D.7 Managing and monitoring impulse control disorder as an adverse effect of dopaminergic treatment

D.7.1 Predictors for the development of impulse control disorders

Study details	Participants	Methods	Results	Comments
Full citation Antonini,A., Chaudhuri,K.R., Boroojerdi,B., et al. Impulse control disorders during long-term rotigotine treatment: a post hoc analysis, Euopean Journal of Neurology 23, 1556-65, 2016 Country/ies where the study was carried out Multinational Study type Retrospective analysis of cohort studies Aim of the study To evaluate the long term frequency of ICD behaviours in people using rotigotine transdermal patches Source of funding UCB Pharma	Sample size N=786 Long-term follow-up data from 6 studies of rotigotine transdermal patches, with follow-ups from 1 year to 6 years. The trials included had a variety of different inclusion criteria, including differences in serverity of PD and other medicines permitted during the studies.	ICDs were classified using the Medical Dictionary for Regulatory Activities Preferred Terms. Characteristics of individuals were then compared between people who did and did not develop ICDs. Information was collected on age, sex, time since diagnosis, severity of PD and medicines taken, though only some results were presented in a dichotomised way that enabled the calculation of odds ratios.	Results Demographics: mean age 63 (9.7) 65% male duration of disease 4.9 years mean UPDRS II 10.7 mean UPDRS III 24.3 Findings: Male: OR 1.14 (0.68, 1.92) Levodopa use during study: OR 2.35 (0.83, 6.61) Rotigotine dose (12-16mg/day versus 2-10mg/day): OR 0.66 (0.40, 1.08)	CASP quality appraisal checklist 1. Did study address on clearly focused issue? yes 2. Was cohort recruited in acceptable way? yes 3. Was exposure accurately measured to minimise bias? No adjustments made for differences between studies 4. Was outcome accurately measured to minimise bias? 5. Have authors identified all important confounding factors and taken account of these in design/analysis? unclear 6. Was follow-up of subjects complete/long enough? Different lengths of follow-up between studies 7. What are results? significant predictive factors of ICD reported 8. How precise are results? precise 9. Are results believable? yes 10. Can results be applied to local population? yes 11. Do

Study details	Participants	Methods	Results	Comments
				results fit with other available evidence? yes Moderate risk of bias
Full citation Auyeung,M., Tsoi,T.H., Tang,W.K., Cheung,C.M., Lee,C.N., Li,R., Yeung,E., 20120618, Impulse control disorders in Chinese Parkinson's disease patients: the effect of ergot derived dopamine agonist, Parkinsonism & Related Disorders, 17, 635-637, 2011 Ref Id 306788 Country/ies where the study was carried out China Study type cohort study Aim of the study The Authors studies the prevalence and related risk factors of ICD's in Chinese PD patients Study dates	Sample size N=213 Inclusion criteria prospectively entered all PD patients who presented to clinic from 1999 onwards into a PD databank. Dementia was screened and anly patient with an MMSE of <26 would be sent to a cognitive neurologist for demenita assessment. From aug 1999 to aug 2010 authors screened all non-demented PD patients diagnosed by brain bank criteria who attended the PD clinic and had thier information entered into the databank. Exclusion criteria	Details pre-designed structured screening questionnaire for ICD was constructed by combining both questionnaires for the QUIP and the hedonistic homeostatic dysregulation screening conducted by a well-trained RA who was blinded to medications patient was taking both patients and carers interviewed as far as possible patients who gave at least 1 positive answer to the questionnaire were seen by a neurologist and a diagnosis of ICD was made according to previously defined criteria those patients who were still sufering from an ICD were labelled as active ICD and those who had a previous ICD were regarded as prior ICD patients	Results demographic mean age at onset 58 (11.1) mean age 67.5 (9.9) 127 male duration of disease 9.3 (5.0) 113/213 DA exposure Dode DA LLED (mg) 98.7 (113.7) total LLED mg 674.9 (387.5) HY 2.3 (0.9) UPDRS 28.1 (17.4) young onset (<50 years) 57/213 findings identified 15/213 (7%) subjects with ICD multivariate analysis revealed following factors to be significantly predictive of IC: young age onset OR = 4.1 (95% CI: 1.1 to 15.9) subjects with anxiety or depression: OR = 10.0 (95% CI:2.0 to 50.8) dose of dopamine agonist /100mg 2.4 (95% CI:1.2 to 4.3)	Overall Risk of Bias CASP quality appraisal checklist 1. Did study address on clearly focused issue? yes 2. Was cohort recruited in acceptable way? yes 3. Was exposure accurately measured to minimise bias? yes 4. Was outcome accurately measured to minimise bias? yes, however PD patients asked to recall symptoms and medications, details etc at that time. Prone to significant recall bias 5. Have authors identified all important confounding factors and taken account of these in design/analysis? yes 6. Was follow-up of subjects complete/long enough? NA 7. What are results? significant predictive factors of ICD reported 8. How precise are results?precise 9. Are results believable? yes 10. Can results be applied to local

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr><td>Received 4th Feb 2011, revised 25th May, Accepted 2nd June

Source of funding
Not listed</td><td>Patients with a diagnosis of dementia</td><td>clinical and demographic data was collected , including medication information, UPDRS, and depression

Interventions
NA</td><td></td><td>population? yes 11. Do results fit with other available evidence? yes

low risk of bias</td></tr>
<tr><td>Full citation
Giladi,N., Weitzman,N., Schreiber,S., Shabtai,H., Peretz,C., 20071004, New onset heightened interest or drive for gambling, shopping, eating or sexual activity in patients with Parkinson's disease: the role of dopamine agonist treatment and age at motor symptoms onset, Journal of Psychopharmacology, 21, 501-506, 2007
Ref Id
307571
Country/ies where the study was carried out
Israel
Study type
case-control study</td><td>Sample size
N=203 consecutive PD patients and 190 age and gender matched healthy individuals

Inclusion criteria
Consecutive patients diagnosed with PD according to UK brain bank criteria and being treated at tge Movement disorders unit and national parkinson's disease centre of tertiary care

Exclusion criteria
the following groups of patients were excluded:
Patients with dementia according</td><td>Details
Patients underwent cognitive screening during neurological interview. Medical, medical history, ADL H&Y stage, UPDRS, disease duration and treatments were all recorded.
Behavioural aspects of patients and controls were assessed by a personal interview that included general personal and medical history. New onset of gambling, shopping, eating, or sexual behaviour (GSES) were assessed by direct questions to both the patient and the spouse or immediate caregiver.</td><td>Results
demographics
mean age = 67.5 (10.9) for PD and 66.7 (11.6) for control
mean age at time of diagnosis = 57.7 years (12.2)
122/193 (63%) were male
27/193 (14%) of patients were found to have new onset heightened interest or drive in GSES which had developed after onset of PD motor symptoms.
behavior:
gambling n=6 (3.1%);
shopping n=6 (3.1%);
eating n=7 (3.6%);
sexual n=17 (8.8%);
number of patients with >1 GSES n=10 (5.0%).

characteristic comparisons
<table><tr><td>male (%)</td><td>78</td><td>56</td><td>p = 0.09</td></tr><tr><td>age of motor symptom onset</td><td>51.5 (12.2)</td><td>58.7 &12.1)</td><td>p=0.006</td></tr></table></td><td>Overall Risk of Bias
No quantification of how diagnosis of ICD was made. only behavioral interview. Adjusted odds ratio not clear on what is adjusted for. Also not clear at all why healthy control population was recruited?

1. Did study address on clearly focused issue? yes 2. Was cohort recruited in acceptable way? yes, consecutive recruitment 3. Was exposure accurately measured to minimise bias? NO - only GSES behavioural interview 4. Was outcome accurately measured to minimise bias? NO- ICD diagnosis not formally made. behaviours only recorded via interview, no</td></tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>Aim of the study
To examine the prevalence and risk factors for new onset heightened interest or drive in gambling, shopping, eating, or sexual activity in patients with Parkinson's disease.

Study dates
Published 2007; no other information reported

Source of funding
None acknowledged</td>
<td>to DSM IV criteria or if their MMSE was <25.
Patients with a psychiatric illness that required psychotropic medication prior to the onset of PD.
Patients with diaganosed and treated OCD</td>
<td>A heightened interest or drive in GSES was diagnosed if:
patient was frequently (>1x p/w) involved in shoppping or buying merchandise or gifts that both patients and caregiver agreed were unnecessary
patient was involved in active gambling and was attracted to gambling several times per week
the patient developed compulsive, uncontrolled eating habits
the patient and the spouse or caregiver reported heightened sexual drive and freuquent sexual thoughts coupled with demanding behaviour or the amount of time a patient spent engaging with pornographic material

Interventions
na</td>
<td>
<table>
<tr><td>disease duration</td><td>10.3 (4.9)</td><td>9.7 (6.6)</td><td>0.667</td></tr>
<tr><td>Patients on DA</td><td>70</td><td>58</td><td>0.24</td></tr>
<tr><td>mean duration of DA</td><td>4.4 (2.4)</td><td>3.7 &3.1)</td><td>0.324</td></tr>
<tr><td>n on ropinerole (%)</td><td>48.2</td><td>31.3</td><td>0.09</td></tr>
<tr><td>n on pergolide (%)</td><td>22.2</td><td>5.3</td><td>0.737</td></tr>
<tr><td>n on apomorphine (%)</td><td>22.2</td><td>4.2</td><td>p=0.009</td></tr>
<tr><td>n on amantadine (%)</td><td>63</td><td>51.2</td><td>0.25</td></tr>
<tr><td>n on selegeline (%)</td><td>29.7</td><td>25.9</td><td>0.68</td></tr>
</table>
new behavioural change n=27, no behavioural change n=166

Risk factors for development of new heightened interests of drive in GSES among all PD patients.
Multivariate logistic regression:
<table>
<tr><td></td><td>adj OR</td><td></td></tr>
<tr><td>age at PD symptoms onset</td><td>0.99</td><td>95%CI: 0.99 to 1.00</td></tr>
<tr><td>gender male</td><td>1.10</td><td>95%CI:1.00 to 1.22</td></tr>
</table>
</td>
<td>diganostic criteria used. 5. Have authors identified all important confounding factors and taken account of these in design/analysis? yes 6. Was follow-up of subjects complete/long enough? na 7. What are results? risk factors for development of ICD reported 8. How precise are results? unclear- very tight confidence intervals in multivariate analysis, but not clear what OR's are adjusted for/ Control data collected in methods, however not reported. Unclear why collected control data or how it was used? 9. Are results believable? unclear 10. Can results be applied to local population? yes 11. Do results fit with other available evidence? results report lower OR than other studies within the clinical area 12. What are implications for practice? some factors may be associated with increased likelihood of ICD in PD

serious risk of bias.</td>
</tr>
</table>

Study details	Participants	Methods	Results	Comments
			duration of treatment with DA <2 years: 0.95; 95%CI:0.84 to 1.08 duration of treatment with DA <2 years: 1.04; 95%CI: 0.91 to 1.18 duration of treatment with DA <2 years: 1.18; 95%CI: 1.00 to 1.39	
Full citation Imamura,A., Geda,Y.E., Slowinski,J., Wszolek,Z.K., Brown,L.A., Uitti,R.J., Medications used to treat Parkinson's disease and the risk of gambling, European Journal of Neurology.15 (4) (pp 350-354), 2008.Date of Publication: April 2008., 350-354, 2008 Ref Id 307832 Country/ies where the study was carried out	Sample size 11 PD patients who developed onset of PG between 1995 and 2006; 37 age and sex matched ontrols; N=48 Inclusion criteria cases = diagnosis of PD by a neurologist; no history of PG; new onset of G in period between 1995 and 2006 controls = patient with PD but did not have PG	Details Cases and controls recruited from hospital database which records information on all PD patients. Every case who met inclusion criteria considerd for study. All potential controls selected randomly from among patients fullfilling age and sex match criteria IV in this study was presence of PG in a patients with PD. Exposure ascertainment done by neurologist who	Results 11 cases identified. Matched with 37 controls median age at onset PD 61 years (48-72); 100% males; PD duration 9.6 years (5.2) cases; 7.8 years (5.3) controls total LEDD (mg/day) case = 574 (548); control = 879 (558) (NS difference) pramixepole (mg/day)dose case = 4.3 (2.1), control 2.8 (2.2) (significantly higher dose in cases, p<0.0001) - patients who took premixepole were 3.65 times more likely to develop PG compared to patients who do not take it pramixepole used more frequently in cases vs control, trend t/w significant; OR = 3.65, 95%CI: 0.89 to 14.9 ropinerole and entacapone more common in cases than controls however numbers taking this were small (1 case 3 controls); OR = 1.13, 95%CI: 0.11 to 12.3 for both	Overall Risk of Bias **NICE case-control study checklist:** 1. The study addresses an appropriate and clearly focused question? yes 2. Cases and controls from comparable populations? yes - well matched 3. Same exclusion criteria used for both cases and controls? yes 4. What was participation rate for each group? Cases: controls: NA - data used from database

Study details	Participants	Methods	Results	Comments
USA Study type case control Aim of the study To assess whether dopamine agonist therapy is associated with pathological gambling in patients with PD Study dates received 26th Jan 2007, accepted December 2007 Source of funding Partially supported by Morris K Udall PD research center of excellence awarded to Mayo clinic Jacksonville. Y>E>G supported in part by National institute of health/National institute of mental health grant	Exclusion criteria secondary causes of Parkinsonism and record of unresponsiveness to levodopa. controls excluded in presence of previous history of PG	was uninformed of case control status information on antiPD meds was extracted on de-indentified records Interventions NA	levodopa use not significantly different between cases and controls OR = 0.27 (0.05 to 1.29) combination therapy including levodopa and pramipexole not signif different, OR = 1.96 (0.3 to 8.79)	5. Participants and non-participants are compared to establish their similarities or differences? yes 6. Cases are clearly defined and differentiated from controls s 7. It is clearly established that controls are not cases? yes 8. Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment? yes - blinded 9. Exposure status is measured in a standard, valid, and reliable way? yes - exposure ascertainment done clearly differentiated in terms of behaviour, however no diagnostic criteria for pathological gambling provided 10. Main potential confounders are identified and taken into account in the design and analysis yes 11. Have confidence intervals been provided? yes
Full citation	Sample size	Details	Results	**Overall Risk of Bias**

Study details	Participants	Methods	Results	Comments
Joutsa,J., Martikainen,K., Vahlberg,T., Kaasinen,V., Effects of dopamine agonist dose and gender on the prognosis of impulse control disorders in Parkinson's disease, Parkinsonism and Related Disorders.18 (10) (pp 1079-1083), 2012.Date of Publication: December 2012., 1079-1083, 2012 Ref Id 307925 Country/ies where the study was carried out Finland Study type Cohort study Aim of the study to conduct a large-sclae prospective study to investigate the predictive and prognostic factors of ICD's in patients with PD Study dates	N=290 patients with PD Inclusion criteria urbey sent to 1000 patients on PD database. 575 responded and second survey sent to these, of these 290 responded in full to second dataset and were included. No further information; authors refer to another previous publication Joutsa et al., 2012 Exclusion criteria no information provided authors refer to another previous publication Joutsa et al., 2012 ;	surveys sent out included demographic dta, including year of diagnosis, alcohol consumption, caffeine, smoking. medical treatments and symptom profile information also collected. Levodopa equivalent daily dose (LEDD) calculated. ICD's and related behaviours assessed using the QUIP and depression with Beck depression inventory. Interventions	demographics 181/290 = male median follow up time 449 days (440 - 456) multiariate analyses for icd at baseline male gender OR = 6.10, 95%CI: 2.16 to 17.18 higher dopamine LEDD at baseline, for 100mg increase OR = 2.25, 95%CI 1.29 to 3.91 No differences in ICD outcomes between patients treated with pramipexole or ropinerole in patients with no ICD at baseline, increase in BDI score between baseline and follow up was only factor associated with ICD at follow up (OR = 1.095, 95%CI: 1.004 to 1.195) no differences in aseline BDI scores between patients who developed novel ICD's compared to patients without ICD's at neither time point medication or demographic factors were not associated with novel ICD's in univariate analysis at both time points patients with ICD's had higher BDI scores compared to patients without ICD	1. Did study address on clearly focused issue? Yes 2. Was cohort recruited in acceptable way? yes - survey mail out to whole database 3. Was exposure accurately measured to minimise bias? yes, although self reported so potentially open to fabrication 4. Was outcome accurately measured to minimise bias? Yes - QUIP used to inform ICD diagnosis 5. Have authors identified all important confounding factors and taken account of these in design/analysis? yes 6. Was follow-up of subjects complete/long enough? yes - 15 months 7. What are results? reports on prdictive factors of ICD 8. How precise are results? imprecise - quite wide CI's 9. Are results believable? yes 10. Can results be applied to local population? yes 11. Do results fit with other available evidence? yes 12. What are implications for practice? inform patients of increased risk of ICD's, especially in light of

Study details	Participants	Methods	Results	Comments
received March 2012 revised and published June 2012 Source of funding This work was supported by the Finish Alcohol research foundation, the Finnish medical foundation, the Turku university hospital funds, Turku university hospital foundation,the Paulo foundaton, and the Finnish Parkinson's foundation				highlighted predictive factors
Full citation Lee,J.Y., Kim,J.M., Kim,J.W., Cho,J., Lee,W.Y., Kim,H.J., Jeon,B.S., 20100524, Association between the dose of dopaminergic medication and the behavioral disturbances in Parkinson disease, Parkinsonism & Related Disorders, 16, 202-207, 2010 Ref Id 308116	Sample size N=1167 Inclusion criteria consecutive patients who visited movement disorder clinics at 6 referral hospitals between March and July 2008 were recruited inclusion criteria were: 1) ideopathic PD diagnosis as defined by UKBB criteria	Details subjects assessed for current symptoms suggestive of an ICD using modification of Minnesota impulsive disorders interview (MIDI) data also collected on all demographic, cognitive, PD symptoms, medications, and presence of motor complications of DRTi.e. fluctuations and dyskinesia	Results demographics 57.3% women age 64.9 (9.8) years age at PD onset 58.3 (10.5) disease duration 6.6 (4.3) durtion of DRT 5.0 (3.8) total LLED = 657.5 (387.1) mg/day prevalence ICD 118/1167 (10.1%) patients had ICD punding most common 4.3% eating 3.4% sex 2.8% buying 2.5% gambling 1.3%	**Overall Risk of Bias** CASP quality appraisal checklist 1. Did study address on clearly focused issue? yes 2. Was cohort recruited in acceptable way? yes - consecutive reruitment 3. Was exposure accurately measured to minimise bias? yes 4. Was outcome accurately measured to minimise bias? yes - using Minesota impulsive disorders interview 5. Have authors identified all

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>Country/ies where the study was carried out
South Korea
Study type
cross sectional survey

Aim of the study
To survey the point prevalence of impulse control disorder and repetitive behaviour disorders in patients with PD and to determine the relationship between PD medication dose and risk of ICD's

Study dates
received July 2009, revised November, published December 2009

Source of funding
Korea health research project grant</td>
<td>2) having been taking stable DRT for at least 3 months

Exclusion criteria
patients who were unable to complete questionnaires due to cognitive impairment</td>
<td>questionnaires used to assess symptoms was a modified version of MIDI and was comprised of 5 ICD modules: compulsive buying, gambling, eating, sexual behaviour, and punding behaviour
presence of an ICD was defined as answering in the affirmative to one or more of the remaining questions on the ICD module. In the interview, current symptoms of an ICD that commenced after begginning the DRT were considered to be positive.</td>
<td>of those 118 patients, 34 (28.8%) had symptoms of 2 or more ICDs
factors contributing to development of ICD
NB: OR's are adjusted for age at PD onset, gender, and PD duration Agonist LLED mg/d
<table>
<tr><th>risk factor</th><th>ICD (buy, gam, sex)</th><th>Eating</th><th>Punding</th></tr>
<tr><td>agonist LLED 60 - 160 mg/d</td><td>3.3 (1.3 - 9.1)</td><td>1.1 (0.4 - 2.8</td><td>1.1 (0.5 - 2.4)</td></tr>
<tr><td>>160 mg/d</td><td>4.3 (1.6 - 11.9)</td><td>1.0 (0.3 - 2.8)</td><td>0.6 (0.2 - 1.7)</td></tr>
<tr><td>daily dose l-dopa 450 - 750</td><td>0.8 (0.4 - 1.6)</td><td>0.9 (0.4 - 2.1)</td><td>2.2 (1.0 - 5.1)</td></tr>
<tr><td>>750</td><td>1.0 (0.5 - 2.1)</td><td>1.8 (0.8 - 4.1)</td><td>3.5 (1.5 - 8.2)</td></tr>
</table>
</td>
<td>important confounding factors and taken account of these in design/analysis? yes 6. Was follow-up of subjects complete/long enough? NA - no follow up 7. What are results? predictive factors of ICD reported 8. How precise are results?precise - tight CI's in OR model 9. Are results believable? yes 10. Can results be applied to local population? yes 11. Do results fit with other available evidence? yes 12. What are implications for practice? patients taking DA therapy be advised of risk of developing ICD</td>
</tr>
<tr>
<td>Full citation
Pontone,G., Williams,J.R., Bassett,S.S., Marsh,L., 20061108, Clinical features associated</td>
<td>Sample size
N=100; n with ICD = 9, n without ICD = 91</td>
<td>Details
individuals were recruited as above. Participants received a clinical interview, with current and past psychiatric</td>
<td>Results
Psychiatric interviews revealed ICD's in 6 men and 3 women, yeilding a prevalence of 9% for the three types of ICD's: hypersexuality PG, and excessive spending.</td>
<td>Overall Risk of Bias
recruitement strategy unclear: unclear if consecutive recruitment; unclear exclusion criteria. Non</td>
</tr>
</table>

Study details	Participants	Methods	Results	Comments
with impulse control disorders in Parkinson disease, Neurology, 67, 1258-1261, 2006 Ref Id 308671 Country/ies where the study was carried out USA Study type Retrospective cohort study Aim of the study To identify factors associated with the development of ICD's. In particular, the paper investigated the association of non-pharmacologic clinical features of patients with PD with the presence of ICD's. Study dates Study dates not listed. Published 2006. Source of funding Not listed	Inclusion criteria n=66 men and n=34 women with ideopathic PD, based on UK brain bank criteria, recruited from outpatient clinics, ongoing research programs, and community outreach to participate. Individuals were 65 years or younger, non demented, and had no evidence of a current substance abuse or psychotic disorder, or a history of neurosurgical treatment for PD. Exclusion criteria None listed	diagnoses established according to the clinical interview and diagnosis (SCID) for DSM IV and supplemental question regarding axis 1: disorders not in the SCID i.e ICD. the neuropsychiatric inventory (NPI) was administered directly to the patient, and was used to rate individual psychiatric phenomena. Participants rated according to UPDRS and H&Y staging system, and MMSE. Interventions NA	No significant differences in PD-related or demographic variables. demographics mean age ICD = 48.9 (10.0), non ICD = 55.1 (7.4) mean age on set PD ICD = 44.3 (9.0), no IVD = 48.6 (9.0) mean duration PD ICD = 4.6 (2.2), no ICD = 6.5 (5.5) psychiatric comorbidities comorbid anxiety disorder ICD n = 5/9; non ICD n = 30/91 comorbid depressive disorder ICD n = 3/9, no ICD n = 20/91 comorbid psychotic symptoms ICD n = 5/9; no ICD = 27/91 NPI depression ICD mean score = 4.3 (5.0), no ICD = 1.1 (2.5) NPI anxiety mean score ICD = 3.4 |(4.6), non ICD = 1.3 (2.8) NPI total mean score ICD = 19.7(17.6), no ICD = 8.1 (9.2) medication regimen association All patients with ICD taking a DA and at time of ICD onset used combined L-dopa/DA therapy. in non ICD group 71/91 taking L-dopa, 56/91 used DA (pramixepole n=36; ropinerole n=11; pergolide n=6; bromocriptine n=2; sumanirole n=1) and 35 were taking DA + L-dopa. Only DA were associated with ICD as a class: OR = 11.9 95%CI: 3.93 to 51.4 Associated found for pramipexole OR = 5.35 (95%CI: 1.05 to 27.2)	demented was inclusion criteria, however one subject in ICD group had MMSE of 22. N very small for ICD group. CASP quality appraisal checklist 1. Did study address on clearly focused issue? yes 2. Was cohort recruited in acceptable way? No - recruitment stretegy unclear 3. Was exposure accurately measured to minimise bias? yes 4. Was outcome accurately measured to minimise bias? yes 5. Have authors identified all important confounding factors and taken account of these in design/analysis? yes 6. Was follow-up of subjects complete/long enough? NA =- no follow up 7. What are results? number of predictive factors for ICD listed 8. How precise are results? Not precise - no CI's listed 9. Are results believable? yes 10. Can results be applied to local population? yes 11. Do

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>results fit with other available evidence? yes</td></tr>
<tr><td>Full citation
Voon,V., Thomsen,T., Miyasaki,J.M., de,Souza M., Shafro,A., Fox,S.H., Duff-Canning,S., Lang,A.E., Zurowski,M., Factors associated with dopaminergic drug-related pathological gambling in Parkinson disease, Archives of Neurology.64 (2) (pp 212-216), 2007.Date of Publication: February 2007., 212-216, 2007
Ref Id
309316
Country/ies where the study was carried out
Canada
Study type
Case-control

Aim of the study
To evaluate factors associated with pathological gambling in PD

Study dates</td><td>Sample size
21 patients with PD and PG identified ; patients with PDPG compared to 286 patients with PD and no PG (previously described in Von et al., 2006)

Inclusion criteria
Inclusion criteria included: PG diagnosis according to DSM IV and ideopathic PD diagnosis according to UKBB criteria

Exclusion criteria
DSM IV-defined dementia diagnosis</td><td>Details
All patients with PD and PG onset after iitiation of receiving dopaminergic medications were ID through movement disorders clinic at Toronto western hospital through clinical presentation or through 3 month prevalence screening 297 patients with PD.
For controls, sequential patients with PD attending follow-up appointments at the movement disorders clinic.
patients and controls completed patient-rated scales and were assessed by neurologist and a psychiatrist - clinical information was collected including age at onset, current medications, MMSE, motor features UPDRS, frontal assessment battery, depression inventory.</td><td>Results
21 patients with PDPG identified. 1 patient PG onset after DBS to STN; separate analyses excluding this patient did not alter results.
76 potential controls contacted.
Patients with PG compared to 42 controls with PD without compulsive behaviors and with 286 patients with PD but without PG previously.
<table>
<tr><td>characteristic</td><td>PD PG N=21</td><td>PD controls N=42</td><td>MD (95%CI)</td></tr>
<tr><td>age at PD onset</td><td>50.9 (8.8)</td><td>58.4 (10.1)</td><td></td></tr>
<tr><td>PD duration</td><td>9.2 (5.2)</td><td>6.9 (4.2)</td><td></td></tr>
<tr><td>DA LEDD</td><td>268.3 (194.3)</td><td>192.1(105.3)</td><td></td></tr>
<tr><td>Left hemisphere onset PD, N</td><td>16</td><td>15</td><td>OR =</td></tr>
<tr><td>Beck depression inventory</td><td>12.4 (6.0)</td><td>10.3 (7.9)</td><td></td></tr>
<tr><td>family hist alcohol use disorder, N</td><td>12</td><td>8</td><td>OR =</td></tr>
<tr><td>Barratt impulsivity (total)</td><td>65.2 (12.2)</td><td>54.1 (10.1)</td><td></td></tr>
</table></td><td>Overall Risk of Bias

NICE case-control checklist
1. The study addresses an appropriate and clearly focused question? yes
2. Cases and controls from comparable populations?
yes 3. Same exclusion criteria used for both cases and controls? yes
4. What was participation rate for each group? Cases: controls: full participation
5. Participants and non-participants are compared to establish their similarities or differences?
yes 6. Cases are clearly defined and differentiated from controls yes 7. It is clearly established that controls are not cases?
yes 8. Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment? yes
9. Exposure status is measured in a standard, valid, and reliable way?</td></tr>
</table>

Study details	Participants	Methods	Results	Comments
patients recruited between June 2003 and June 2005, study published February 2007 Source of funding No financial disclosure reported		Pathological gambling, compulsive shopping, hypersexuality, and compulsive medication use were diagnosed. Past and present mood disorders, anxiety, substance abuse disorders were diagnosed via clinical interview using structured clinical interview DSM IV axis. impulsivity measures Barratt impulsivity score which assesses planning, attention, and motor factors. Novelty seeking and harm avoidance were assessed using the temperament character inventory. Interventions NA	<table><tr><td>Novelty seeking score</td><td>20.3 (6.6)</td><td>10.9 (4.2)</td><td></td></tr><tr><td>N recieving DA adjunctive therapy. N</td><td>20</td><td>30</td><td>OR =</td></tr></table>	yes 10. Main potential confounders are identified and taken into account in the design and analysis: yes 11. Have confidence intervals been provided? yes **no serious risk of bias**
Full citation Weintraub,D., Siderowf,A.D., Potenza,M.N., Goveas,J., Morales,K.H., Duda,J.E., Moberg,P.J., Stern,M.B., 20060807, Association of	Sample size N=272 Inclusion criteria Outpatients diagnosed with ideopathic PD, predominantly of mild to moderate	Details 2 trained research assistants administered the screening battery, which included open ended questions about the existance(lifetime, anytime during PD, and currently) of recurrent compulsive buying,	Results demographic age rage 35 - 91 years 137/272 (50.4%) participants taking a DA at screening For patients taking DA, no difference between both groups in LEDD 21/272 patient positive for ICD - 2 did not meet MIDI criteria and one was lost to follow up so final N ICD = 18	Overall Risk of Bias For subjects who had experienced and ICD at any stage of their PD, were asked to recall symptoms and medications, details etc at that time. Prone to significant recall bias.

Study details	Participants	Methods	Results	Comments
dopamine agonist use with impulse control disorders in Parkinson disease, Archives of Neurology, 63, 969-973, 2006 Ref Id 309365 Country/ies where the study was carried out USA Study type cohort study - unstructured screening interview for ICD's followed by telephone administered structured interview for screen positive patients Aim of the study To determine the frequency and correlates of ICD's in PD Study dates Patients screened between July 2004 and June 2005. Paper published July 2006 Source of funding	severity, confirmed by movement disorders specialist. Subjects were established patients of one of two movement disorder clinics and were thought to represent a cross-section of the clinic's populations Exclusion criteria Patients unable to provide written consent due to cognitive impairment	gambling, or sexual behaviours. Subjects also administered the 15 item geriatric depresion scale and MMSE as part of screening. Those who screened positive for ICD during course of their PD were contacted by phone and administered a modified MIDI, which includes queries for the presence of clinically-significant compulsive gambling, sexual, and buying behaviours Patients were instructed to answer questions based on based on their state at the time they were symptomatic ICD's defined as answering in the affirmative to 1 (compulsive sexual behaviour and compulsive shopping) or 2 (compulsive gambling) gateway questions plus 1+ affirmative answer to remianing ICD questions PI reviewed medical charts of all patients to verify answers	compulsive sexual behaviour as common as compulsive gambling, both N = 7 , compulsive buying N = 4 (all for anytime during PD) results On univariate analysis, younger age, longer PD duration, history of ICD symptomology prior to PD, and use of DA or amantadine were associated with presence of an ICD, with suggestion of higher LEDD all 11 active ICD cases were taking a DA all 18 ICD cases (any time) were taking DA at time of symptoms 7 became unsymptomatic; 4 = discontinuation of DA, 2 = reduction in DA , 1 = counselling In multivariate model taking all significant univarate factors into account, dopamine agonist use and history of ICD behaviour/symptomology prior to PD were the only significant factors predictive of an ICD : prior ICD symptoms, OR = 15.54, unadjusted 95%CI: 2.83, 76.16 DA use, OR = 16.27, unadjusted 95%CI: 2.61, upper limit approaches infinity) No significant differences between the 3 DA's and incidence of ICD; in patients who had experienced an ICD, ropinerole = 8, pramipexole =7, pergolide = 3 DA dosage In patients currently taking a DA, ICD's were associated with exposure to higher daily doses of pergolide (T13 = -3.38, p=0.05), but not pramipexole (t 71 = -2.14, p=0.06), or ropinerole (t47 = -0.81, p=0.4) Using LEDD's and examining the 3 dopamine agonists as a class, treatment with higher doses was	CASP quality appraisal checklist 1. Did study address on clearly focused issue? yes 2. Was cohort recruited in acceptable way? yes 3. Was exposure accurately measured to minimise bias? yes 4. Was outcome accurately measured to minimise bias? yes, however PD patients asked to recall symptoms and medications, details etc at that time. Prone to significant recall bias 5. Have authors identified all important confounding factors and taken account of these in design/analysis? yes 6. Was follow-up of subjects complete/long enough? NA 7. What are results? significant predictive factors of ICD reported 8. How precise are results?precise 9. Are results believable? yes 10. Can results be applied to local population? yes 11. Do results fit with other available evidence? yes **low risk of bias**

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>study supported by grant from NIMH and by mental illness research, education,and clinical centers at the Philadelphia and West Haven veterans affairs medical centers</td>
<td></td>
<td>LEDD's calculated for DA's and DA +L-dopa (total LEDD)
to probe for possible risk factors in development of ICD in PD, data obtained for factors that have been previously reported as associated with ICD's in PD i.e. type and ose of dopaminergic therapy, disease duration, age, and sex) or were factors of interest (history of ICD, cognition, education, marital status).

Interventions
NA</td>
<td>associated with the presence of an ICD (t135 = -4.06, p=0.001).

<table>
<tr><td>Variable</td><td>No active ICD (261)</td><td>Active ICD (11)</td><td>Odds ratio (95%CI) or MD (95% CI)**Calculated from raw data</td></tr>
<tr><td>age</td><td>68.6 (10.2)</td><td>59.5 (9.4)</td><td></td></tr>
<tr><td>male, N</td><td>182 (69.7)</td><td>10 (90.9%)</td><td>OR =4.34 (0.5463 to 34.4871)</td></tr>
<tr><td>L-dopa mg/d</td><td>448.1 (335.2)</td><td>543.6 (453.5)</td><td></td></tr>
<tr><td>total LEDD mg/d</td><td>5699.3 (369.1)</td><td>925.5 (534.9)</td><td></td></tr>
<tr><td>DA use, N</td><td>126 (48.3)</td><td>11 (100%)</td><td>OR =24.6 (1.4 to 422.44)</td></tr>
<tr><td>amantadine use, N</td><td>49(18.8)</td><td>6 (54.5%)</td><td></td></tr>
<tr><td>PD duration, years</td><td>6.9 (5.8)</td><td>11.2 (7.5)</td><td></td></tr>
<tr><td>GDS</td><td>4.0 (3.8)</td><td>6.0 (5.5)</td><td></td></tr>
<tr><td>prior ICD behaviour, N</td><td>9 (3.5)</td><td>4 (36.4)</td><td>OR =16 (3.957 to 64.68)</td></tr>
</table>
</td>
<td></td>
</tr>
</table>

Study details	Participants	Methods	Results	Comments
Full citation Weintraub,D., Koester,J., Potenza,M.N., Siderowf,A.D., Stacy,M., Voon,V., Whetteckey,J., Wunderlich,G.R., Lang,A.E., 20100701, Impulse control disorders in Parkinson disease: a cross-sectional study of 3090 patients, Archives of Neurology, 67, 589-595, 2010 Ref Id 309372 Country/ies where the study was carried out USA and Canada Study type Cross sectional cohort study Aim of the study To ascertain point prevalence estimates of 4 ICD's in PD and examine their associations with dopamine-replacement therapies and other clinical characteristics	Sample size N=3090 patients with PD Inclusion criteria Subjects diagnosed as having ideopathic PD by a movement disorder specialist, aged 30 - 75 years, recruited from 46 movement disorder clinics in US and canada. Inclusion criteria required patients had treatment with a PD medication for at least 1 year with demonstrated response Exclusion criteria Dopamine agonist treatment could not be initiated or terminated in the 6 months prior to evaluation	Details Semi structred interview using formal diagnostic criteria assessed current frequency of 4 different ICD's: pathological gambling compulsive sexual behaviour compulsive buying binge eating All participants informed primary purpose of study was to study ICD and the association with PD medication Participants answered atudy questions individually but corroborative evidence was taken from informant where available. Patients recruited regularly during clinic visits based on set selection process such that every third patient on given clinicl day was assessed for suitability by researcher with no knowledge of patient's ICD status and PD medication. The following semi-structure diagnostic	Results 3030/3091 taking either levodopa or a DA 2040/2090 taking 1 or more DA's 2682/2090 were taking levodopa, including the 991 not taking a DA 59 patients taking neither ICD prevalence at leas one active ICD identified in 13.6% of patients 3.9% experienced 2 or more ICD's clinical characteristics by ICD: Those with ICD more likely to be Young. age <65 v > 65 = 302/420 (ICD) vs 1322/2670 (no ICD) OR = 2.5 (1.98 to 3.15) currently smoke = 28/420 vs 90/2670 - OR = 1.70 (1.07 to 2.70) report familial gambling = 30/420 vs 94/2670 - OR = 2.08 (1.33 to 3.25) not married vs married - OR = 1.48 (1.16 to 1.89 dopamine agonist treatment - OR = 2.72 (2.07 to 3.57) levodopa treatment - OR = 1.51 (1.09 to 2.09) men more likely women to have compulsive sexual behaviour - OR = 11.98, 95%CI: 4.87 to 29.48 men less likely compulsive buying - OR = 0.55; 95%CI: 0.40 to 0.74 men less likely binge eating disorder - OR = 0.57, 95%CI: 0.4 to 0 patients with history of gambling problems had higher rate of: problem gambling- OR = 2.97, 95%CI: 1.71 to 5.17 compulsive buying OR = 1.97, 95%CI: 1.08 to 3.58 binge eating OR =2.49, 95%CI:1.43 to 4.64	CASP quality appraisal checklist 1. Did study address on clearly focused issue? yes 2. Was cohort recruited in acceptable way? yes 3. Was exposure accurately measured to minimise bias? yes 4. Was outcome accurately measured to minimise bias? yes, however PD patients asked to recall symptoms and medications, details etc at that time. Prone to significant recall bias 5. Have authors identified all important confounding factors and taken account of these in design/analysis? yes 6. Was follow-up of subjects complete/long enough? NA 7. What are results? significant predictive factors of ICD reported 8. How precise are results?precise 9. Are results believable? yes 10. Can results be applied to local population? yes 11. Do results fit with other available evidence? yes **low risk of bias**

Study details	Participants	Methods	Results	Comments
Study dates published May 2010 Source of funding study funded by and designed by jointly by Boehringer Ingleheim and the scientific advisory board (consisting of Drs Weintraub, Potenza, Siderowf, Stacy, Voon, and Lang)		instruments were administered by trained research staff to capture clinically significant symptoms: Massachusetts gambling screen , ≥ 5 endorsed for pathological gambling, 3 - 4 endorsed for problem gambling Minessota Impulsive Disorders interview for compulsive buying and sexual behaviour - both disorders positive response to gateway question plus ≥ 1 secondary question for that sub section DSM IV proposed research criteria for binge-eating disorder. Positive response to gateway question plus ≥ 3 secondary questions Interventions N/A	ICD frequency in those with and without DA's. No DA vs DA Patients treated with DA had higher frequency iof ICD compared to those not taking DA - OR 2.72 (2.08 to 3.54) problem gambling: OR = 2.82 (1.81 to 4.39) pathological gambling - OR = 2.15 (1.26 to 3.66) compulsive sexual behaviour - OR = 2.59 (1.55 to 4.33) compulsive buying - OR = 2.53 (1.69 to 3.78) binge eating - OR = 3.34 (2.01 to 5.53) Examining only patients on DA (n=2040) no dopamine agonist dosage effect any levodopa use and higher levodopa use assocuated with current ICD - OR = 1.43 (95% CI: 1.03 to 2)	
Full citation Weintraub,D., Sohr,M., Potenza,M.N., Siderowf,A.D., Stacy,M., Voon,V., Whetteckey,J.,	Sample size (see Weintraub et al., 2010a) Inclusion criteria	Details (see Weintraub et al., 2010a) Interventions NA	Results see (see Weintraub et al., 2010a) for demographic details results	CASP quality appraisal checklist 1. Did study address on clearly focused issue? yes 2. Was cohort recruited in acceptable way? yes 3. Was

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>Wunderlich,G.R., Lang,A.E., Amantadine use associated with impulse control disorders in Parkinson disease in cross-sectional study, Annals of Neurology.68 (6) (pp 963-968), 2010.Date of Publication: December 2010., 963-968, 2010
Ref Id
309373
Country/ies where the study was carried out
USA
Study type
cross section study - See Weintraub et al., 2010a

Aim of the study
secondary analysis of the DOMINION data (see Weintraub et al., 2010a) to determine the frequency of ICD's in patients treated with amantadine

Study dates
published July 2010 - (see Weintraub et al., 2010a)</td>
<td>(see Weintraub et al., 2010a)

Exclusion criteria
(see Weintraub et al., 2010a)</td>
<td></td>
<td>At least 1 active ICD identified in 17.6% amantadine users compared with 12.4% of patients not taking amantadine (p = 0.0001) (see table below)

<table>
<tr><td>Any ICD</td><td>OR = 1.49 (95%CI: 1.19 to 1.87)</td></tr>
<tr><td>PG</td><td>OR = 1.78 (95%CI: 1.27 to 2.50)</td></tr>
<tr><td>compulsive sexual</td><td>OR = 1.70 (95%CI:1.13 to 2.56)</td></tr>
<tr><td>compulsive buying</td><td>OR = 1.60 (95%CI:1.15 to 2.22)</td></tr>
<tr><td>binge eating disorder</td><td>OR = 1.03 (95%CI: 0.68 to 1.54)</td></tr>
</table>
Patients treated with amantadine compared with those who no amantadine use were: younger, had longer PD duration, more sever PD based on H&Y, more likely to have undergone DBS, had more formal education, were likely to be treated with a DA and were taking higher levodopa dosage. see below:

<table>
<tr><td>variable</td><td>amantadine use (n=728)</td><td>no amantadine use (n=2357)</td><td>p value</td></tr>
<tr><td>gender, male</td><td>463 (63.6)</td><td>1515 (64.3)</td><td>0.69</td></tr>
<tr><td>age <65 years</td><td>446 (61.3)</td><td>1177 (49.9)</td><td>na</td></tr>
</table>
</td>
<td>exposure accurately measured to minimise bias? yes 4. Was outcome accurately measured to minimise bias? yes, however PD patients asked to recall symptoms and medications, details etc at that time. Prone to significant recall bias 5. Have authors identified all important confounding factors and taken account of these in design/analysis? yes 6. Was follow-up of subjects complete/long enough? NA 7. What are results? significant predictive factors of ICD reported 8. How precise are results?precise 9. Are results believable? yes 10. Can results be applied to local population? yes 11. Do results fit with other available evidence? yes

low risk of bias</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>Source of funding
Boehringer Ingelheim</td>
<td></td>
<td></td>
<td>
<table>
<tr><td>PD duration, median yrs</td><td>10.0 (6.4-14.0)</td><td>5.7 (3.3 - 9.2)</td><td>0.0001</td></tr>
<tr><td>H&Y stage</td><td>n=724</td><td>n=2354</td><td>0.0001</td></tr>
<tr><td>current smoking, Y</td><td>n=33</td><td>n=85</td><td>0.2</td></tr>
<tr><td>curent alcohol, Y</td><td>n=281</td><td>n=990</td><td>0.1</td></tr>
<tr><td>fam hist gambling, Y</td><td>n=32</td><td>n=94</td><td>0.6</td></tr>
<tr><td>fam hist alcohol abuse, Y</td><td>n=155</td><td>n=571</td><td></td></tr>
<tr><td>DA use, Y
Levodopa LEDD, median mg/d</td><td>n=521
468.75</td><td>1517
450</td><td>0.0003
0.0001</td></tr>
</table>

Multiple logistic model stepwise selection of ICD correlates
<table>
<tr><td>1</td><td>age (<65 v > 65)</td><td>OR = 2.40 (95%CI: 1.91 to 3.02)</td><td>p < 0.0001</td></tr>
</table>
</td>
<td></td>
</tr>
</table>

Study details	Participants	Methods	Results	Comments
			2 | DA use (Y v N) | OR = 2.64 (95%CI: 2.01 to 3.46) | p < 0.0001 3 | L-dopa LEDD (median > 450 mg/d) | OR = 1.50 (95%CI: 1.21 to 1.86) | p = 0.0002 4 | amantadine use (YvN) | OR = 1.29 (95%CI: 1.02 to 1.63) | p = 0.0342	
Full citation Sharma,A., Goyal,V., Behari,M., Srivastva,A., Shukla,G., Vibha,D., 20150306, Impulse control disorders and related behaviours (ICD-RBs) in Parkinson's disease patients: Assessment using "Questionnaire for impulsive-compulsive disorders in Parkinson's disease" (QUIP), Annals of Indian Academy of Neurology, 18, 49-59, 2015 **Ref Id** 371219 **Country/ies where the study was carried out** India	**Sample size** N=299 consecutive patients with PD **Inclusion criteria** patients with ideopathic PD according to UKBB criteria aged 30 - 75 years on treatment with DRT for >1 year with documented response and whose treatment was not modified based on prior reporting of ICD RB's **Exclusion criteria** patient not consenting for study cognitive abnormaility of MMSE <24	**Details** participants and their spouses asked to fill out QUIP based on behaviours that ocurred anytime during PD that lasted at least 4 consecutive weeks. following cut offs used to represent a poaitive screen based on QUIP validation study data: compulsive gambling = 2/5 items, sexual behaviour = 1/5, buying = 1/5, eating = 2/5, plus other compulsive behaviours i.e. hobbyism, punding demographic details collected along with UPDRS motor score in 'on' state, H&Y score in on state, and details of antiparkinsonian medication regimen **Interventions** NA	**Results** demographics: age = 57.7 (11.4) disease duration = 6.9 (4.7) males = 74.9% females = 25.1% 296/299 taking LD or DA N=245 on a DA At least one ID RB present in 93 (31.1%) of patients frequency of ICD RB in subjects exposed only to LD (20.3%) was lower than those on DA monotherapy (24.2%) which was lower than those on both (55.5%) Bivariate and multivariate analysis results taken here only from ICD (NOT ICDRB) dataset independent predictors of ICD after multivariate analysis were younger age at onset, being unmarried, smoking and higher DA and total LEDD **MULTIVARIATE** analysis controlling for age of onset, being unmarried, smoking, disease duration, Ldopa LEDD, DA LEDD, total LEDD (positive factors from univariate analyses) | | OR | 95%CI low | 95%CI high	**Overall Risk of Bias** CASP quality appraisal checklist 1. Did study address on clearly focused issue? yes 2. Was cohort recruited in acceptable way? yes 3. Was exposure accurately measured to minimise bias? yes 4. Was outcome accurately measured to minimise bias? yes 5. Have authors identified all important confounding factors and taken account of these in design/analysis? yes 6. Was follow-up of subjects complete/long enough? NA 7. What are results? significant predictive factors of ICD reported in univariate and multivariate anayses 8. How precise are

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>Study type
cross-sectional study

Aim of the study
ascertain prevalence of ICDRB's and association of these behaviours with dopamine replacement therapy

Study dates
study conducted from March 2012 to May 2013

Source of funding</td>
<td></td>
<td></td>
<td>
<table>
<tr><td>age onset <40 vs >40</td><td>0.96</td><td>0.93</td><td>0.99</td></tr>
<tr><td>unmarried</td><td>6.92</td><td>1.84</td><td>25.94</td></tr>
<tr><td>smoker</td><td>7.67</td><td>3.28</td><td>17.93</td></tr>
<tr><td>disease duration</td><td>NA</td><td></td><td></td></tr>
<tr><td>L-dopa</td><td>NA</td><td></td><td></td></tr>
<tr><td>DA LEDD 150 - 300mg
DA LEDD >300 mg</td><td>4.52
4.53</td><td>1.6
2.26</td><td>12.5
13.06</td></tr>
<tr><td>total LEDD 400 - 800mg
total LEDD >800mg</td><td>1.38
4.41</td><td>0.5
1.62</td><td>3.82
11.98</td></tr>
</table>
UNIVARIATE ANALYSES
<table>
<tr><td>variables</td><td>OR</td><td>95%CI LOW</td><td>95%CI HIGH</td></tr>
<tr><td>pramipexole use</td><td>3.03</td><td>1.73</td><td>5.30</td></tr>
<tr><td>entacapone</td><td>1.47</td><td>0.75</td><td>2.9</td></tr>
<tr><td>rasagaline</td><td>0.98</td><td>0.5</td><td>1.9</td></tr>
<tr><td>amantadine</td><td>3.48</td><td>2.02</td><td>6.01</td></tr>
</table>
</td>
<td>results? precise 9. Are results believable? yes 10. Can results be applied to local population? yes - although this cohort is from India, unknown how comparable this PD population is to UK PD population and relevance of predictive factors i.e. smoking, alcohol intake, and marital status, which are culturally-dependent variables 11. Do results fit with other available evidence? yes</td>
</tr>
</table>

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>unmarried</td><td>9.6</td><td>2.9</td><td>31.3</td></tr>
<tr><td>smoker</td><td>7.5</td><td>3.5</td><td>16.15</td></tr>
<tr><td>alcohol intake</td><td>4.0</td><td>2.0</td><td>8.05</td></tr>
<tr><td></td><td></td><td></td><td></td></tr>
</table>
</td><td></td></tr>
<tr><td>Full citation
Rizos,A., Sauerbier,A., Antonini,A., Weintraub,D., Martinez-Martin,P., Kessel,B., Henriksen,T., Falup-Pecurariu,C., Silverdale,M., Durner,G., Rokenes,Karlsen K., Grilo,M., Odin,P., Chaudhuri,K.R., A European multicentre survey of impulse control behaviours in Parkinson's disease patients treated with short- and long-acting dopamine agonists, Eur J Neurol, 23, 1255-1261, 2016
Ref Id
675546</td><td>Sample size
425

Inclusion criteria
PD patients diagnosed according to the UK Brain Bank criteria
Data from patients already taking ropinirole-IR/XL, pramipexole-IR/PR and rotigotine, as well as those initiating treatment with these DAs

Exclusion criteria
Patients who had dementia or parkinsonism not due to idiopathic PD</td><td>Details
This medical record survey was registered as an audit and the prospective component was part of a longitudinal study of motor and non-motor symptoms in PD and the impact of PD treatments. Assessment was based on established clinical records and chart review.

Interventions
N/A</td><td>Results
Main demographic and PD historical characteristics:
<table>
<tr><td>Demographic characteristics</td><td>All cases (n=425)</td><td>ICD cases (n=57)</td></tr>
<tr><td>Male gender (%)</td><td>259(60.9)</td><td>45(78.9)</td></tr>
<tr><td>Mean age in years (range)</td><td>68.3(37-90)</td><td>62.7(42-85)</td></tr>
<tr><td>Mean duration of PD in years (range)</td><td>7.5(0-37)</td><td>7.0(0-24)</td></tr>
<tr><td>Median H&Y stage (range)</td><td>2.5(1.0-5.0)</td><td>3.0(1.0-5.0)</td></tr>
</table>
ICD rates on immediate- and extended release DAs:
Pramipexole pooled (IR+PR): 13.8%
Pramipexole-IR: 19%
Pramipexole-PR: 6.6%
Ropinirole pooled (IR+XL): 13.9%</td><td>Overall Risk of Bias
CASP quality appraisal checklist
1. Did study address on clearly focused issue? Yes. 2. Was cohort recruited in acceptable way? Yes. 3. Was exposure accurately measured to minimise bias?
Unclear. 4. Was outcome accurately measured to minimise bias? Yes. 5. Have authors identified all important confounding factors and taken account of these in design/analysis?
Unclear. 6. Was follow-up of subjects complete/long enough?
NA - no follow up
7. What are results? Incidence of ICD in PD patients treated</td></tr>
</table>

Study details	Participants	Methods	Results	Comments
Country/ies where the study was carried out UK, Spain, Denmark and Romania Study type A retrospective and prospective survey based on medical records and clinical interviews Aim of the study To assess the occurrence of ICDs in PD patients across several European centres treated with short- or long-acting (ropinirole; pramipexole) and transdermal (rotigotine skin patch) DAs, based on clinical survey as part of routine clinical care. Study dates Not reported Source of funding No funding			Ropinirole-IR: 14% Ropinirole-XL: 13.9% Rotigotine: 4.9%	with short- or long-acting DAs. 8. How precise are results? Precise. 9. Are results believable? Yes. 10. Can results be applied to local population? yes 11. Do results fit with other available evidence? Unclear. 12. What are implications for practice? patients taking DA therapy be advised of risk of developing ICD Overall risk of bias: Low.

<table>
<tr><th>Study details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>Full citation
Wang,X.P., Wei,M., Xiao,Q., A survey of impulse control disorders in Parkinson's disease patients in Shanghai area and literature review, Transl Neurodegener., 5, 4-, 2016
Ref Id
675547
Country/ies where the study was carried out
Shanghai
Study type
Survey

Aim of the study
To investigate the incidence of ICD in Chinese PD patients from Shanghai area, explore the association of ICD with dopamine replacement therapy.

Study dates
March to October 2013

Source of funding
National Natural Science Foundation of</td>
<td>Sample size
217

Inclusion criteria
Idiopathic PD patients, based on UK Brain Bank clinical diagnostic criteria

Exclusion criteria
Atypical parkinsonism
secondary parkinsonism
cognitive abnormality that might have problem in understanding and giving feedback of questionnaire</td>
<td>Details
The modified version of Minnesota Impulsive Disorders Interview (Chinese version) was used to assess gambling, compulsive shopping, hypersexuality, binge eating, and punding.

Interventions
N/A</td>
<td>Results
Comparison between patients with and without ICD behaviours (mean±SD, n, %, p):
<table>
<tr><td></td><td>Non-ICD</td><td>ICD</td></tr>
<tr><td>Number of case</td><td>208</td><td>9</td></tr>
<tr><td>Age, yr</td><td>67.25±8.82</td><td>63.67±10.55</td></tr>
<tr><td>Male, n(%)</td><td>114(54.8%)</td><td>6(66.7%)</td></tr>
<tr><td>Disease duration, yr</td><td>5.76±4.38</td><td>6.44±3.17</td></tr>
<tr><td>Dose of l-dopa (mg/d)</td><td>425±327.26</td><td>791.67±802.73</td></tr>
<tr><td>DA-LED (mg/d)</td><td>60.5±80.5</td><td>119.4±86.4</td></tr>
<tr><td>TLED (mg/d)</td><td>503.78±359.13</td><td>912.81±878.73</td></tr>
<tr><td>H&Y stage</td><td>1.41±0.52</td><td>2.33±0.87</td></tr>
<tr><td>Use of agonists, n(%)</td><td>94(45.2%)</td><td>7(77.8%)</td></tr>
</table>
</td>
<td>Overall Risk of Bias
CASP quality appraisal checklist
1. Did study address on clearly focused issue? Yes. 2. Was cohort recruited in acceptable way? Yes. 3. Was exposure accurately measured to minimise bias? Yes. 4. Was outcome accurately measured to minimise bias? Yes. 5. Have authors identified all important confounding factors and taken account of these in design/analysis? Yes. 6. Was follow-up of subjects complete/long enough? NA - no follow up 7. What are results? Incidence of ICD in PD patients treated with dopamine replacement therapy. 8. How precise are results? Imprecise – only 9/208 had ICD. 9. Are results believable? Unclear. 10. Can results be applied to local population? Unclear. 11. Do results fit with other available evidence? Unclear. 12. What are implications for practice? patients taking DA</td>
</tr>
</table>

Study details	Participants	Methods	Results	Comments
China and the Natural Science Foundation of Shanghai				therapy be advised of risk of developing ICD. Overall risk of bias: Low to moderate.