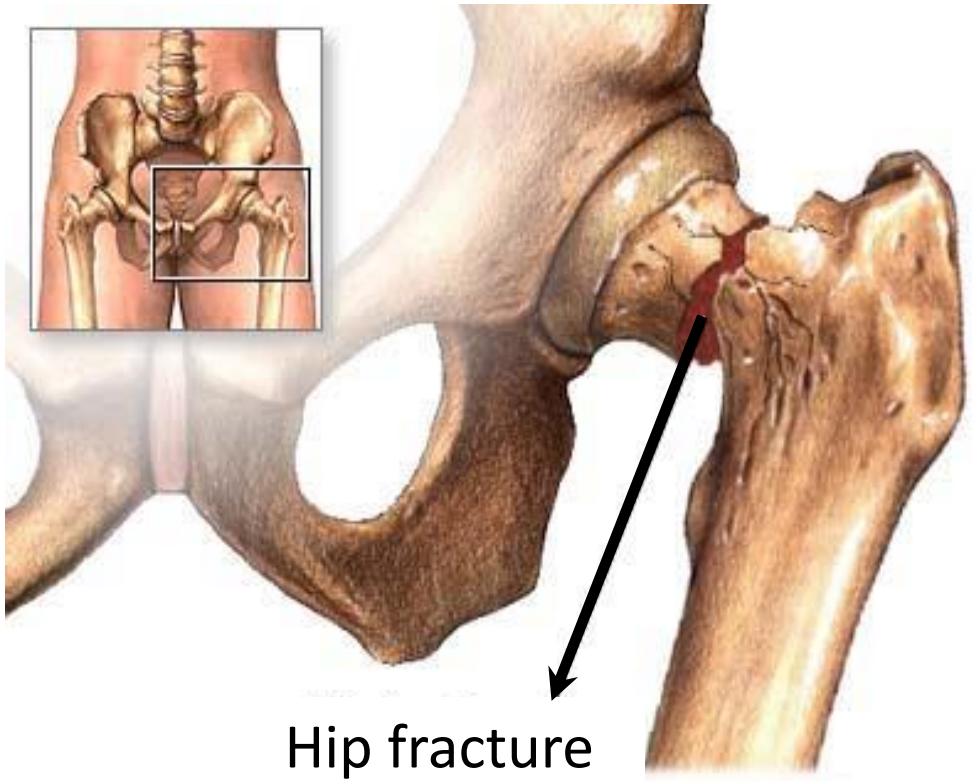
Pickering et al., Mov Disord 2007;22:1892-1900

Fear of falls in Parkinson disease

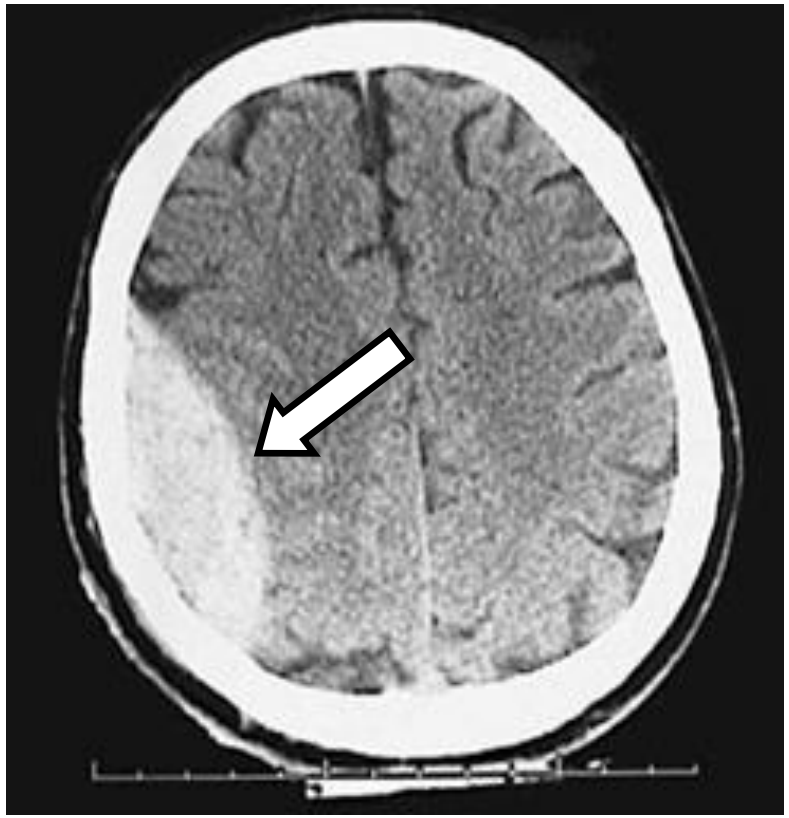


Bloem et al., J Neurol 2001;87:950-958

Injuries in Parkinson disease



Hip fracture



Epidural hematoma

RESEARCH ARTICLE

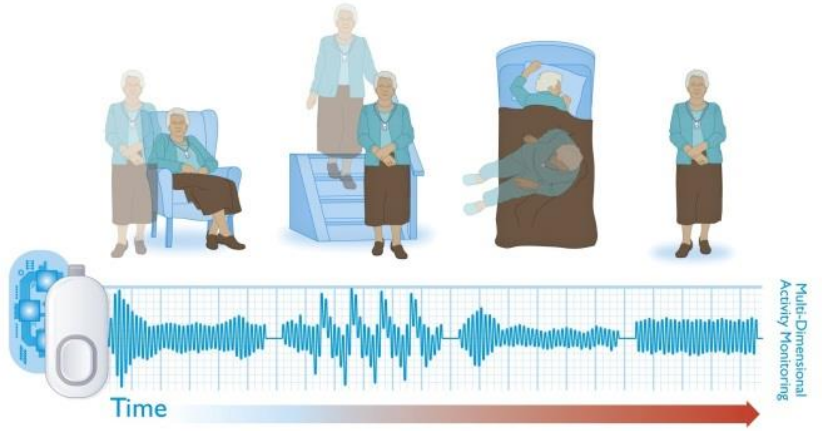
Home-Based Monitoring of Falls Using Wearable Sensors in Parkinson's Disease

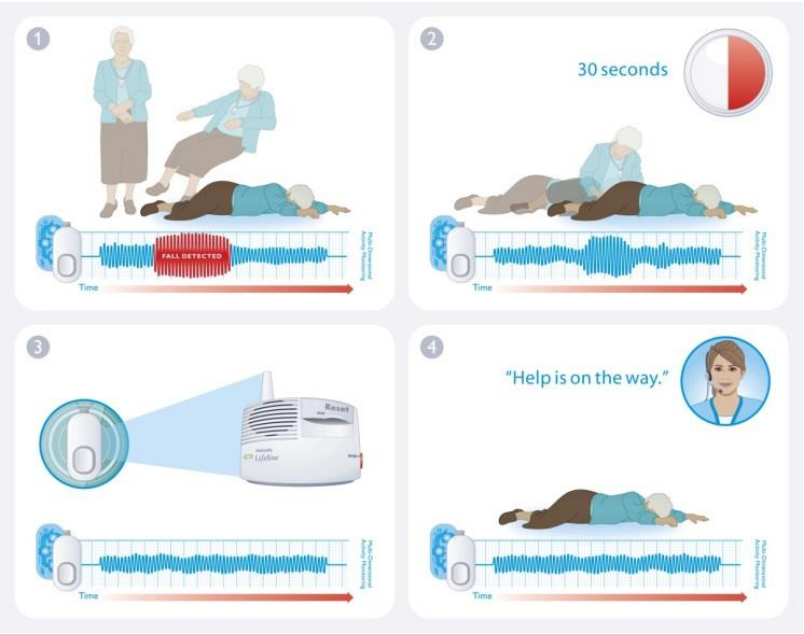
Ana Lígia Silva de Lima, PhD,[1] Tine Smits, MSc,[2] Sirwan K. L. Darweesh, MD, PhD,[1,3,4] Giulio Valenti, PhD,[2] Mladen Milosevic, PhD,[5] Marten Pijl, PhD,[2] Heribert Baldus, PhD,[2] Nienke M de Vries, PhD,[1] Marjan J. Meinders, PhD,[1,6] and Bastiaan R. Bloem, MD, PhD[1*]

[1]*Department of Neurology, Radboud University Medical Center, Donders Institute for Brain, Cognition and Behavior, Nijmegen, The Netherlands*
[2]*Philips Research, Department Personal Health, Eindhoven, the Netherlands*
[3]*Department of Epidemiology, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands*
[4]*Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA*
[5]*Philips Research North America, Acute Care Solutions Department, Cambridge, Massachusetts, USA*
[6]*Radboud University Medical Center, Radboud Institute for Health Sciences, Scientific Center for Quality of Healthcare, Nijmegen, the Netherlands*

Movement Disorders, 2019

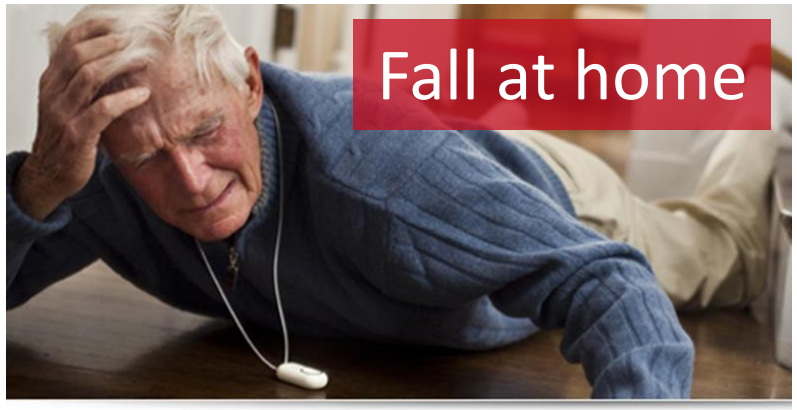
Automated falls detection

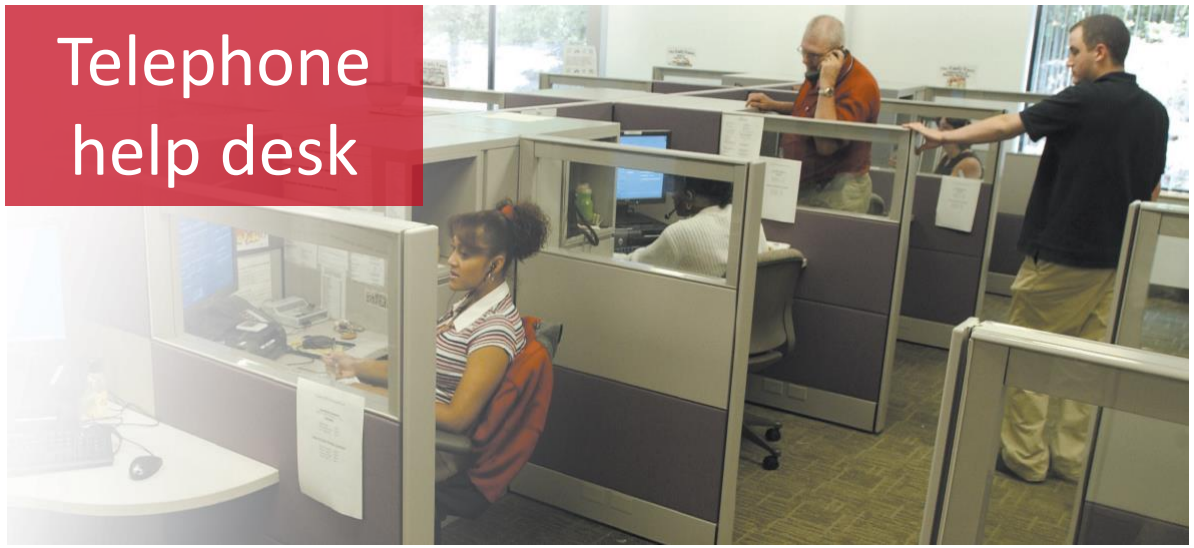




- 3 linear accelerometers
- 1 height sensor
- Algorithms validated (?)

Connection to help desk

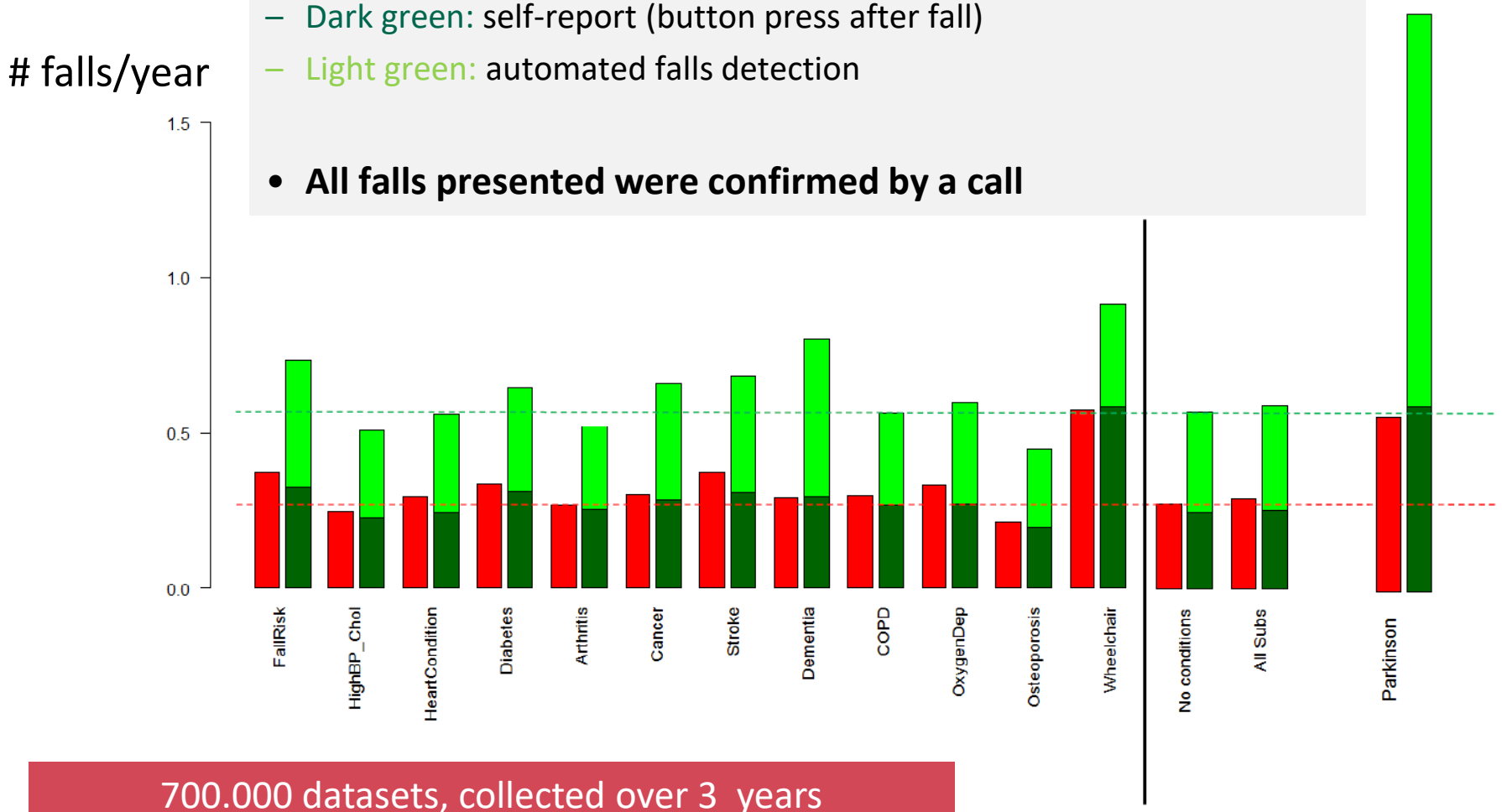




Documented falls (top 12 conditions)

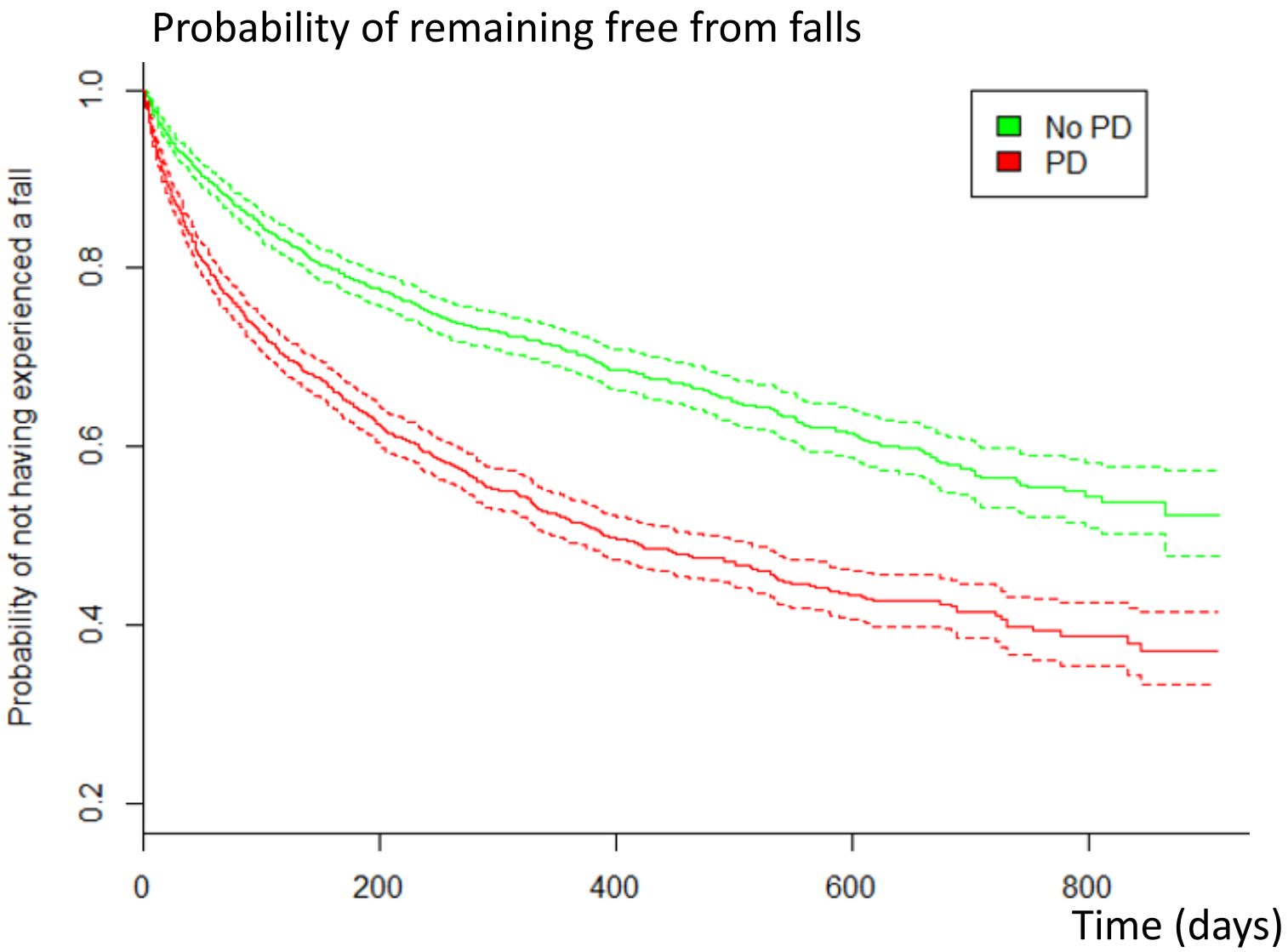
- Red: self-report on device without sensors (button press after fall)
- Green: device with sensors
  - Dark green: self-report (button press after fall)
  - Light green: automated falls detection

- **All falls presented were confirmed by a call**



700.000 datasets, collected over 3 years

Risk of first fall



“Take home” message!

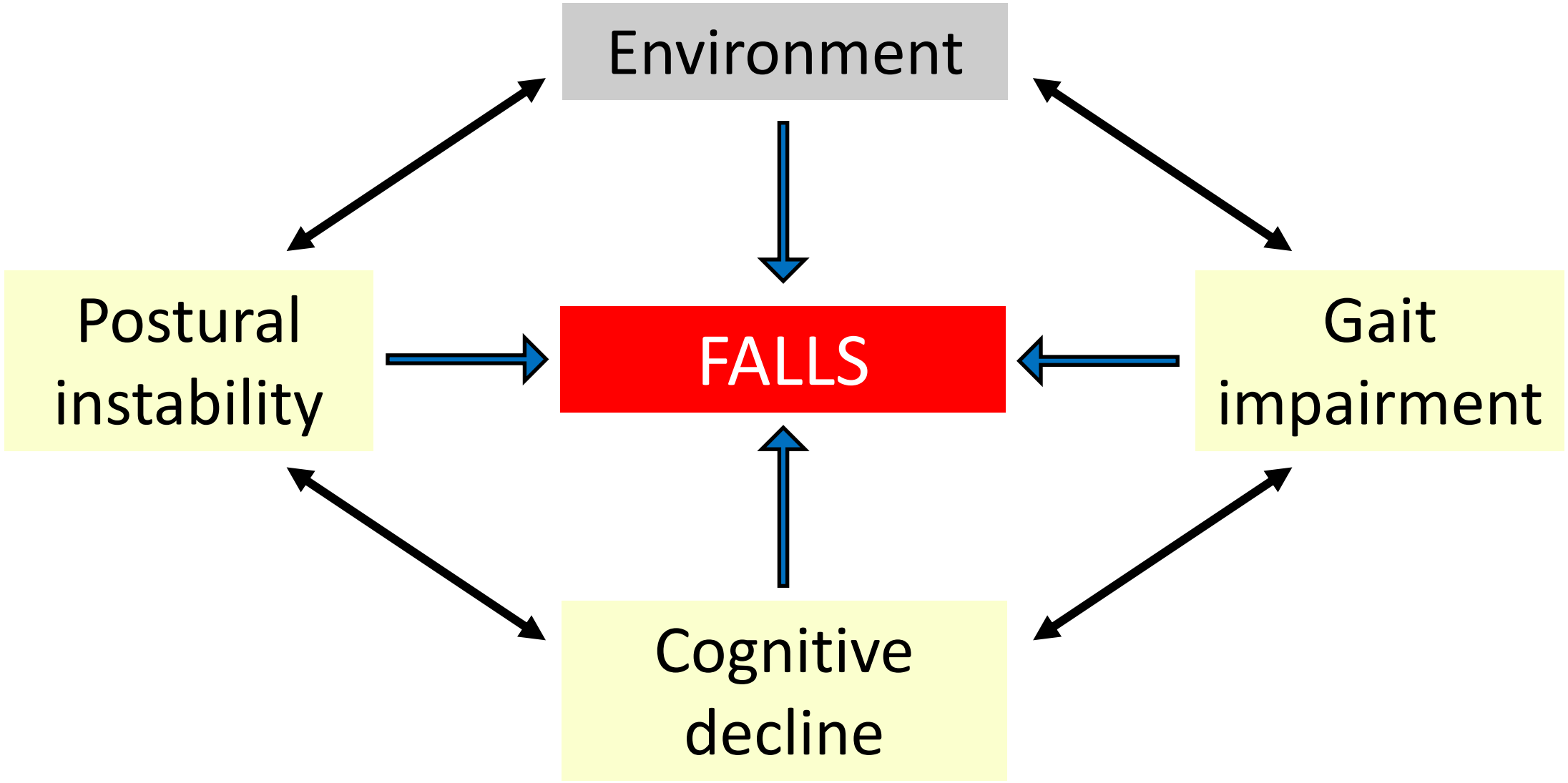
Parkinson’s disease is the

number 1 falling disorder

Causes of falls

= patient-related (“intrinsic”)

= outside the patient (“extrinsic”)



Also common in COGNITIVE disorders

OPEN ACCESS Freely available online

PLoS one

Incidence and Prediction of Falls in Dementia: A Prospective Study in Older People

Louise M. Allan[1]*, Clive G. Ballard[2], Elise N. Rowan[1], Rose Anne Kenny[3]

1 Institute for Ageing and Health, Wolfson Research Centre, Newcastle General Hospital, Newcastle upon Tyne, United Kingdom, **2** Wolfson Centre for Age Related Disorders, King's College London, London, United Kingdom, **3** Trinity College Institute of Neuroscience, Trinity College Dublin, Dublin, Ireland

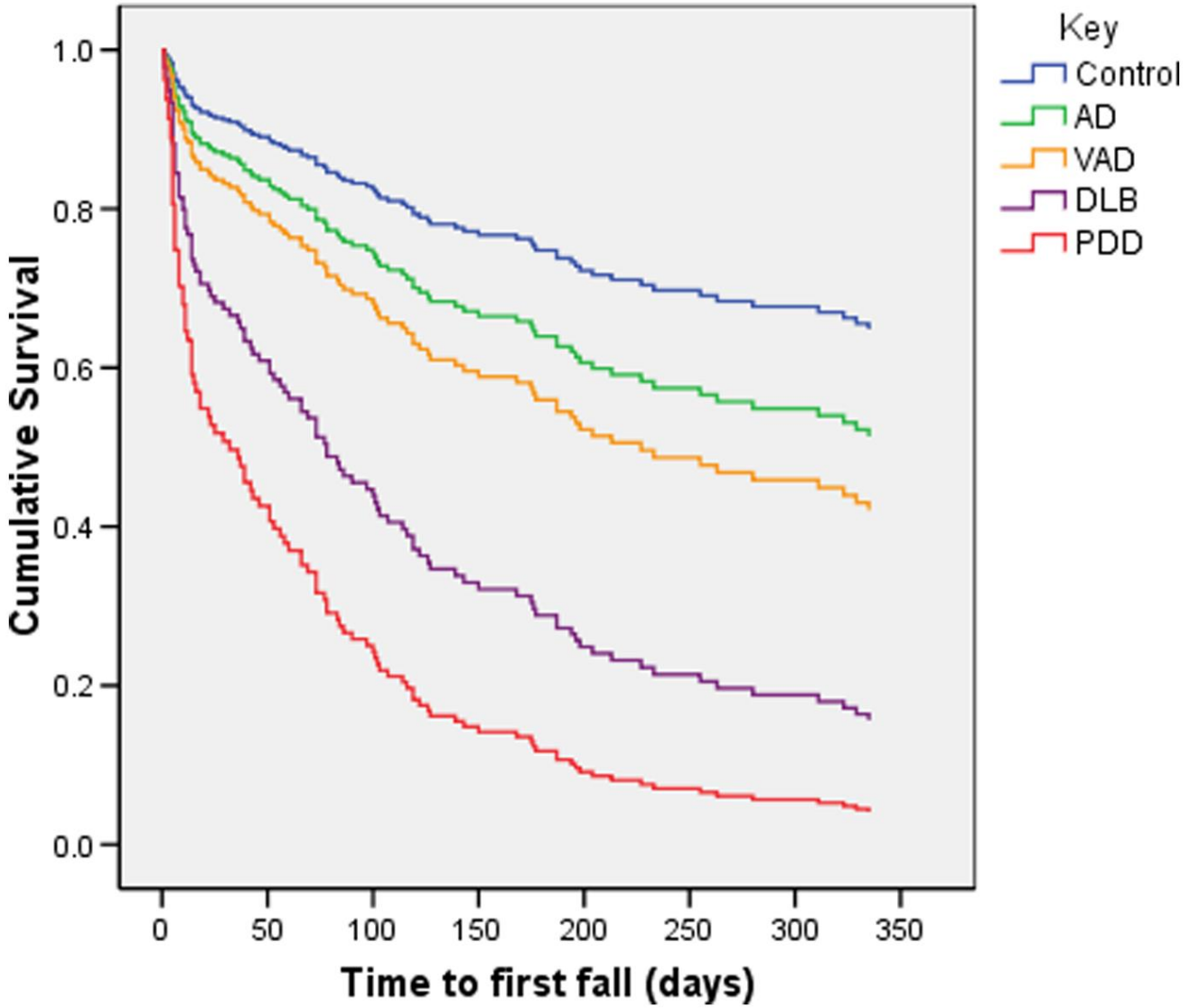
Abstract

Background: Falls are a major cause of morbidity and mortality in dementia, but there have been no prospective studies of risk factors for falling specific to this patient population, and no successful falls intervention/prevention trials. This prospective study aimed to identify modifiable risk factors for falling in older people with mild to moderate dementia.

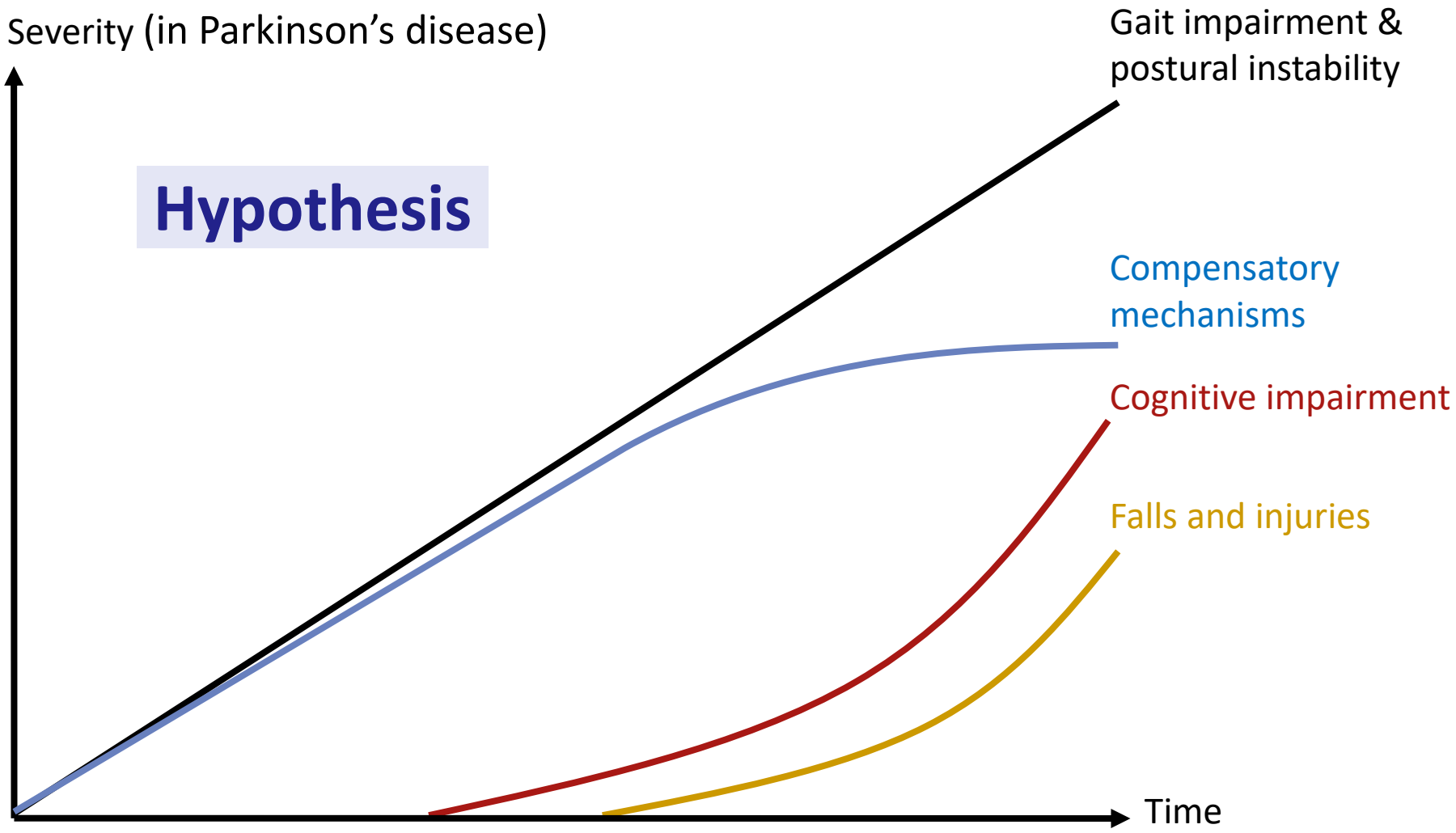
Methods and Findings: 179 participants aged over 65 years were recruited from outpatient clinics in the UK (38 Alzheimer's disease (AD), 32 Vascular dementia (VAD), 30 Dementia with Lewy bodies (DLB), 40 Parkinson's disease with dementia (PDD), 39 healthy controls). A multifactorial assessment of baseline risk factors was performed and fall diaries were completed prospectively for 12 months. Dementia participants experienced nearly 8 times more incident falls (9118/1000 person-years) than controls (1023/1000 person-years; incidence density ratio: 7.58, 3.11–18.5). In dementia, significant univariate predictors of sustaining at least one fall included diagnosis of Lewy body disorder (proportional hazard ratio (HR) adjusted for age and sex: 3.33, 2.11–5.26), and history of falls in the preceding 12 months (HR: 2.52, 1.52–4.17). In multivariate analyses, significant potentially modifiable predictors were symptomatic orthostatic hypotension (HR: 2.13, 1.19–3.80), autonomic symptom score (HR per point 0–36: 1.055, 1.012–1.099), and Cornell depression score (HR per point 0–40: 1.053, 1.01–1.099). Higher levels of physical activity were protective (HR per point 0–9: 0.827, 0.716–0.956).

Conclusions: The management of symptomatic orthostatic hypotension, autonomic symptoms and depression, and the encouragement of physical activity may provide the core elements for the most fruitful strategy to reduce falls in people with dementia. Randomised controlled trials to assess such a strategy are a priority.

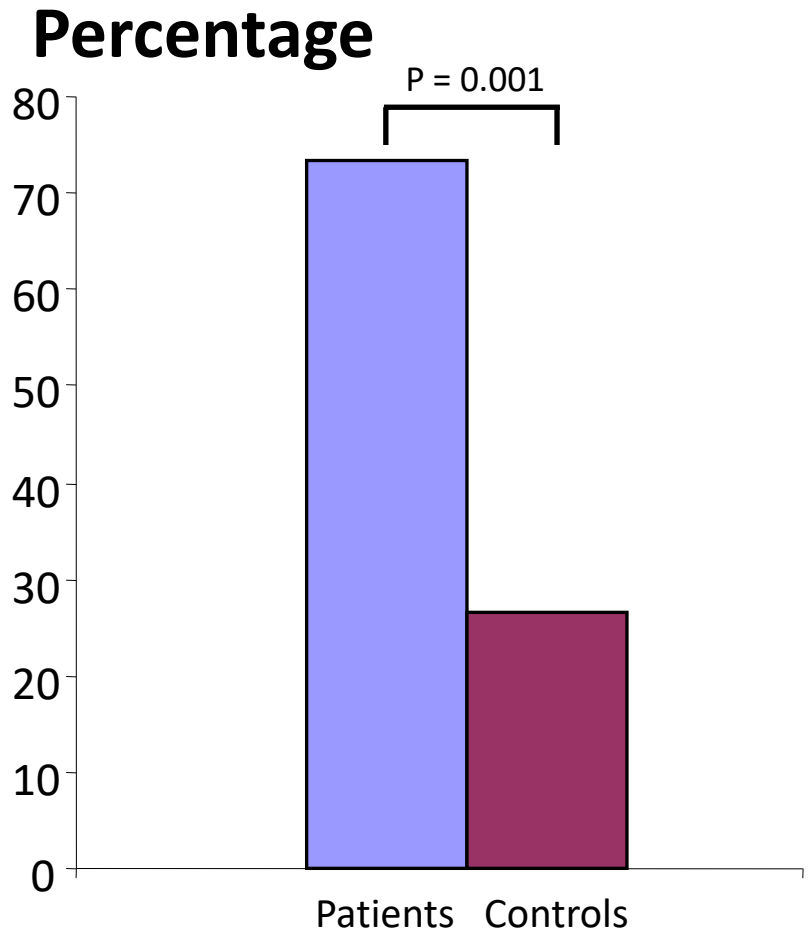
Falls are common in dementias



Perhaps even particularly cognitive?



Multiple tasking and falls in PD



Bloem et al, J Neurol 2001;87:950-958

ELSEVIER

Journal of the Neurological Sciences 248 (2006) 196 – 204

Journal of the Neurological Sciences

www.elsevier.com/locate/jns

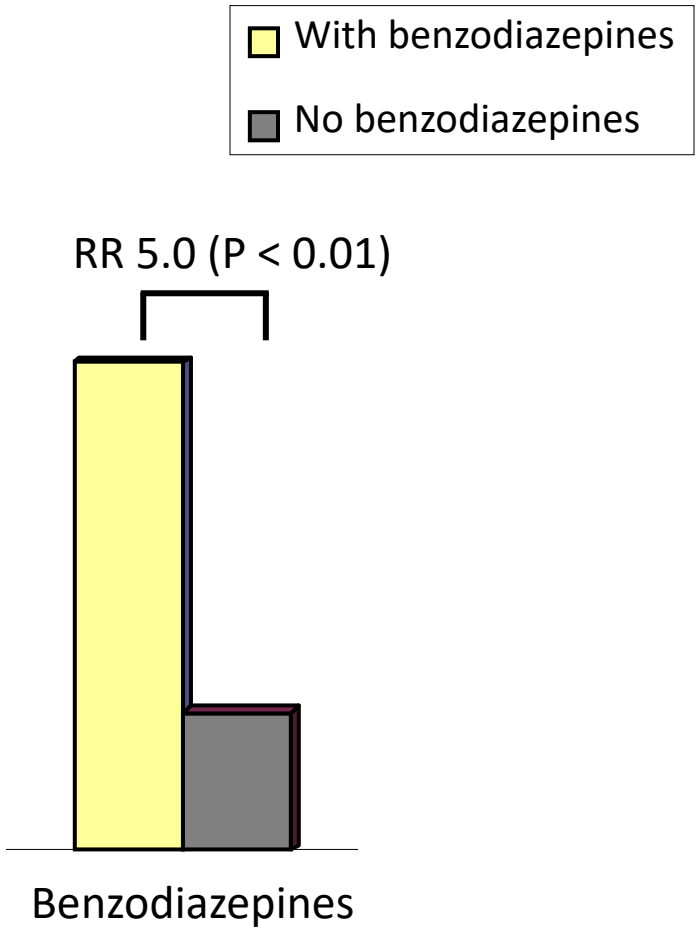
The "posture second" strategy: A review of wrong priorities in Parkinson's disease

Bastiaan R. Bloem [a,*], Yvette A.M. Grimbergen [b], J. Gert van Dijk [b], Marten Munneke [a]

[a] *Department of Neurology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands*
[b] *Department of Neurology, Leiden University Medical Centre, The Netherlands*

Available online 27 June 2006

Avoid benzodiazepines!

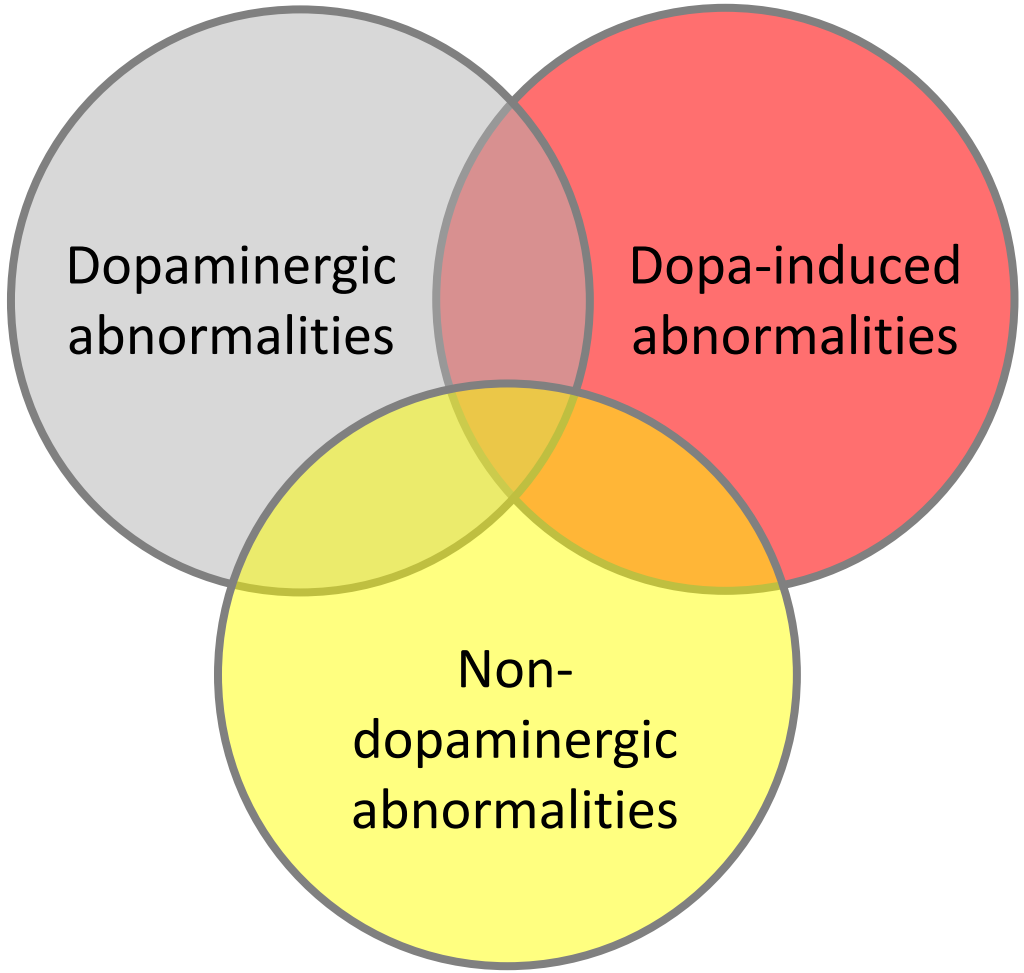


Bloem et al., J Neurol 2001;248:950-958

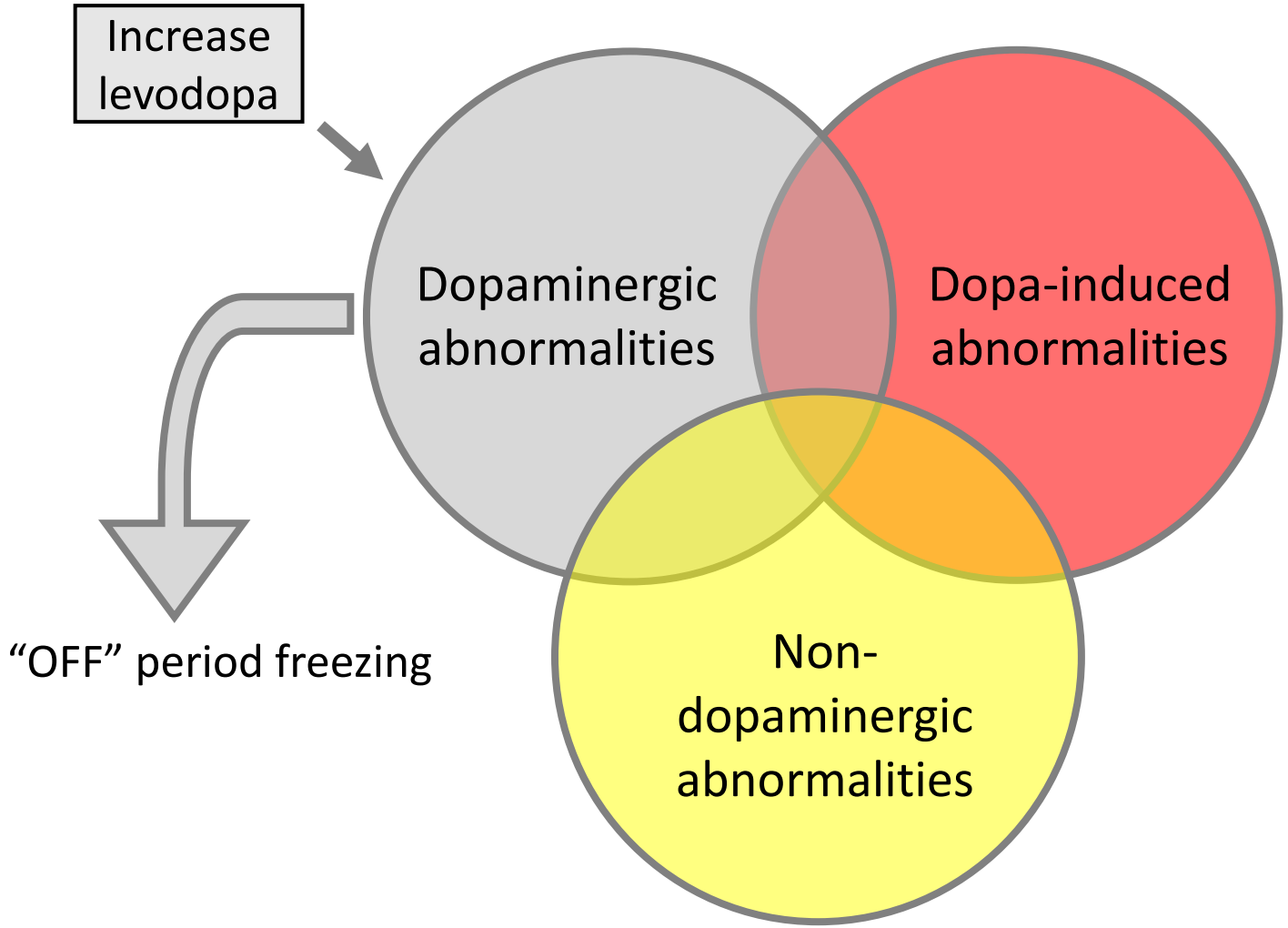
Example of falling due to freezing

Treatment of gait & balance / prevention of falls

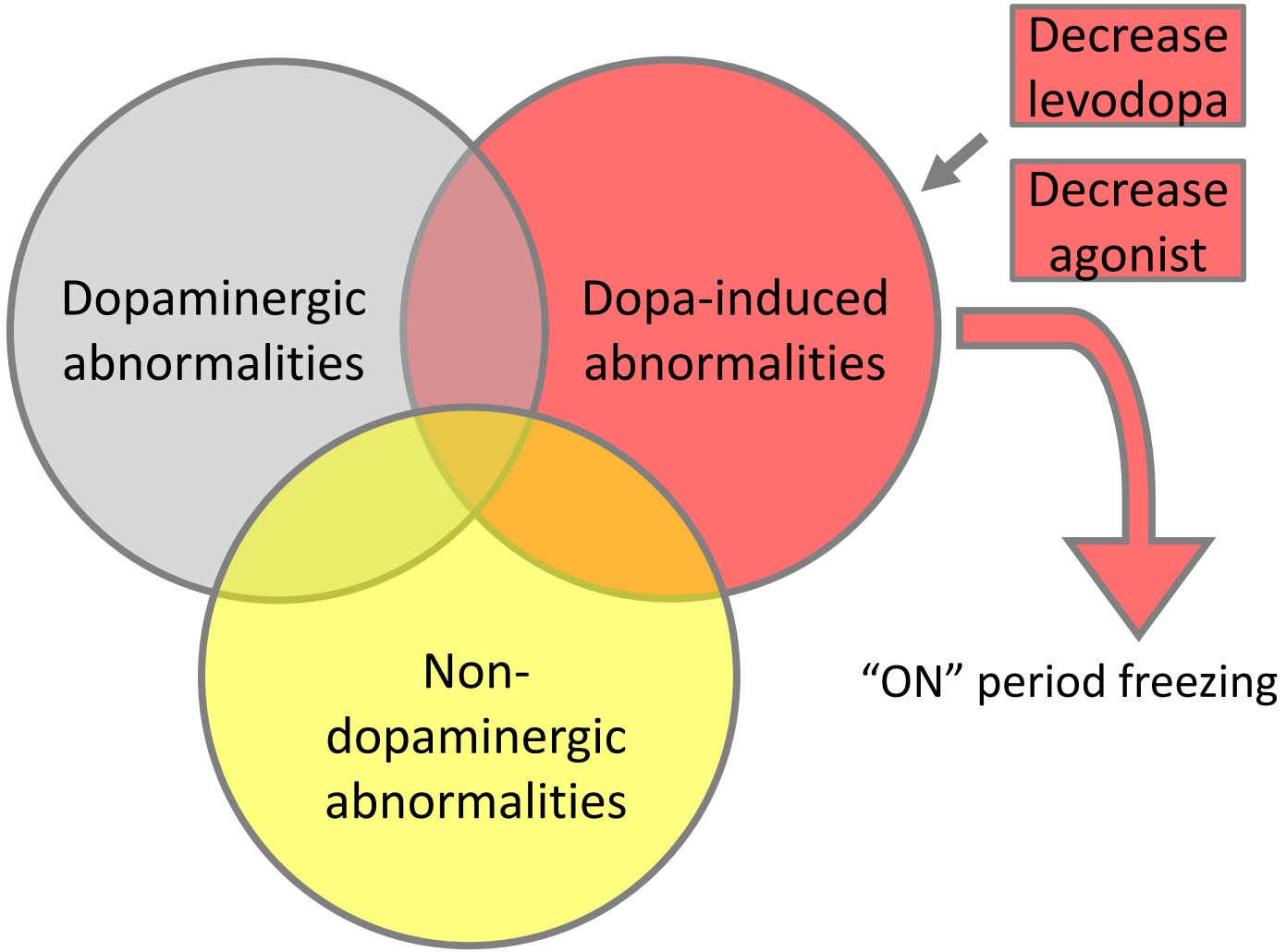
Clinical state in relation to falls



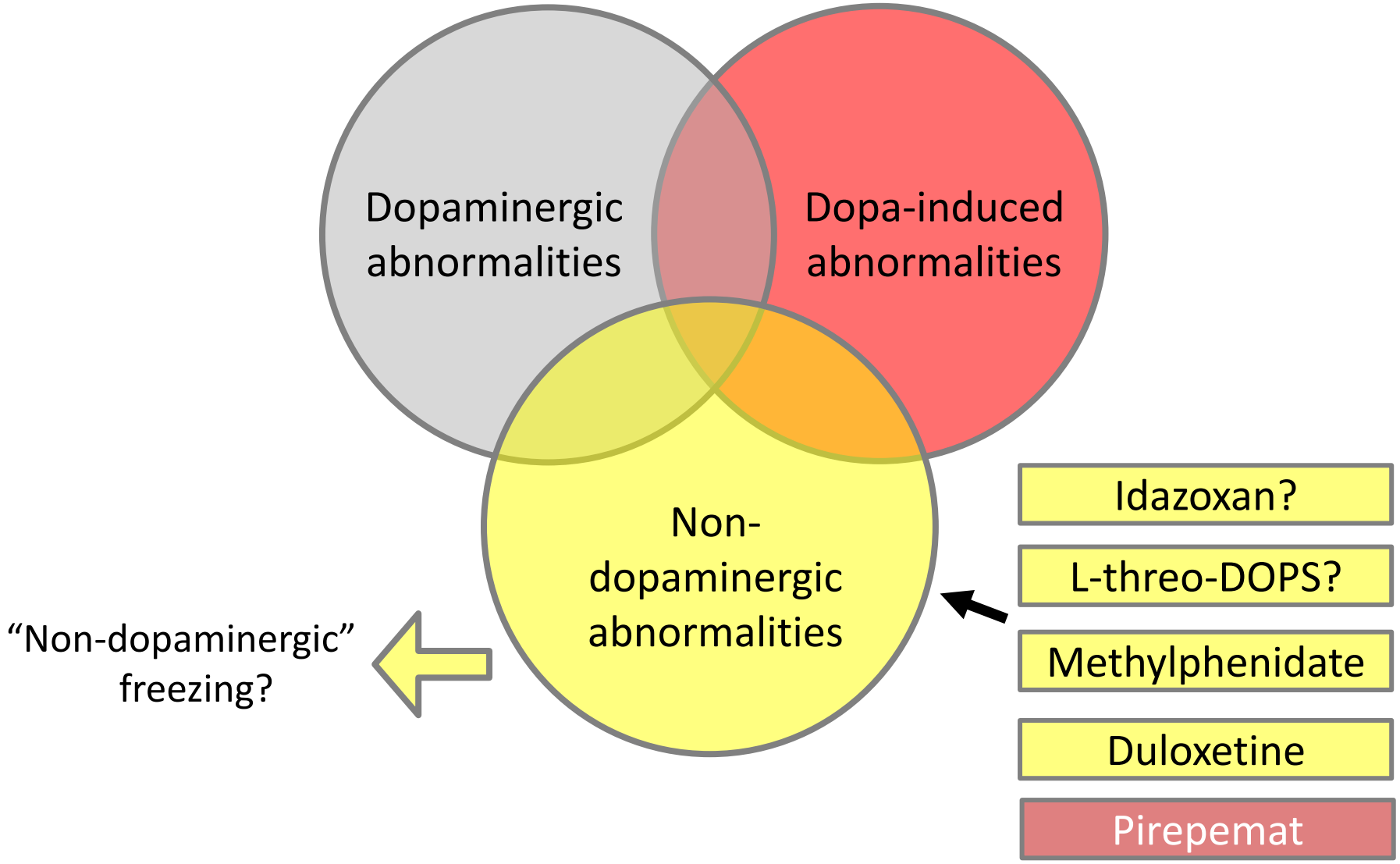
Clinical state in relation to falls



Clinical state in relation to falls



Clinical state in relation to falls




THANK YOU!

Pirepemat Phase IIb: Impaired balance/Falls

Primary objective in study IRL752C003

- Effects on **falls frequency**

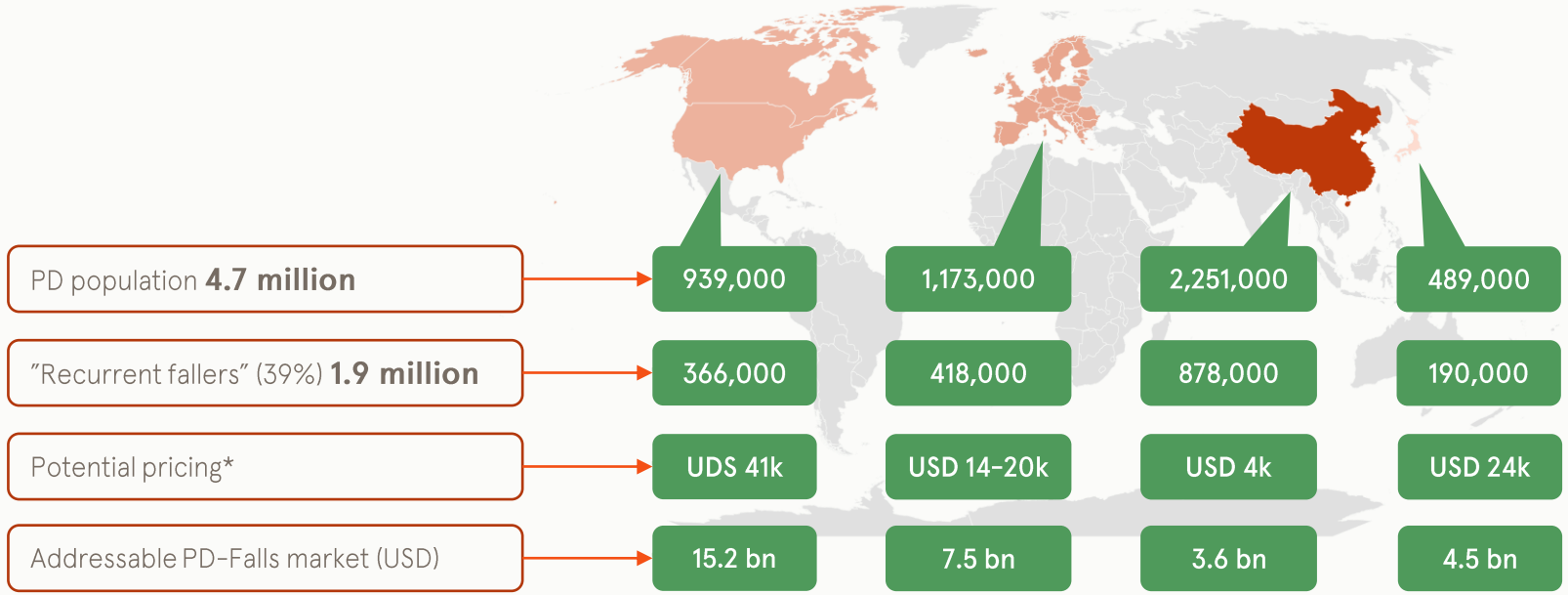
Secondary & other objectives

- Effects on **cognitive functions** (Montreal Cognitive Assessment) (MoCA)
- Effects on **Parkinson's disease symptoms** (MDS-UPDRS)
- Effects on **postural dysfunction** (tandem walking and single leg stance test)
- Effects on **global function** assessed with Clinicians Global Impression of Severity (CGIS)
- PK/PD relationships

"A Phase IIb study to evaluate the effects of pirepemat on falls frequency as compared to placebo."

Q&A

Pirepemat – Market opportunity



Total addressable market for pirepemat is about **USD 30 bn**

IRLAB

Source: Global Data 2020. Europe represented by "EU5" (GE, FR, IT, SP and UK)
* Pricing based on health economy calculations and relations between countries from IHS Markit poli, 2017

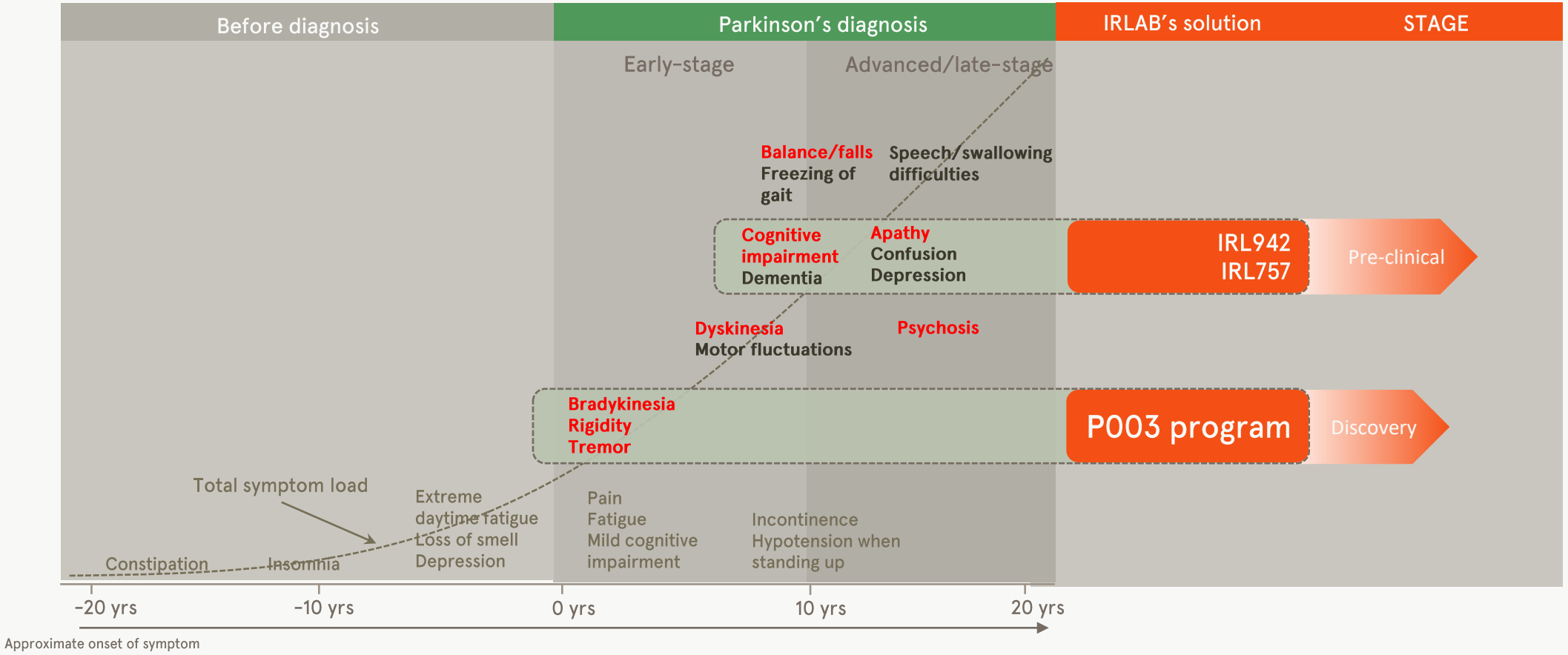
IRLAB

Preclinical portfolio to accelerate IRLAB's growth

IRL942 and IRL757: To improve cognitive function, brain health and treat apathy (target populations: PD, dementias, schizophrenia, depression)

P003: Long-acting Parkinson treatment with better efficacy than L-DOPA or apomorphine and reduced risk of side effects

Living with Parkinson's: IRLAB transforms the treatment algorithm



References: Based on Kalia, LV. and Lang, AE. Lancet 2015;386-912.

IRL942 – Aimed at improving cognitive function and brain health across neurological indications

IRL942 opportunity

- **12 %** of adults aged 65 years or more experience **cognitive decline** (CDC)

Problem

- **Disruption of frontal-subcortical circuits** are implicated in the pathogenesis of cognitive decline*

IRLAB's solution

- IRL942 show a **unique ability** to activate frontal-subcortical circuits and **improve cognitive function in animal models**
- **Potential for both symptomatic relief and disease modification**

* TN Chase, Neurotox Res (2011) 19:266–278 DOI 10.1007/s12640-010-9196-9 Graph:

IRL757 – Aimed at the huge untreated problem with APATHY

IRL757 opportunity

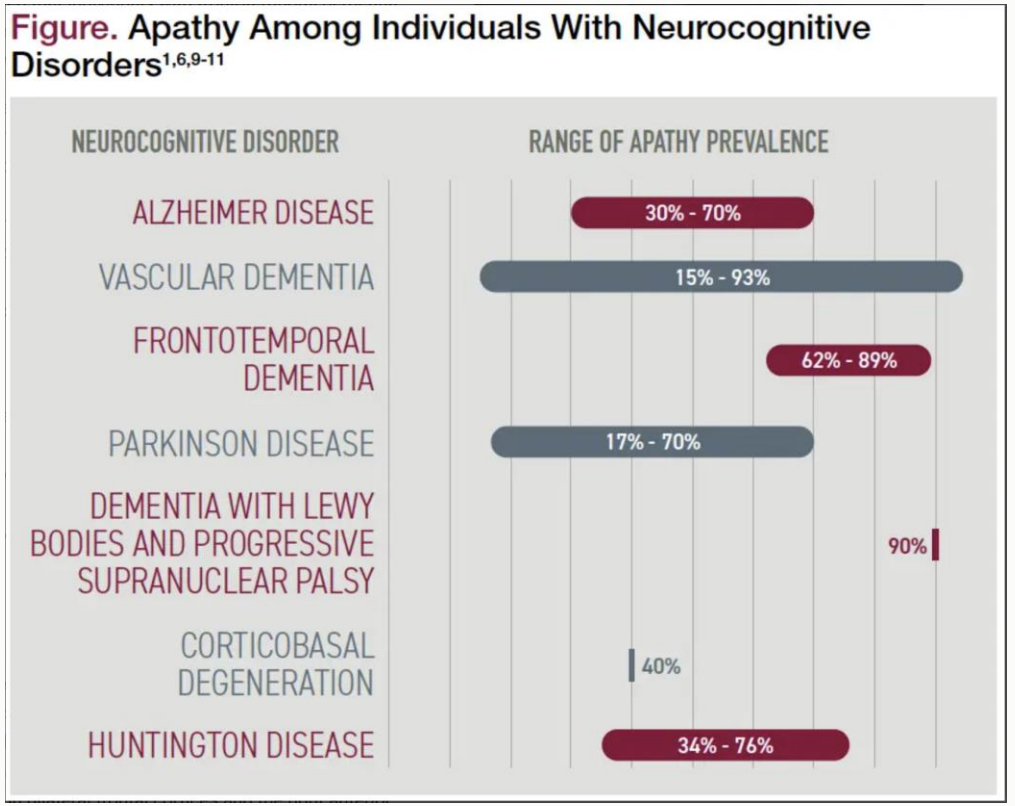
- **Over 10 million US and EU citizens each** may be affected by apathy
- Apathy occurs in 20-70% in people with PD **and** In 20-90% of people with AD and other CNS disorders

Pathophysiological background

- **Disruption of frontal neurocircuits** are implicated in apathy

IRLAB's solution

- IRL757 promotes a unique ability to **increase neuronal activity** in these circuits
- **Potential for both symptomatic relief and disease modification**

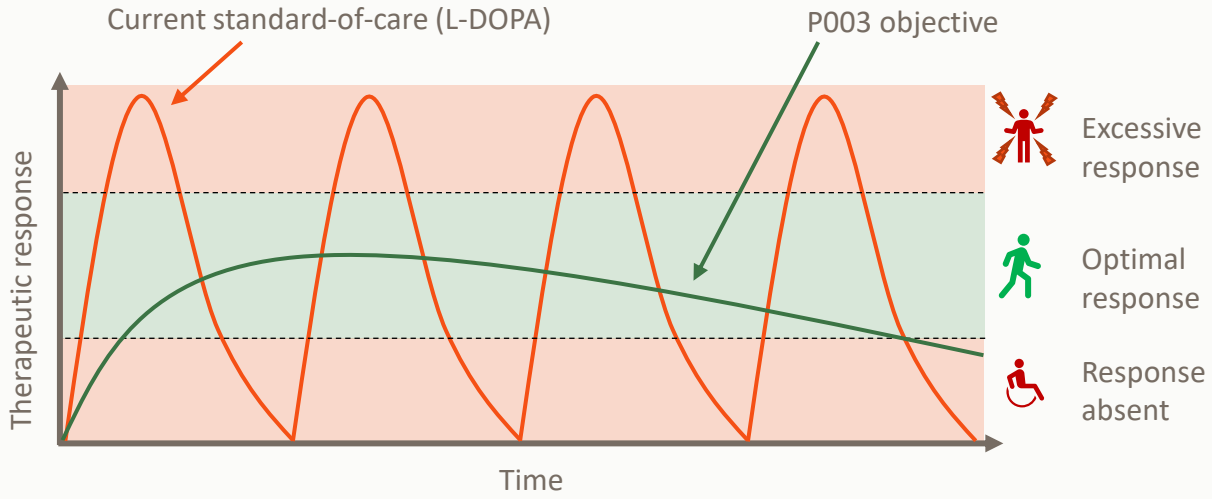


* TN Chase, Neurotox Res (2011) 19:266–278 DOI 10.1007/s12640-010-9196-9

Graph: from R. R. Tampi, Psychiatric Times, Vol 38, Issue 7, July 14, 2021

P003 – Parkinson treatment beyond levodopa

- Total market (16 largest markets): 8.3 million people diagnosed with PD in 2022*
- Aimed at treatment of core symptoms of Parkinson's disease
- Long-acting Parkinson treatment with efficacy better or equivalent to L-DOPA / apomorphine
- Reduced risk of side effects compared to L-dopa / apomorphine
- Opportunity: potential to transform treatment paradigm in PD



P003 ongoing work

- 1st generation: lead optimization on-going
- 2nd generation: candidate identification through structural chemistry on-going

* Source: Global Data Epidemiology data base

Q&A

Well positioned to deliver

- Two “first in class” programs in late-stage **clinical Phase IIb**
- Addressing **large global markets**
- Partnership with **Ipsen** – a leading global neuroscience company
- Preclinical development **candidates towards** clinical Phase I
- Highly efficient **discovery platform** for **“first in class”**

Strong momentum in operations

- **Well ahead** of competition
- Strong **cash position**
- Mesdopetam **fully financed through Phase III** and marketing
- **Strong newsflow** 2022-2024

IRLAB

Contact:
Nicholas Waters, CEO, nicholas.waters@irlab.se, Viktor Siewertz, CFO, viktor.siewertz@irlab.se

IRLAB discovers and develops novel treatments of Parkinson’s disease and other disorders of the brain. The company's most advanced drug candidates, mesdopetam (IRL790) and pirepemat (IRL752), are in Phase IIb and are designed to treat some of the most difficult symptoms related to Parkinson's disease. In 2021, IRLAB entered an exclusive and worldwide license with Ipsen for the development and marketing of mesdopetam.

Through ISP, its proprietary research platform, IRLAB has discovered and developed all its experimental drug candidates and continues to discover innovative drug candidates for the treatment of disorders of the brain. In addition to IRLAB’s strong clinical pipeline, IRLAB runs several preclinical programs with IRL942 and IRL757 currently in development towards Phase I. IRLAB is listed on Nasdaq Stockholm. More information on www.irlab.se.