
# Malattia di Parkinson: Differenze di genere

Roma, 4 Maggio 2019

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# Outline

Epidemiologia

Sintomi motori e non motori

Cognitività

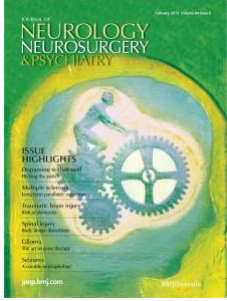
Biomarcatori

Implicazioni e prospettive


Raffaello, Madonna con bambino, 1503

SHORT REPORT

*J Neurol Neurosurg Psychiatry* 2004;**75**:637–639.




# Are men at greater risk for Parkinson's disease than women?

**G F Wooten, L J Currie, V E Bovbjerg, J K Lee, J Patrie**

## Incidence: Meta-analysis including>2500 PD patients from 17 studies

| Study location | Year | Population Age (years) | Size | Number of | Mean age of | Age-standardised M:F |
|---|---|---|---|---|---|---|
| Western populations | | | | | | |
| Southwest Finland[2] | 1976 | All | 402 | | | |
| Poznan, Poland[2] | 1989 | All | 1 30 | | | |
| Ferrara, Italy[2] | 1991 | All | 187 | | | |
| Manhattan, USA[2] | 1995 | All | 213 | | | |
| Navarra, Spain[2] | 1999 | All | 523 | | | |
| Olmstead, USA[2] | 1999 | All | 95 0 | | | |
| Turku, Finland[2] | 1999 | All | 196 | | | |
| Italy[3] | 2000 | 65–84 | 4341 | | | |
| Tartu, Estonia[4] | 2003 | All | 156 | | | |
| California, USA[5] | 2003 | All | 4 77 perso | | | |
| Rotterdam, The Netherlands[6] | 2004 | ⩾55 | 6839 | | | |
| Central Spain[7] | 2004 | ⩾65 | 5160 | | | |
| Cambridge, UK[8] | 2004 | All | 700 | | | |
| Aberdeen, UK[9] | 2006 | All | 148 | | | |
| Pooled age-adjusted M:F ratio | | | | | | |
| Asian populations | | | | | | |
| 29 provinces, China[2] | 1991 | All | 3 86 | | | |
| Ilan County, Taiwan[2] | 2001 | All | 75 5 | | | |
| Wakayama, Japan[10] | 2002 | All | 1 08 | | | |
| Pooled age-adjusted M:F ratio | | | | | | |
| Total pooled age-adjusted M:F ratio | | | | | | |

M:F, male:female.
*Age-adjusted RR from original publication.
†Mean age calculated crudely from age-stratified number of cases.

REVIEW

Pringsheim

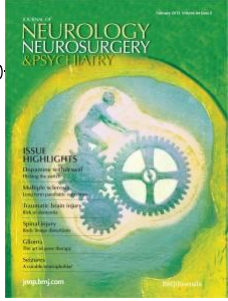
## The Prevalence of Parkinson's Disease: A Systematic Review and Meta-analysis

**TABLE 4.** Prevalence of PD by sex and geographic location (per 100,000)
47 studies

| Geographic location | Female | Male |
|---|---|---|
| Asia (21 studies) | 306<br>95% CI 184, 511<br>$I^2$ 98.6 | 371<br>95% CI 219, 629<br>$I^2$ 98.8 |
| Europe/North America/Australia (17 studies) | 1,267<br>95% CI 1,005, 1,595<br>$I^2$ 82.8 | 1,535<br>95% CI 1,188, 1,983<br>$I^2$ 83.9 |
| South America (4 studies) | 808<br>95% CI 356, 1,832<br>$I^2$ 88.5 | 1,267<br>95% CI 583, 2,752<br>$I^2$ 89.3 |

RESEARCH PAPER

Moisan F, *et al*. *J Neurol Neurosurg Psychiatry* 2015;**0**:1–6. doi:10.1136/jnnp-



OPEN ACCESS

# Parkinson disease male-to-female ratios increase with age: French nationwide study and meta-analysis

Frédéric Moisan,[1] Sofiane Kab,[1,2,3] Fatima Mohamed,[2,3] Marianne Canonico,[2,3] Morgane Le Guern,[1] Cécile Quintin,[4] Laure Carcaillon,[4] Javier Nicolau,[5] Nicolas Duport,[4] Archana Singh-Manoux,[2,3] Marjorie Boussac-Zarebska,[5] Alexis Elbaz[1,2,3]

French Nationwide study including 188.562 persons being treated for PD

Meta-analysis including 22 studies involving 7616 Men and 6510 women with PD≥40 years

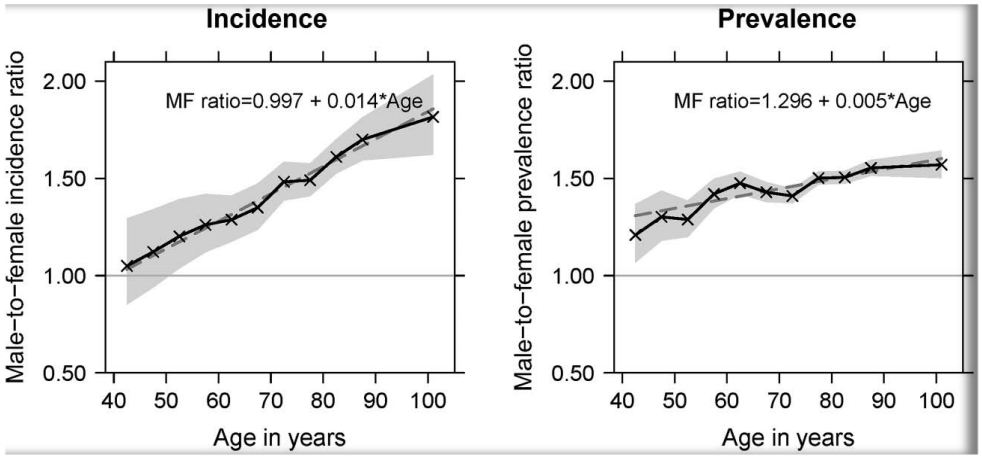



**Figure 1** Age-specific male-to-female incidence and prevalence ratios of Parkinson's disease (France, 2010). Solid line, observed age-specific male-to-female ratios estimated by modelling prevalence and incidence through Poisson regression. Grey area, 95% CIs of observed male-to-female ratios. Dashed line, linear regression of male-to-female ratios weighted by the inverse of their variance on age (in years, centred at 40 years).

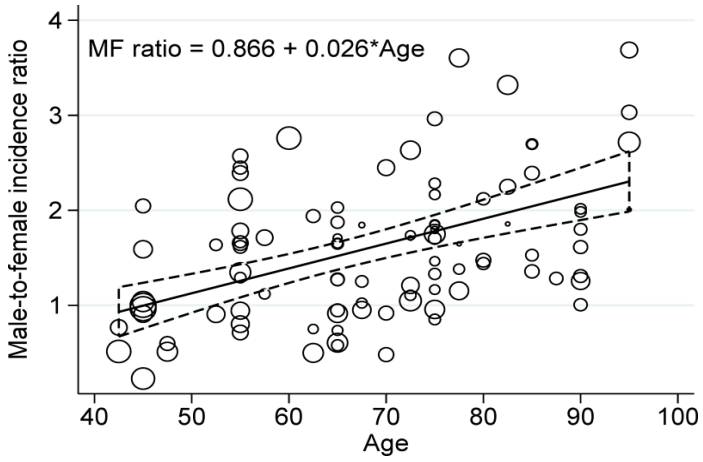
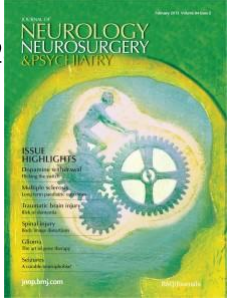



**Figure 2** Systematic review of age-specific male-to-female incidence ratios of Parkinson's disease. Circles represent observed male-to-female incidence ratios for each study by age-by-sex strata, estimated by modelling incidence through Poisson regression; their size is proportional to the variance of the male-to-female incidence ratios, and more precise estimates are represented by larger circles. Solid line, linear regression of male-to-female incidence ratios weighted by the inverse of their variance on age (in years, centred at 40 years). Dashed line, 95% CIs of the linear regression.

OPEN ACCESS

RESEARCH PAPER

Moisan F, *et al*. *J Neurol Neurosurg Psychiatry* 2015;**0**:1–6. doi:10.1136/jnnp-2015-3122




# Parkinson disease male-to-female ratios increase with age: French nationwide study and meta-analysis

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## Possible explanations

Genetic contribution to PD is stronger at younger ages. Mendelian and non-mendelian forms have a younger age of onset

Non-genetic PD risk or protective factors are differently distributed in men and women and their role increases with age.

Risk factors: Chemicals and toxic factors

Protective factors: Oestrogens

**MEN**

**WOMEN**

Contents lists available at ScienceDirect

Experimental Neurology

journal homepage: www.elsevier.com/locate/yexnr

Review

# Sex differences in Parkinson's disease and other movement disorders

Kara M. Smith *, Nabila Dahodwala

Experimental Neurology 259 (2014) 44–56

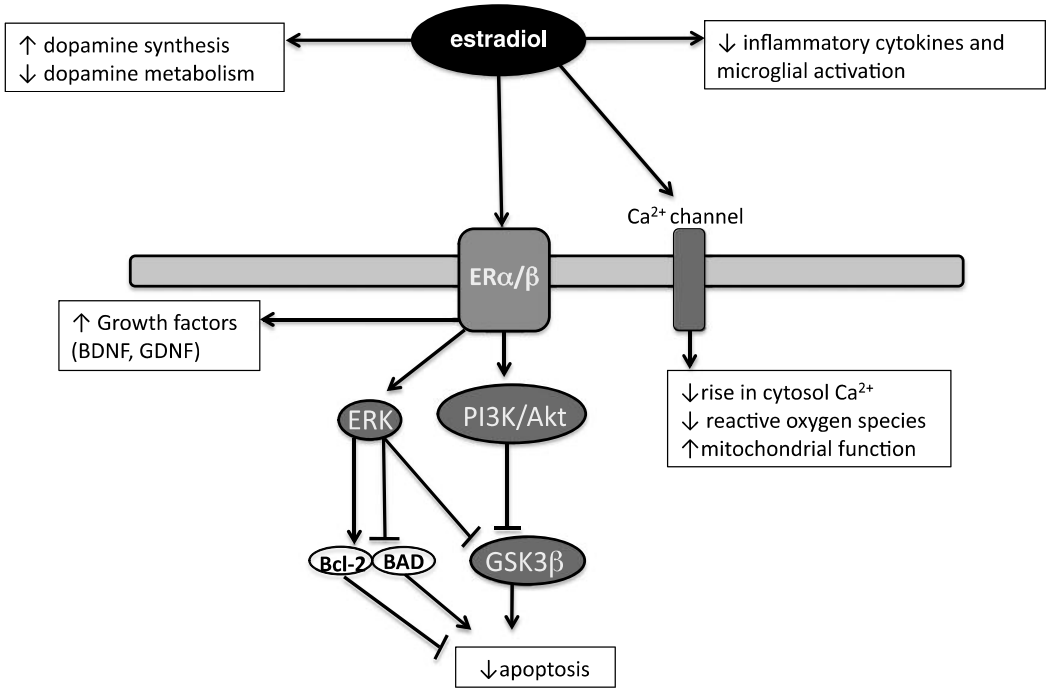
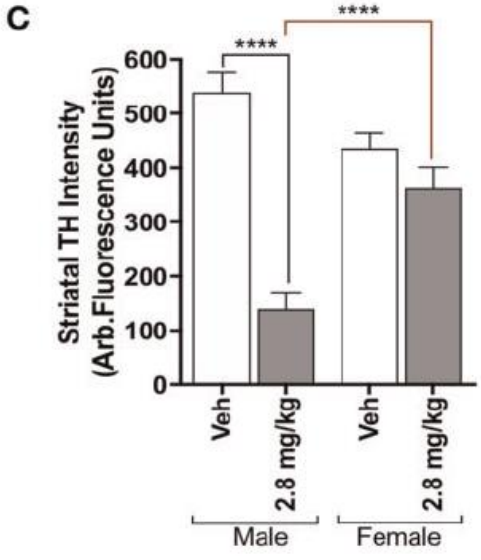
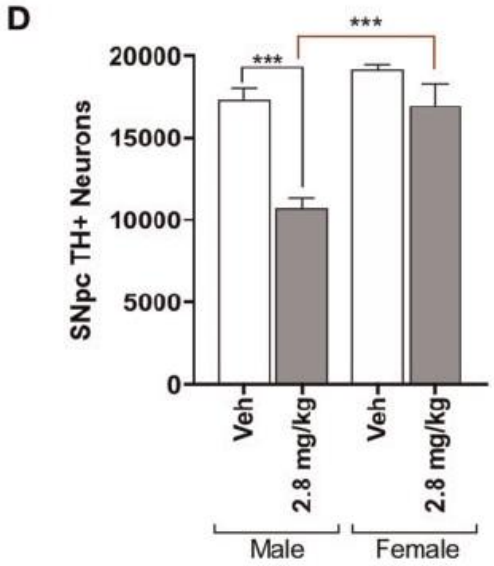


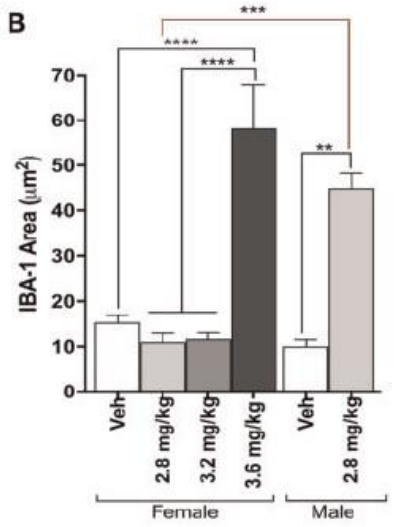

**Fig. 1.** Potential neuromodulatory and neuroprotective mechanisms of estradiol and related compounds. Abbreviations: ER, estrogen receptor; BDNF, brain derived neurotrophic factor; GDNF, glial derived neurotrophic factor; ERK, extra-cellular signal regulated kinase; PI3K, phosphatidylinositol 3 kinase; GSK3β, glycogen synthase kinase 3β. Schematic presentation of estradiol's potential effects in the striatum and substantia nigra. Binding of ER by estradiol activates signal cascades that ultimately decrease apoptosis of neurons.

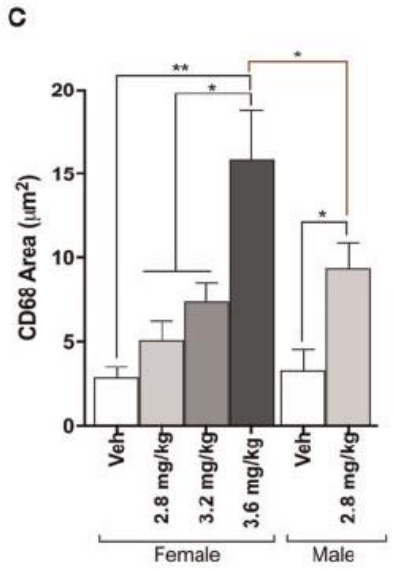
# Sex Differences in Rotenone Sensitivity Reflect the Male-to-Female Ratio in Human Parkinson's Disease Incidence

Briana R. De Miranda,[*,†] Marco Fazzari,[‡,§,¶] Emily M. Rocha,[*,†] Sandra Castro,[*,†] and J. Timothy Greenamyre[*,†,1]




Toxicol Sci, 2019

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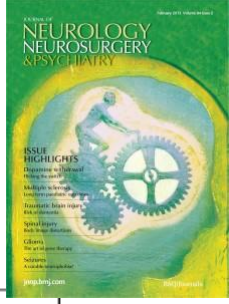
Implicazioni e prospettive

Vermeer, La ragazza con l'orecchino di Perla, 1665-1666

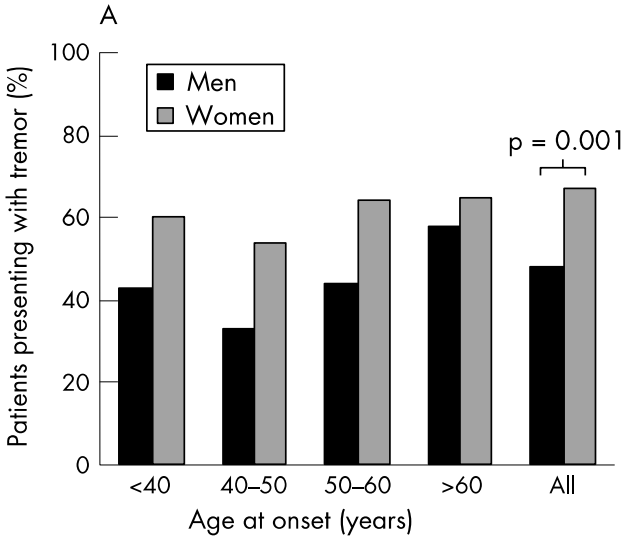
# Gender differences in Parkinson's disease

**Charlotte A Haaxma, Bastiaan R Bloem, George F Borm, Wim J G Oyen, Klaus L Leenders, Silvia Eshuis, Jan Booij, Dean E Dluzen, Martin W I M Horstink**

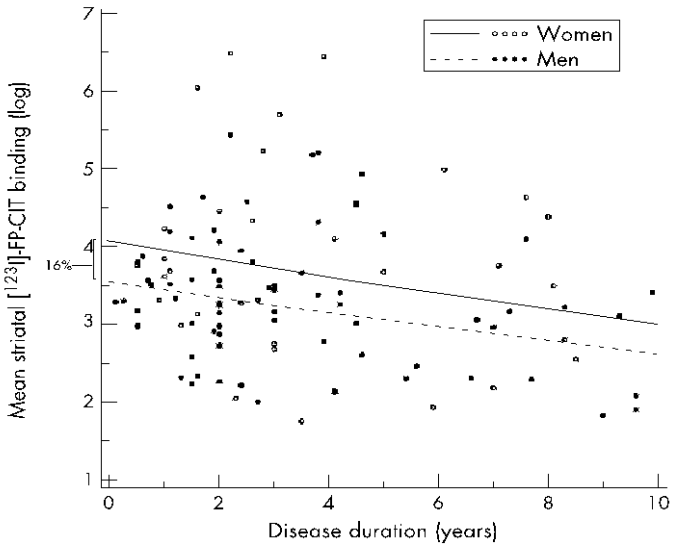


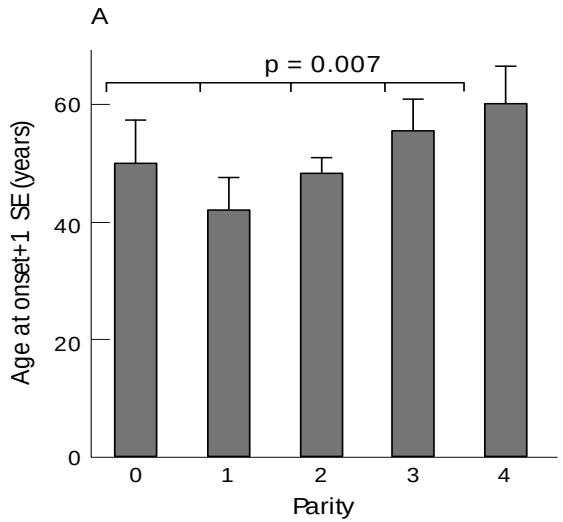

253 drug-naive PD patients (156M/97W)

Women have higher striatal uptake




- At onset W were 2.1 years older than men
- W presented more frequently with tremor



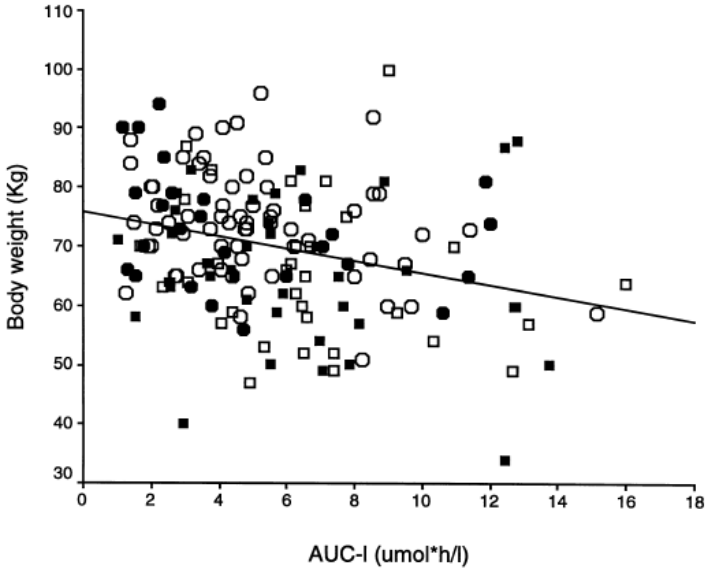


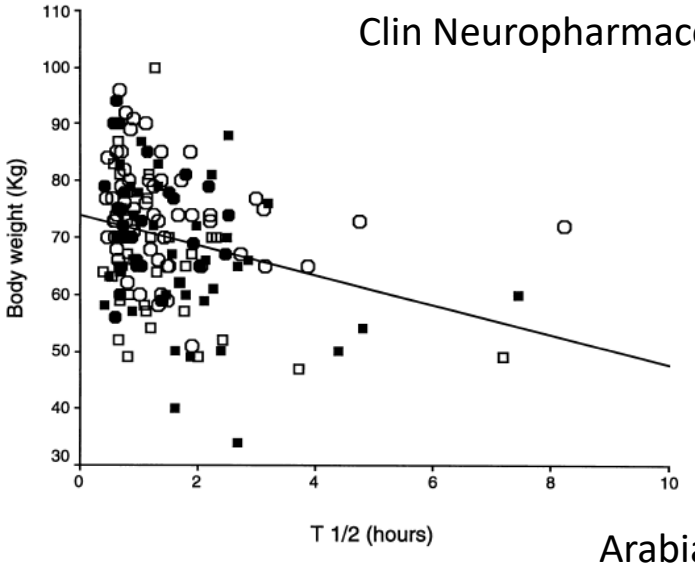
This more benign phenotype is related with oestrogen status (parity, age at menopause and fertile life span)

*Neurol Neurosurg Psychiatry* 2007;**78**:819–824.

# Body Weight Influences Pharmacokinetics of Levodopa in Parkinson's Disease

*†Mario Zappia, †Lucia Crescibene, *Gennarina Arabia, †Giuseppe Nicoletti, †Angelo Bagalà, †Loredana Bastone, †Manuela Caracciolo, ‡Simona Bonavita, ‡Alfonso Di Costanzo, †Massimo Scornaienchi, *†Antonio Gambardella, and *†Aldo Quattrone




Clin Neuropharmacol 2002

Arabia et al 2002

| | Men (n=91) | | Women (n=73) | | *p* value |
|---|---|---|---|---|---|
| Age, years | 66.0 | (8.9) | 64.9 | (9.0) | NS[b] |
| Body weight, kg | 73.9 | (9.4) | 65.3 | (12.2) | <0.001[b] |
| Duration of disease, months | 78.1 | (59.7) | 90.7 | (59.4) | NS[b] |
| Duration of levodopa treatment, months | 59.4 | (56.1) | 71.3 | (56.5) | NS[b] |
| Daily levodopa dosage, mg[a] | 450 | (100–1350) | 500 | (100–1390) | NS[c] |
| UPDRS-ME at baseline[a] | 18 | (5.0-39.5) | 20 | (3.5-51.0) | NS[c] |
| Hoehn-Yahr score[a] | 2.5 | (1–5) | 2.5 | (1–5) | NS[c] |
| Dyskinetic subjects, n (%) | 26 | (28.6) | 39 | (53.4) | 0.001[d] |
| AUC-l, µmol/l h | 4.94 | (2.93) | 6.45 | (3.32) | 0.002[b] |

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

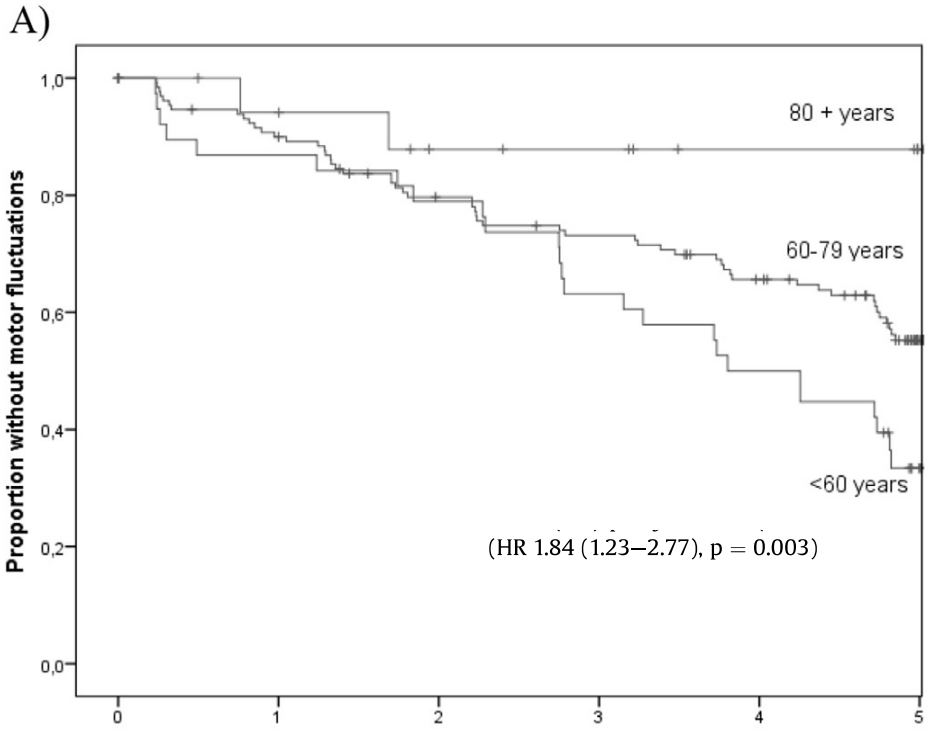
journal homepage: www.elsevier.com/locate/parkreldis

# Risk and course of motor complications in a population-based incident Parkinson's disease cohort

Anders Bjornestad [a, d, *], Elin B. Forsaa [a, d], Kenn Freddy Pedersen [a, d], Ole-Bjorn Tysnes [b, c], Jan Petter Larsen [a], Guido Alves [a, d]

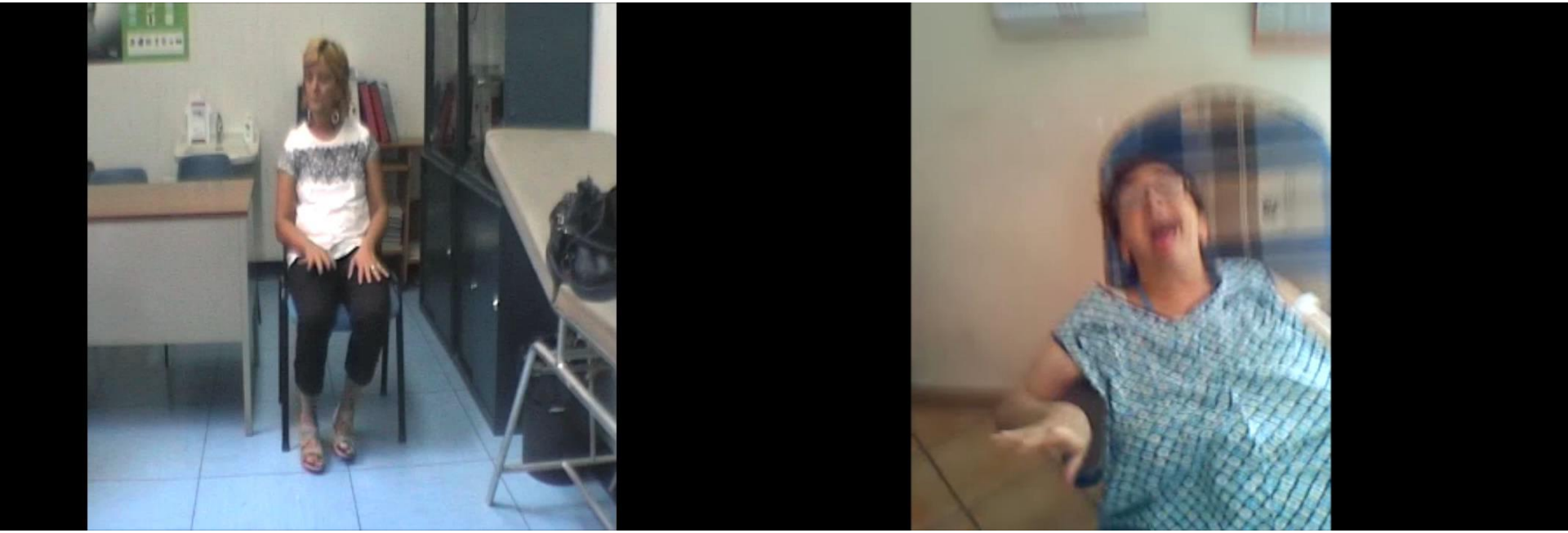
## Gender

A)




older. In contrast, gender was the most important independent predictor of dyskinesias, with an almost 3-fold increased risk in females. This confirms previous findings of gender as a strong, individual predictor of dyskinesias, proposed to overcome potential protective effects of genetic factors such as dopamine receptor D2 polymorphisms [29]. It has been proposed that the gender-difference in risk of dyskinesias observed in our cohort and other studies could be due to lower body weight in females than males [30]. This is, however, not supported by our findings, suggesting that other factors, e.g. genetic predisposition, may be more important. In addition, we found no association between dyskine-

# Dyskinesia occur in women irrespective to body weight



# Outline

Epidemiologia

Sintomi motori e non motori

Cognitività

Biomarcatori

Implicazioni e prospettive future

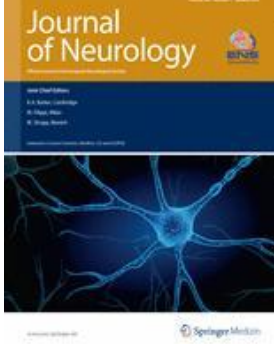
Goya, Maya desnuda, 1797

Goya, Maya vestida, 1800

ORIGINAL COMMUNICATION

# Gender differences in non-motor symptoms in early, drug naïve Parkinson's disease

Marina Picillo · Marianna Amboni · Roberto Erro · Katia Longo · Carmine Vitale · Marcello Moccia · Angela Pierro · Gabriella Santangelo · Anna De Rosa · Giuseppe De Michele · Lucio Santoro · Giuseppe Orefice · Paolo Barone · Maria Teresa Pellecchia




93 Healthy Controls
60/33 M/W

NMS evaluated with NMS-Questionnaire (NMS-Q)

| | Total PD patients, *n* (%) | Female PD patients, *n* (%) | Male PD patients, *n* (%) | *p* |
|---|---|---|---|---|
| Sex difficulties | 23 (11.5) | 1 (1.4) | 22 (17.5) | 0.001 |
| Taste/smelling | 41 (20.5) | 9 (12.2) | 32 (25.4) | 0.024 |

200 PD Patients
126/74 M/W

J Neurol (2013) 260:2849–2855

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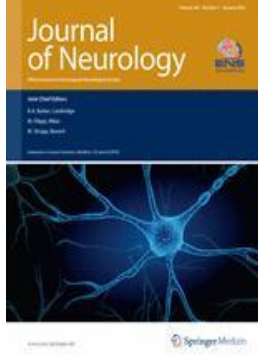
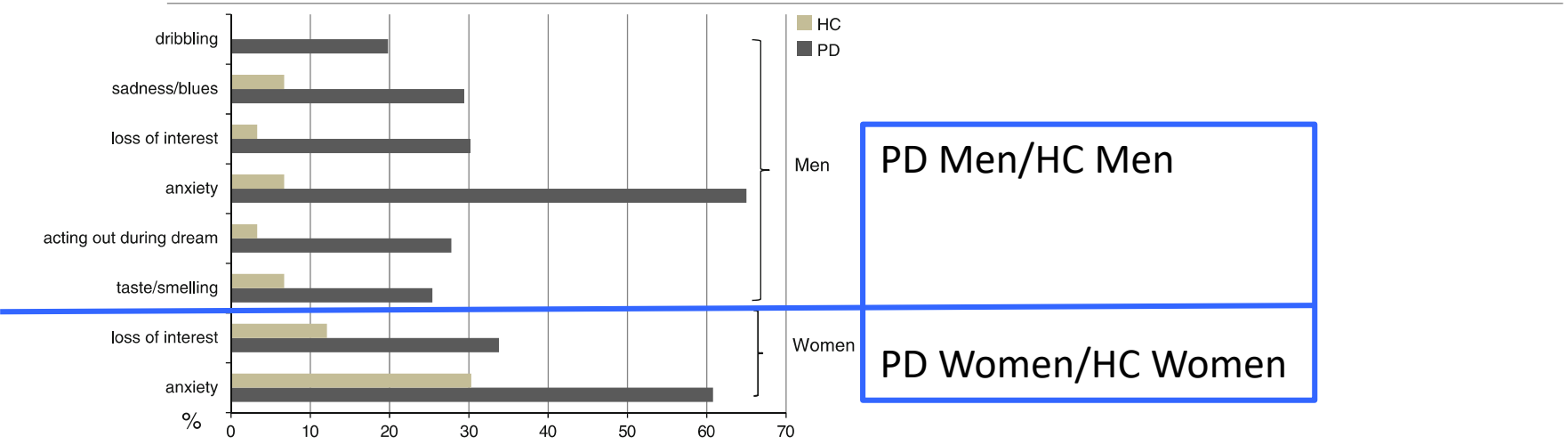
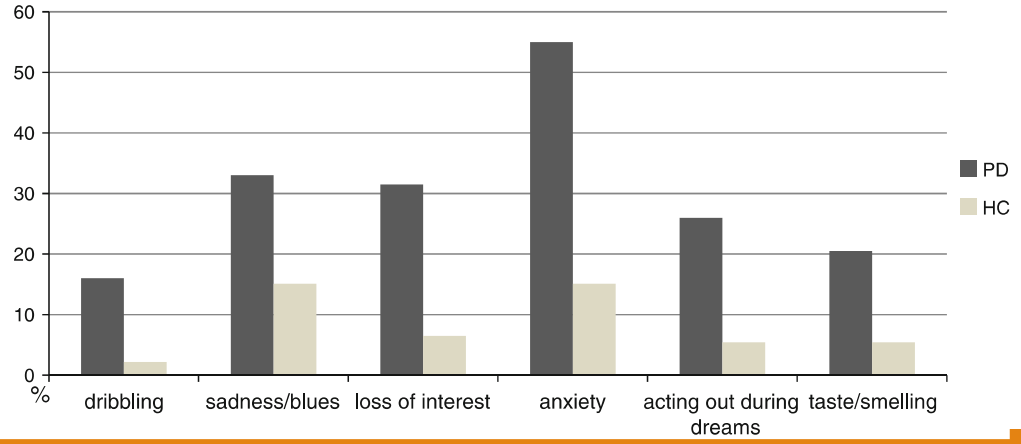



PD Men/HC Men

PD Women/HC Women

NMS featuring prodromal PD segregate in men




J Neurol (2013) 260:2849–2855

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

# Gender differences in non-motor symptoms in early Parkinson's disease: A 2-years follow-up study on previously untreated patients

Marina Picillo [a,b], Roberto Erro [c], Marianna Amboni [b,d], Katia Longo [d], Carmine Vitale [d,e], Marcello Moccia [a], Angela Pierro [b], Sara Scannapieco [b], Gabriella Santangelo [f], Emanuele Spina [a], Giuseppe Orefice [a], Paolo Barone [b,*], Maria Teresa Pellecchia [b]

Same cohort of PD patients was prospectively followed for 2 years

Aim: to assess the gender-related effect of dopaminergic therapy in early PD

Patients taking meds other than levodopa, dopamine agonists and i-MAO were excluded

| | Men | Women | p |
|---|---|---|---|
| NMS-Q, total (baseline) | 4.4 (3.2) | 3.8 (2.9) | 0.3 |
| NMS-Q, total (2-year follow up) | 4.5 (2.9) | 3.1 (2.2) | **0.005** |
| NMS improved | swallowing<br>sadness/blues<br>anxiety | sadness/blues<br>dizziness | NA |
| NMS worsened | urinary urgency<br>sex drive<br>weight change | ---------- | NA |

NMS evaluated with NMS-Questionnaire (NMS-Q)

# Gender effect on non-motor symptoms in Parkinson's disease: are men more at risk?

A. Nicoletti [a], R. Vasta [a], G. Mostile [a], G. Nicoletti [b], G. Arabia [c], G. Iliceto [d], P. Lamberti [d], R. Marconi [e], L. Morgante [f], P. Barone [g], A. Quattrone [b, c], M. Zappia [a, *]

NMS and PD multivariate analysis, logistic regression, stratified by sex.

| | *Men* | | | | Adj OR | 95%CI | *p-value* | *Women* | | | | Adj OR | 95%CI | *p-value* |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | PD (n = 348) | | Controls (n = 168) | | | | | PD (n = 237) | | Controls (n = 313) | | | | |
| | n | % | n | % | | | | n | % | n | % | | | |
| Gastrointestinal dist. | 194 | 55.7 | 31 | 18.4 | 6.81 | 4.26–10.87 | <0.0001 | 144 | 60.7 | 95 | 30.3 | 2.84 | 1.96–4.13 | <0.0001 |
| Urinary dist. | 102 | 29.3 | 26 | 15.5 | 2.52 | 1.54–4.11 | <0.0001 | 90 | 38.0 | 34 | 10.9 | 3.64 | 2.29–5.80 | <0.0001 |
| Sexual dysfunction [a] | 80 | 41.7 | 13 | 26.0 | 1.96 | 0.94–4.06 | 0.07 | 19 | 36.5 | 23 | 22.5 | 1.64 | 0.77–3.52 | 0.2 |
| Sleep disturbances | 210 | 60.5 | 49 | 29.1 | 3.83 | 2.57–5.71 | <0.0001 | 145 | 61.7 | 127 | 40.6 | 1.86 | 1.29–2.68 | 0.0001 |
| Hallucination | 42 | 12.1 | 0 | 0 | / | / | / | 37 | 15.6 | 0 | 0 | / | / | / |
| Cognitive impairment [b] | 55 | 15.8 | 6 | 3.6 | 5.44 | 2.27–12.98 | <0.0001 | 37 | 15.6 | 14 | 4.5 | 2.82 | 1.43–5.56 | <0.0001 |
| Mild depression [c] | 95 | 27.4 | 2 | 1.2 | 30.88 | 7.50–126.93 | <0.0001 | 85 | 35.9 | 11 | 3.5 | 12.72 | 6.49–24.95 | <0.0001 |
| Major depression [d] | 59 | 17.0 | 1 | 0.60 | 33.84 | 4.64–246.61 | 0.001 | 56 | 23.6 | 5 | 1.60 | 14.74 | 5.69–38.18 | <0.0001 |

PD women showed a significantly higher frequency of depression and urinary disturbances than parkinsonian men

Parkinsonism Relat Disord 2017

# Non motor fluctuations

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

# Gender and non motor fluctuations in Parkinson's disease: A prospective study

Marina Picillo [a], Raffaele Palladino [b, c], Marcello Moccia [d], Roberto Erro [e], Marianna Amboni [f], Carmine Vitale [f, g], Paolo Barone [a], Maria Teresa Pellecchia [a, *]

- 47 PD (16W/31M) followed for 4 years since diagnosis
- Non motor fluctuations evaluated with WOQ-19

Frequency of motor and non motor wearing off symptoms as reported by the WOQ-19 at 4-year follow up for the whole population and according to gender.

| WO symptoms, n (%) | Patients | | | |
|---|---|---|---|---|
| | All (47) | Women (16) | Men (31) | p |
| **Motor** | | | | |
| Tremor | 12 (25.5) | 4 (25) | 8 (25.8) | 0.62 |
| Difficulty in speech | 6 (12.8) | 3 (18.8) | 3 (9.7) | 0.32 |
| Weakness | 8 (17) | 4 (25) | 4 (12.9) | 0.25 |
| Problems with balance | 5 (10.6) | 3 (18.8) | 2 (6.5) | 0.2 |
| Slowness of movements | 19 (40.4) | 7 (43.8) | 12 (38.7) | 0.48 |
| Reduced dexterity | 16 (34) | 6 (37.5) | 10 (32.3) | 0.48 |
| General stiffness | 8 (17) | 4 (25) | 4 (12.9) | 0.25 |
| Muscle cramps | 2 (4.3) | 1 (6.3) | 1 (3.2) | 0.57 |
| Getting out of chair | 2 (4.3) | 0 (0) | 2 (6.5) | 0.43 |
| **Non Motor** | | | | |
| Anxiety | 10 (21.3) | 6 (37.5) | 4 (12.9) | **0.05** |
| Sweating | 0 (0) | 0 (0) | 0 (0) | 1 |
| Mood changes | 9 (19.1) | 6 (37.5) | 3 (9.7) | **0.03** |
| Numbness | 5 (10.6) | 3 (18.8) | 2 (6.5) | 0.20 |
| Panic attacks | 1 (2.1) | 1 (6.3) | 0 (0) | 0.34 |
| Cloudy mind | 4 (8.5) | 1 (6.3) | 3 (9.7) | 0.58 |
| Abdominal discomfort | 0 (0) | 0 (0) | 0 (0) | 1 |
| Feelings of hot/cold | 2 (4.3) | 1 (6.2) | 1 (3.2) | 0.57 |
| Pain | 6 (12.8) | 5 (31.3) | 1 (3.2) | **0.01** |
| Aching | 2 (4.3) | 2 (12.5) | 0 (0) | 0.11 |
| WOQ-19 Total score $\geq 2$ | 26 (55.3) | 12 (75) | 14 (45.2) | **0.04** |
| WOQ-19 Motor score $\geq 1$ | 28 (59.6) | 12 (75) | 16 (51.6) | 0.1 |
| WOQ-19 Non motor score $\geq 1$ | 18 (38.3) | 10 (62.5) | 8 (25.8) | **0.01** |

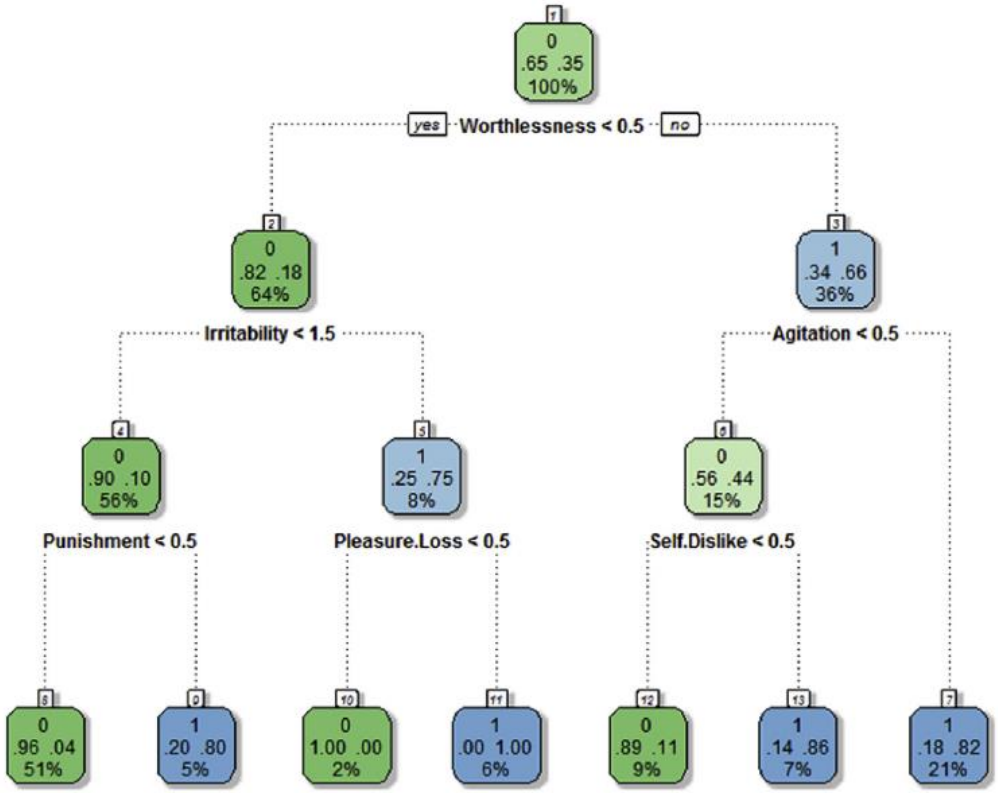
In conclusion, we conducted a prospective study on early, drug-naïve PD patients followed for 4 years since diagnosis and showed that female gender represents a major risk factor for the development of NMF. No gender differences in medication intake were noticed, supporting the hypothesis that NMF in women remain mostly underestimated and undertreated. From a practical standpoint, our findings prompt the clinician to consider the role of gender in the management of NMF in PD.

Short communication

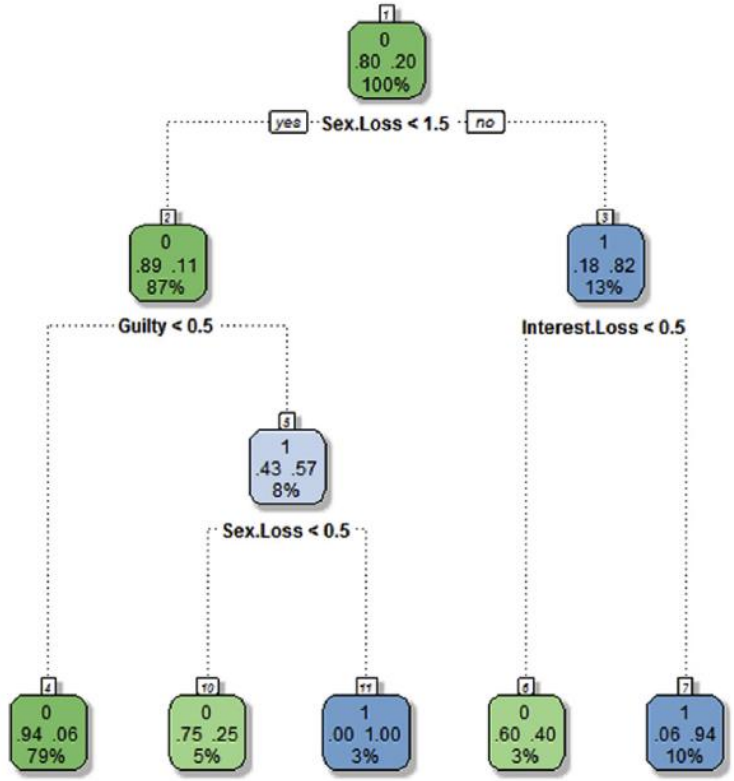
# Gender differences in Parkinson's disease depression

Andrew J. Perrin [a, c, *], Ekaterina Nosova [b], Kim Co [b], Adam Book [b, c], Oscar Iu [b], Vanessa Silva [b, c], Christina Thompson [b], Martin J. McKeown [c], A. Jon Stoessl [c], Matthew J. Farrer [b], Silke Appel-Cresswell [c, **]

**Women**

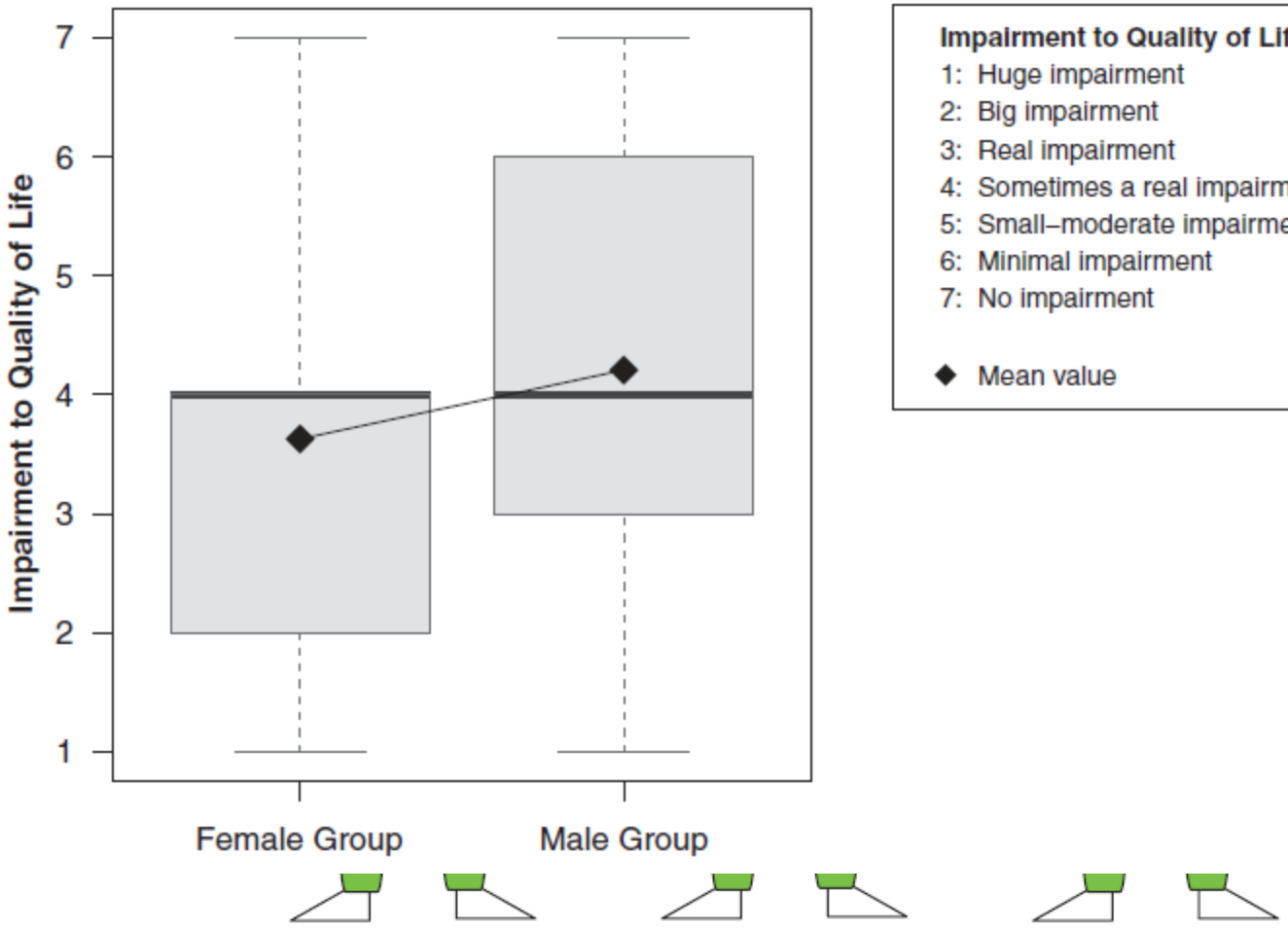



**Men**



# Landscape of pain in Parkinson's disease: impact of gender differences

Maria Angela Samis Zella[a,b], Caroline May[c], Thomas Müller[d], Maike Ahrens[c], Lars Tönges[a], Ralf Gold[a], Katrin Marcus[c] and Dirk Woitalla[a,b]




Neurol Res, 2019

# Outline

Epidemiologia

Sintomi motori e non motori

Cognitività

Biomarcatori

Implicazioni e prospettive

Artemisia Gentileschi, Self-portrait as the allegory of painting, 1638-1639

# Longitudinal study of normal cognition in Parkinson disease

Pigott et al


- 55 (63%M) cognitively intact PD patients followed for 6 years
- About 50% developed any kind of cognitive impairment by the end of the study

**Figure 1** Kaplan-Meier survival curve for progression from normal cognition to any cognitive impairment

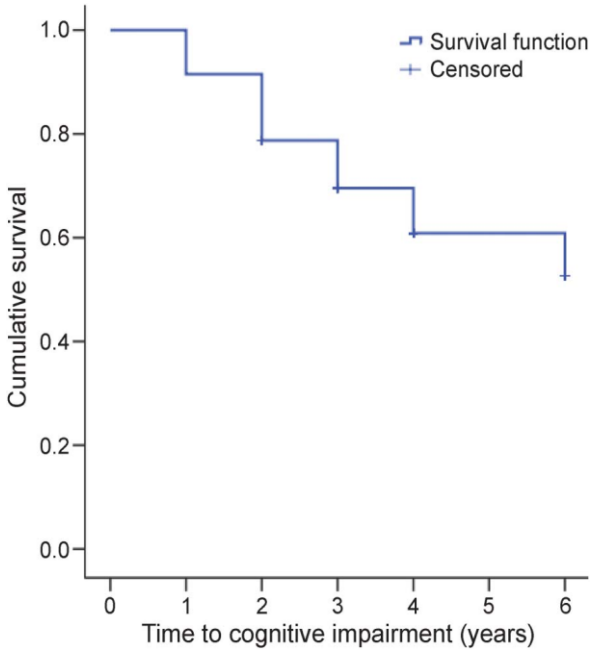



**Table 3** Cox regression model of factors predicting progression to cognitive impairment

| Variable | Wald | *df* | Hazard ratio | 95% CI of hazard ratio | | *p* Value |
|---|---|---|---|---|---|---|
| | | | | Lower | Upper | |
| Sex | 5.755 | 1 | 0.467 | 0.251 | 0.870 | 0.02 |
| Age | 0.025 | 1 | 1.003 | 0.961 | 1.048 | 0.87 |
| Duration of disease | <0.001 | 1 | 1.000 | 0.939 | 1.064 | 0.99 |
| H&Y | 1.308 | 1 | 1.450 | 0.767 | 2.740 | 0.25 |
| UPDRS III motor | 15.539 | 1 | 1.079 | 1.039 | 1.121 | <0.001 |
| GDS-15 score | 1.836 | 1 | 1.073 | 0.969 | 1.189 | 0.18 |
| DRS-2 total score | 14.094 | 1 | 0.809 | 0.724 | 0.904 | <0.001 |

Abbreviations: CI = confidence interval; DRS-2 = Dementia Rating Scale-2; GDS-15 = 15-item Geriatric Depression Scale; H&Y = Hoehn & Yahr; UPDRS = Unified Parkinson's Disease Rating Scale.

Male gender is a risk factor for cognitive impairment in PD

# Predictors of dementia in Parkinson disease

## A prospective cohort study

Anang et al


- 80 (51M/29W) PD patients followed for 4.4 (2.0) years
- 27/80 (22M/5W) developed dementia

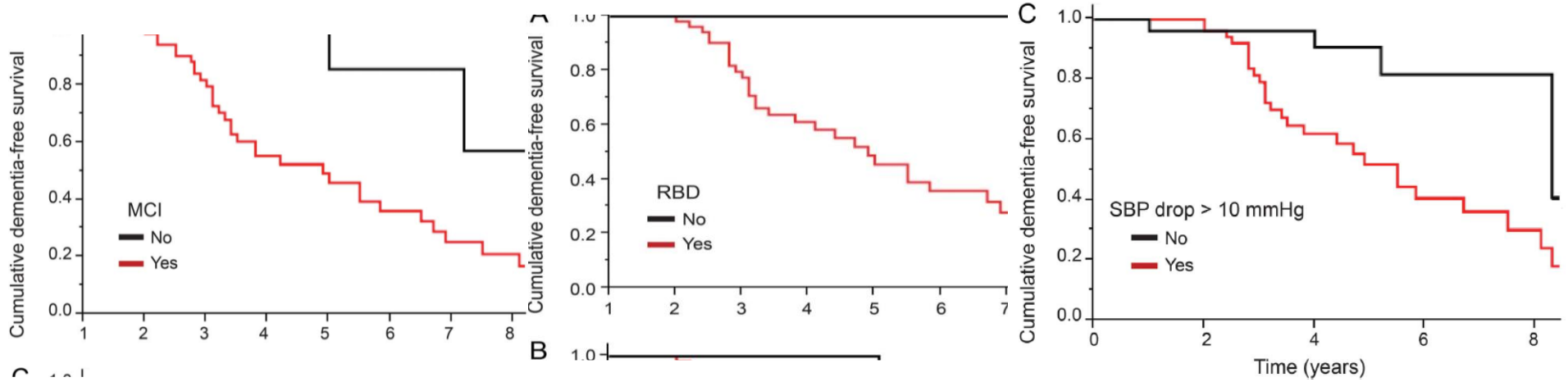



**Table 1** Demographic and motor predictors of dementia

| | All patients (N = 80) | Without dementia (n = 53) | With dementia (n = 27) | Odds ratio (90% CI) | *p* Value |
|---|---|---|---|---|---|
| Age, y | 66.2 (10.9) | 63.6 (8.0) | 70.48 (7.02) | 1.14 (1.07-1.21) | 0.001 |
| Sex, M/F | 51/29 | 29/24 | 22/5 | 3.64 (1.43-9.26) | 0.023 |
| Duration of disease, baseline, y | 5.7 (4.2) | 5.4 (4.0) | 6.02 (4.11) | 1.04 (0.94-1.14) | 0.54 |
| Follow-up duration, y | 4.4 (2.0) | 4.2 (1.9) | 4.70 (2.07) | 1.12 (0.92-1.37) | 0.34 |
| Hoehn and Yahr stage | 2.4 (0.9) | 2.3 (0.9) | 2.8 (0.9) | 1.53 (0.79-2.94) | 0.30 |
| UPDRS part III score | 24.0 (10.7) | 24.0 (10.3) | 23.8 (12.1) | 0.97 (0.92-1.01) | 0.21 |
| Total UPDRS score | 38.6 (15.7) | 37.6 (14.9) | 41.7 (17.8) | 0.99 (0.96-1.03) | 0.73 |

Male gender is a risk factor for development of dementia in PD

*Neurology*® 2014;83:1253-1260

# Outline

Epidemiologia

Sintomi motori e non motori

Cognitività

Biomarcatori

Implicazioni e prospettive

Manet, I bar delle Folies Bergere, 1882

# Prospective study of plasma urate and risk of Parkinson disease in men and women

Gao et al

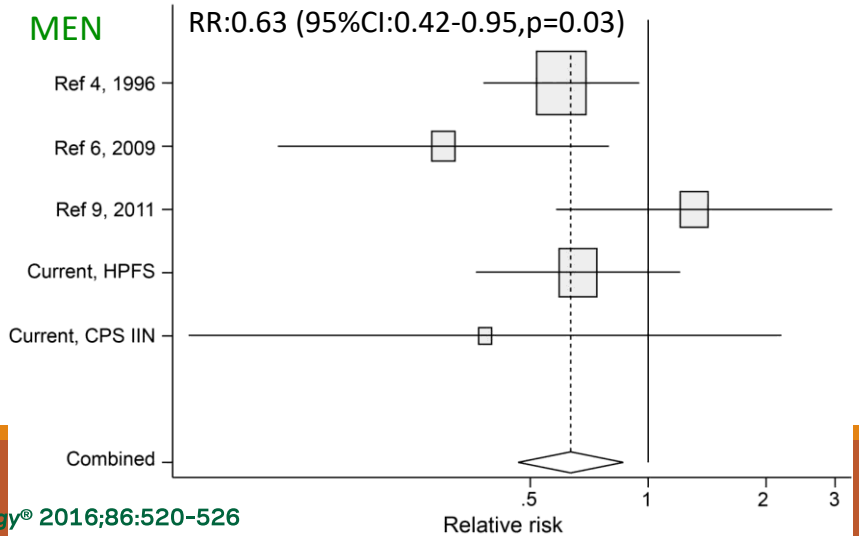

- Urate is a potent antioxidant
- Higher plasma urate is associated with a lower risk of developing PD and with slower disease progression
- Unanswered question: is gender relevant?

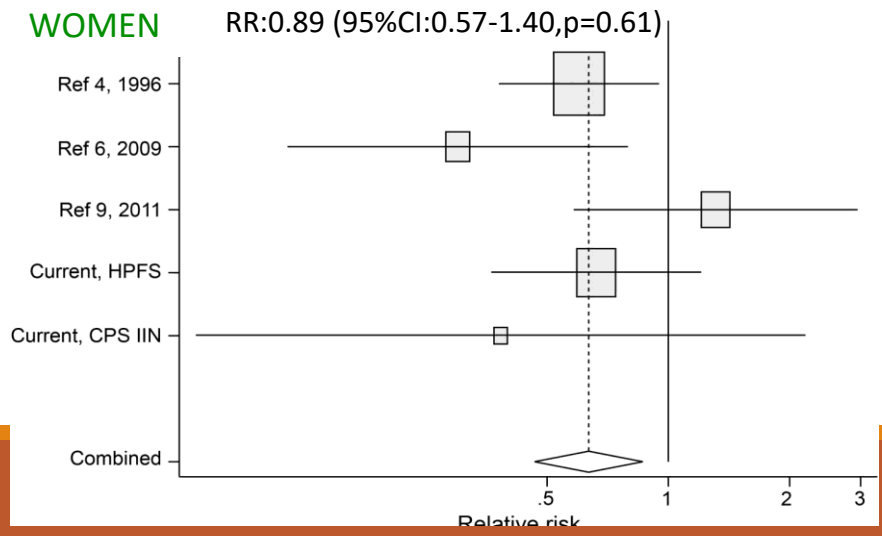
-Data merged from 3 cohort studies including>90.000 men and women

-388 (202M/186W) new incident PD matched with 1.267 controls (446M/821W)

Table 2 Relative risk (RR) of Parkinson disease according to quartiles of plasma/serum urate in the Health Professionals Follow-up Study, Nurses' Health Study, and Cancer Prevention Study II Nutrition cohort

| | Quartile of serum urate | | | | |
|---|---|---|---|---|---|
| | Q1 | Q2 | Q3 | Q4 | $p_{trend}$ |
| Men | | | | | |
| Cases/controls, n | 58/107 | 48/120 | 51/108 | 45/111 | |
| Age- and smoking-adjusted RR | 1 (ref) | 1.00 (0.62, 1.59) | 0.72 (0.24, 2.17) | 0.59 (0.35, 0.99) | 0.018 |
| Multivariate-adjusted RR | 1 (ref) | 0.76 (0.21, 2.66) | 0.76 (0.20, 2.93) | 0.63 (0.35, 1.10) | 0.049 |
| Women | | | | | |
| Cases/controls, n | 42/210 | 48/204 | 51/198 | 45/209 | |
| Age- and smoking-adjusted RR | 1 (ref) | 1.03 (0.40, 2.64) | 1.28 (0.80, 2.03) | 1.06 (0.66, 1.71) | 0.38 |
| Multivariate-adjusted RR | 1 (ref) | 0.62 (0.05, 7.26) | 1.29 (0.78, 2.12) | 1.04 (0.61, 1.78) | 0.44 |




Neurology® 2016;86:520-526

# Outline

Epidemiologia

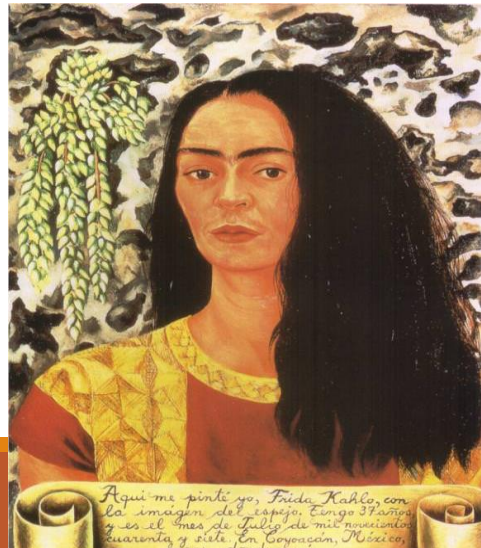
Sintomi motori e non motori

Cognitività

Biomarcatori

Implicazioni e prospettive

- ✓Strategie differenti per identificare i casi prodromici
- ✓Migliorare il trattamento




Frida Kahlo, Self-portrait with loose hair, 1947

# Potential sex differences in nonmotor symptoms in early drug-naive Parkinson disease


Liu et al

PPMI cohort: 414 PD (269M/145W) and 188 HC (121M/67W)

**NMS comparisons between sex in patients with PD and in healthy controls**

| | Healthy controls | | | | PD | | | |
|---|---|---|---|---|---|---|---|---|
| NMS | Total (n = 188) | Male (n = 121) | Female (n = 67) | *p* Value[a] | Total (n = 414) | Male (n = 269) | Female (n = 145) | *p* Value[a] |
| Sleep disorder | | | | | | | | |
| Epworth Sleepiness Scale | 5 (3-8) | 5 (3-8) | 5 (3-7) | 0.74 | 5 (3-8) | 6 (3-8) | 5 (3-8) | 0.37 |
| RBDSQ | 2 (1-4) | 2 (1-4) | 2 (1-4) | 1.00 | 3 (2-6) | 4 (2-6) | 3 (2-5) | 0.16 |
| Olfactory | | | | | | | | |
| UPSIT | 35 (33-37) | 35 (32-37) | 36 (34-38) | 0.28 | 22 (16-29) | 21.5 (15-28) | 24 (19-31) | 0.02[b] |
| Neurobehavioral | | | | | | | | |
| Total anxiety | 53 (46-65) | 52 (46-64) | 54 (45-69) | 0.39 | 61 (51-75) | 60 (50-75) | 64 (53-76) | 0.11 |
| State anxiety | 25 (21-33) | 25 (21-33) | 26 (21-33) | 0.87 | 31 (24-39) | 31 (24-38) | 31 (25-40) | 0.95 |
| Trait anxiety | 27 (23-32.5) | 26 (24-32) | 29 (23-35) | 0.45 | 31 (25-37) | 29 (25-36) | 32 (27-40) | 0.02[b] |
| Geriatric depression | 1 (0-2) | 1 (0-1) | 1 (0-2) | 1.00 | 2 (1-3) | 2 (1-3) | 2 (1-3) | 1.00 |
| Cognitive domains[c] | | | | | | | | |
| Global | 28 (27-29) | 28 (27-29) | 28 (27-29) | 0.52 | 28 (26-29) | 27 (26-29) | 28 (26-29) | 0.0008[b] |
| Memory | 51.8 (45.3-56.8) | 49.7 (43.3-55.0) | 53.7 (48-57.3) | 0.0007[b] | 47.3 (41.7-54.0) | 46 (40.7-52) | 50.7 (43.2-56.3) | 0.0003[b] |
| Visuospatial | 59.5 (53.8-65.2) | 60.9 (56.3-66.7) | 55.8 (50-62.4) | 0.002[b] | 58.7 (52-64.7) | 60.3 (55.1-66.7) | 55.7 (46.6-60.6) | <0.0001[b] |
| Working memory–executive | 53.6 (49.2-58.8) | 53.3 (49.2-58.2) | 53.8 (49.7-60.2) | 0.43 | 53.2 (48-57.3) | 53.2 (47.7-57.5) | 53.3 (48.5-57.2) | 0.72 |
| Attention-processing speed | 50 (43.2-57) | 48.8 (42.5-55) | 52 (45-58.3) | 0.04[b] | 46 (40-51) | 45 (39-49.2) | 47 (41.3-52) | 0.29 |
| Autonomic | | | | | | | | |
| SCOPA-AUT | 5 (3-7) | 5 (3-7) | 6 (4-9) | 0.002[b] | 8 (5-12) | 8 (5-12) | 9 (6-12) | 0.24 |

# Potential sex differences in nonmotor symptoms in early drug-naive Parkinson disease

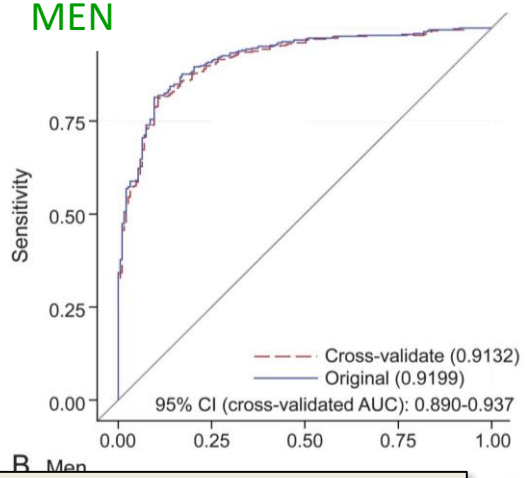
Liu et al


PPMI cohort: 414 PD (269M/145W) and 188 HC (121M/67W)

**Table 3** Significant NMS predictors of PD from multiple stepwise logistic regression analysis

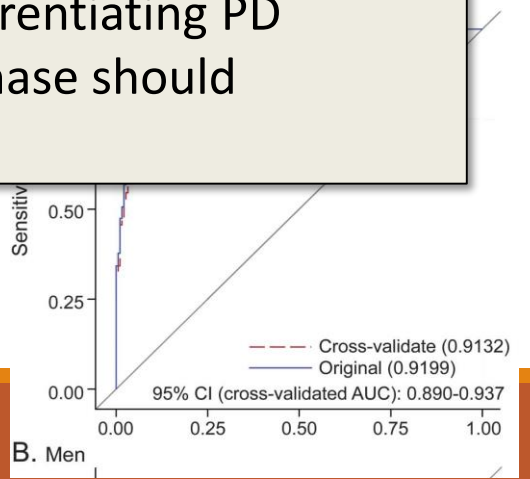
| NMS[a] | Regression coefficient | Standard error | *p* Value | OR[b] | 95% CI |
|---|---|---|---|---|---|
| Overall | | | | | |
| UPSIT | −2.5239 | 0.245 | <0.0001 | 0.08 | 0.05-0.13 |
| SCOPA-AUT | 0.7153 | 0.208 | 0.0006 | 2.05 | 1.36-3.08 |
| MoCA | −0.5219 | 0.177 | 0.003 | 0.59 | 0.42-0.84 |
| State anxiety | 0.3346 | 0.152 | 0.03 | 1.40 | 1.04-1.88 |
| Male | | | | | |
| UPSIT | | | | | |
| SCOPA-AU | | | | | |
| MoCA | | | | | |
| Female | | | | | |
| UPSIT | | | | | |
| RBDSQ | | | | | |
| MoCA | | | | | |

MEN




**Take-home message**

To be effective, strategies aimed at differentiating PD from healthy controls in prodromal phase should consider gender



# Improving therapeutic management

## Gender needs to be considered to better tailor treatment in PD patients

- ✓Disparities in medical management
- ✓Disparities in Deep Brain Stimulation surgery

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Short communication

### Gender and non motor fluctuations in Parkinson's disease: A prospective study

Marina Picillo [a], Raffaele Palladino [b, c], Marcello Moccia [d], Roberto Erro [e], Marianna Amboni [f], Carmine Vitale [f, g], Paolo Barone [a], Maria Teresa Pellecchia [a, *]

Distribution of women and men with subthalamic nucleus (STN) deep brain stimulation (DBS) for Parkinson's disease, in publications worldwide and in specific parts of the world.

| | Worldwide | North America | Europe | Australia | Asia |
|---|---|---|---|---|---|
| No of papers (%) | 135 | 43 (31.9) | 76 (56.3) | 4 (3.0) | 12 (8.9) |
| No of papers (%) in which gender was specified | 119 (88.1) | 37 (86.0) | 68 (89.5) | 3 (75.0) | 11 (91.7) |
| Total no (%) of reported patients | 4700 | 1461 (31.1) | 2736 (58.2) | 135 (2.9) | 368 (7.8) |
| No (%) of patients with gender reported | 3880 (82.6) | 1082 (74.1) | 2432 (88.9) | 77 (57.0) | 289 (78.5) |
| No (%) of men | 2445 (63.0) | 735 (67.9) | 1513 (62.2) | 53 (68.8) | 144 (49.8) |
| No (%) of women | 1435 (37.0) | 347 (32.1) | 919 (37.8) | 24 (31.2) | 145 (50.2) |

### Disparities in deep brain stimulation surgery among insured elders with Parkinson disease

Neurology®2014;82:163-171

Allison W. Willis, MD, MSCI
Mario Schootman, PhD
Nathan Kung, MD
Xiao-Yu Wang
Joel S. Perlmutter, MD
Brad A. Racette, MD

ABSTRACT

**Objective:** To identify sociodemographic, clinical, and physician/practice factors associated with deep brain stimulation (DBS). DBS is a proven surgical therapy for Parkinson disease (PD), but is recommended only for patients with excellent health, results in significant out-of-pocket costs, and requires substantial physician involvement.

**Methods:** Retrospective cohort study of more than 657,000 Medicare beneficiaries with PD. Multivariable logistic regression models examined the association between demographic, clinical, socioeconomic status (SES), and physician/practice factors, and DBS therapy.

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

Parkinsonism and Related Disorders 17 (2011) 146–149

Review

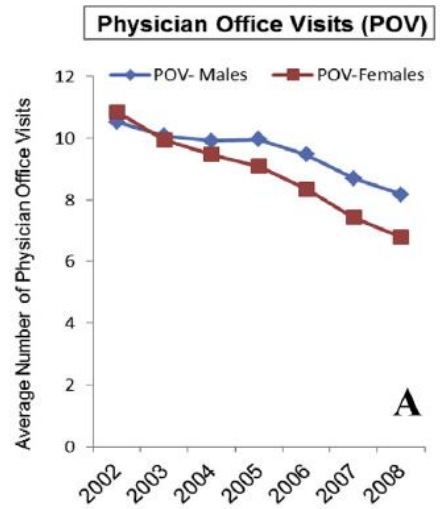
### Gender distribution of patients with Parkinson's disease treated with subthalamic deep brain stimulation; a review of the 2000–2009 literature☆

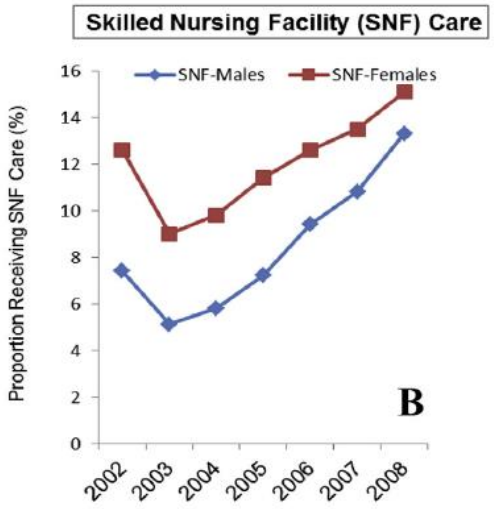
Gun-Marie Hariz [a,b,*], Takeshi Nakajima [c,d], Patricia Limousin [c], Tom Foltynie [c], Ludvic Zrinzo [c], Marjan Jahanshahi [c], Katarina Hamberg [e]

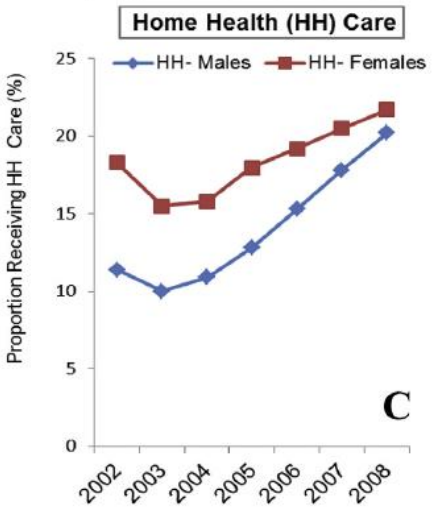
# Sex disparities in health and health care utilization after Parkinson diagnosis: Rethinking PD associated disability

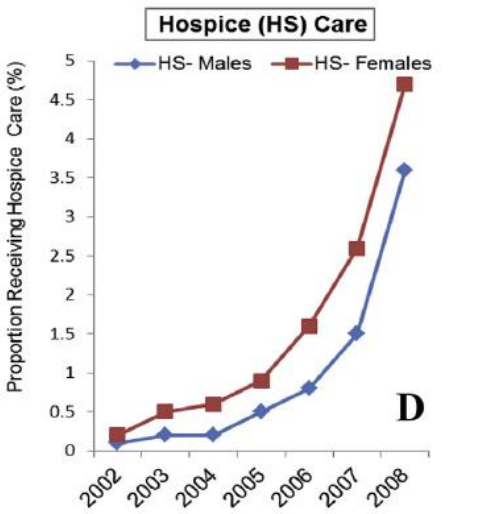
Michelle E. Fullard [a,*], Dylan P. Thibault [a,b], Veronica Todaro [c], Susan Foster [c], Lori Katz [c], Robin Morgan [c], Drew S. Kern [d,j], Jason M. Schwalb [e,j], Enrique Urrea Mendoza [f,j], Nabila Dahodwala [a,j], Lisa Shu

| Disease | IR | LCL | UCL |
|---|---|---|---|
| Arthritis | 1.51 | 1.47 | 1.55 |
| Atrial Fibrillation | 0.89 | 0.86 | 0.92 |
| Cataract | 1.09 | 1.06 | 1.12 |
| Chronic Kidney D | 0.82 | 0.8 | 0.84 |
| Colorectal Cance | 0.88 | 0.8 | 0.97 |
| Congestive Heart | 0.98 | 0.96 | 1 |
| COPD | 0.88 | 0.86 | 0.91 |
| Dementia | 1.02 | 1.01 | 1.04 |
| Depression | 1.52 | 1.49 | 1.55 |
| Diabetes | 1.14 | 1.1 | 1.18 |
| Glaucoma | 1.12 | 1.06 | 1.17 |
| Hip Fracture | 1.59 | 1.53 | 1.66 |
| Ischemic Heart D | 0.96 | 0.93 | 0.98 |
| Lung Cancer | 0.69 | 0.63 | 0.76 |
| Myocardial Infarc | 0.83 | 0.79 | 0.87 |
| Osteoporosis | 2.73 | 2.64 | 2.81 |
| Stroke/TIA | 1.05 | 1.02 | 1.08 |
| Incidence Ratio (I | | | |
| More Affected Se | | | |




Parkinsonism Relat Disord, 2018

# GENDER MATTERS IN PD

**Future studies of gender differences in care needs, care quality, comorbidity related disability, PD progression, and non-clinical factors associated with disability are needed to inform clinical guidelines that may improve quality of life in patients with PD**