

## Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

## Supplementary methods

### PD patients

We used the following criteria to identify incident PD patients between 2005 and 2014 within the National Health Insurance dataset: (i) at least three medical claims (either ambulatory or inpatient care) with a diagnostic code of PD (International Classification of Disease [ICD], 9th Revision, Clinical Modification, ICD-9-CM code 332.0, ICD-10-CM code G20) during 2002-2015; and (ii) at least three anti-Parkinsonism medications claims, including L-dopa or dopamine agonist prescriptions, after PD diagnosis and during 2002-2015. We defined the date of the first inpatient or outpatient record for PD after 2005 as the index date (i.e., we excluded those with inpatient or outpatient record for PD before 2005). Moreover, the first and last outpatient or inpatient visits and anti-parkinsonism medication records should be separated by at least 90 days to avoid accidental inclusion of miscoded patients. We further applied the following exclusion criteria to ensure the validity of the PD diagnosis: (1) age younger than 35 years at the index date because PD is exceptional before that age, (2) diagnostic code of secondary parkinsonism (ICD-9-CM code: 332.1) during the study period, (3) prescription of neuroleptic medications within 180 days prior to the index date, (4) three or more medical claims (either ambulatory or inpatient care) with the diagnostic codes of dementia prior to the index date, and (5) without at least three anti-parkinsonism medication prescriptions within 2 years after the index date.<sup>22</sup>

Based on these inclusion and exclusion criteria, we retained for our analyses incident PD patients diagnosed between 2005 and 2014.

eTable 1: ICD-codes for study variables

|  | ICD 9 code  | ICD 10 code   |
|--|---|---|
| Parkinson's disease (PD)               | 332.0   | G20   |
| Suicide<br>Methods                     | E950-E959,E980-E989   | X60-X84,Y10-Y34,Y87   |
| Hanging/Suffocation                    | E953  | X70   |
| Jumping                                | E957  | X80   |
| Poisoning                              | E950, E980,E982   | X61, X64, X68, X69, Y18, Y19  |
| Charcoal burning                       | E952  | X67   |
| Drowning                               | E954  | X71   |
| Others                                 | E951, 955, 956,958,959  | X60, X62-63,X65-66, X72-79,X81-84   |
| Intent undetermined                    | E981, E983-989  | Y87,Y10-34, excluding Y18,Y19   |
| Dementia                               | 0461,2900,29010,29011,29012,29013<br>,<br>29020,29021,2903,29040,29041,29042,29043,2908,2909,2912,29282,2940,29410,29411,29420,2948,2949,2989,3310,33111,33119,3312,3317,33182,3334,797 | F000,F001,F002,F009,F010,F011, F012,F013,F018,F019,F020,F021, F022,F023,F024,F028,F03,F051,G300,G301,G308,G309,G311 |
| Depression                             | 296.2,296.3,296.82,300.4  | F32, F33, F32.89,F34.1  |
| Mental disorders other than depression | 291-298, 300-316<br>(excluding 296.2, 296.3, 296.82, and 300.4)   | F10-F69,F99<br>(excluding F32, F33, F32.89, and F34.1)  |
| Myocardial infarct                     | 410,412   |   |
| Congestive heart failure               | 428   |   |
| Peripheral vascular disease            | 441,4439,7854,V434  |   |
| Cerebrovascular disease                | 430-438   |   |
| Chronic pulmonary disease              | 490-496,500-505, 5064   |   |
| Rheumatologic disease                  | 7100, 7101, 7104, 7140-7142,725,71484   |   |
| Ulcer disease                          | 531-534   |   |
| Mild liver disease                     | 5712, 5714-5716   |   |
| Diabetes                               | 2500-2503, 2507   |   |
| Diabetes with chronic complications    | 2504-2506   |   |

|   |   |  |  |
|---|---|--|--|
| Hemiplegia or paraplegia                              | 342, 3441   |  |  |
| Renal disease   | 582, 5830-5837,585,586,588                          |  |  |
| Any malignancy,<br>including<br>leukemia and lymphoma | 140-172,174-185,168,187-194, 1951-<br>1958, 200-208 |  |  |
| Moderate or severe liver<br>disease                   | 5722-5728,4560, 4561,45621                          |  |  |
| Metastatic solid tumor                                | 196, 197, 198, 1991                                 |  |  |
| Acquired<br>immunodeficiency<br>syndrome (AIDS)       | 042, 043, 044                                       |  |  |

| eTable 2: Reasons for censoring in Parkinson's disease (PD) patients and referent subjects |                                   |                                  |
|--|-----------------------------------|----------------------------------|
|  | Parkinson's disease<br>(N=35,891) | Referent subjects<br>(N=143,557) |
| Suicide  | 151                               | 300                              |
| Insurance suspended or cancelled   | 80                                | 535                              |
| Onset of PD in control group   | -                                 | 649                              |
| Deep brain stimulation   | 88                                | -                                |
| Causes of death (other than suicide)   |                                   |                                  |
| Cancer   | 2,057                             | 8,725                            |
| Cardiovascular disease   | 3,114                             | 9,169                            |
| Infectious disease   | 513                               | 1,315                            |
| Respiratory disease  | 2,144                             | 5,928                            |
| Accident   | 279                               | 881                              |
| Other natural causes of death  | 4,102 <sup>#1</sup>               | 9,197 <sup>#2</sup>              |
| No event (censored at end of follow-up)  | 23,363                            | 106,858                          |

#1 Hematologic disease, metabolic disease, neurodevelopmental disorder, disease of the nervous system, disease of the digestive system, disease of the skin and subcutaneous tissue, disease of the musculoskeletal system, chromosomal abnormalities, other abnormal clinical conditions.

# 2 Hematologic disease, metabolic disease, neurodevelopmental disorder, disease of the nervous system, disease of the eye and adnexa, disease of the ear and mastoid process, disease of the digestive system, disease of the skin and subcutaneous tissue, disease of the musculoskeletal system, chromosomal abnormalities, other abnormal clinical conditions.



eTable 3: Hazard ratios of suicide in Parkinson's disease (PD) patients compared to referent subjects from the general population

|   | Model 1      | Model 2      | Model 3      | Model 4 <sup>a</sup> | Model 5 <sup>a</sup> | Model 6 <sup>a</sup> |
|---|--------------|--------------|--------------|----------------------|----------------------|----------------------|
| <b>Hazard ratio of suicide in PD (95% CI)</b> | 2.2(1.8-2.7) | 2.2(1.8-2.6) | 2.1(1.7-2.5) | 2.1(1.7-2.5)         | 1.9(1.5-2.3)         | 1.9(1.6-2.3)         |
| <b>Covariates</b>                             |              |              |              |                      |                      |                      |
| <i><b>Insurance premium (USD)</b></i>         |              |              |              |                      |                      |                      |
| 0-36  |              | 1.0 (ref.)   | 1.0 (ref.)   | 1.0 (ref.)           | 1.0 (ref.)           | 1.0 (ref.)           |
| >36-650                                       | -            | 0.9(0.7-1.2) | 0.9(0.7-1.2) | 0.9(0.7-1.2)         | 1.0(0.7-1.3)         | 1.0(0.7-1.3)         |
| >650  | -            | 0.7(0.6-1.0) | 0.7(0.6-1.0) | 0.7(0.6-1.0)         | 0.8(0.6-1.0)         | 0.8(0.6-1.0)         |
| <i><b>Medical comorbidities (CCI)</b></i>     |              |              |              |                      |                      |                      |
| 0   |              |              | 1.0 (ref.)   | 1.0 (ref.)           | 1.0 (ref.)           | 1.0 (ref.)           |
| 1   | -            | -            | 1.1(0.9-1.4) | 1.1(0.9-1.4)         | 1.1(0.8-1.4)         | 1.1(0.8-1.4)         |
| ≥2  | -            | -            | 1.6(1.2-2.0) | 1.5(1.2-2.0)         | 1.5(1.2-1.9)         | 1.5(1.2-1.9)         |
| <i><b>Dementia (reference: no)</b></i>        | -            | -            | -            | 0.9(0.6-1.4)         | -                    | 0.8(0.5-1.2)         |
| <i><b>Mental disorders</b></i>                |              |              |              |                      |                      |                      |
| No  | -            | -            | -            | -                    | 1.0 (ref.)           | 1.0 (ref.)           |
| Depression                                    | -            | -            | -            | -                    | 4.3(2.9-6.2)         | 4.3(2.9-6.3)         |
| Mental disorder other than depression         | -            | -            | -            | -                    | 4.4(3.2-6.1)         | 4.5(3.2-6.3)         |

CCI, Charlson comorbidity index.

Model 1: adjusted for age at index date, age<sup>2</sup>, sex, year of diagnosis, and urbanization.

Model 2: adjusted for age at index date, age<sup>2</sup>, sex, year of diagnosis, urbanization, and insurance premium.

Model 3: adjusted for age at index date, age<sup>2</sup>, sex, year of diagnosis, urbanization, insurance premium, and medical comorbidities.

Model 4: adjusted for age at index date, age<sup>2</sup>, sex, year of diagnosis, urbanization, insurance premium, medical comorbidities, and dementia (time-dependent).

Model 5: adjusted for age at index date, age<sup>2</sup>, sex, year of diagnosis, urbanization, insurance premium, medical comorbidities, and mental disorders (time-dependent).

|   |  |
|---|--|
| Model 6: adjusted for age at index date, age <sup>2</sup> , sex, year of diagnosis, urbanization, insurance premium, medical comorbidities, dementia (time-dependent), and mental disorders (time-dependent). |  |
| <sup>a</sup> Time-dependent Cox model.<br>Note: age and age <sup>2</sup> were modelled in 10-year age bands   |  |



eTable 4: Hazard ratios of suicide in Parkinson's disease patients compared to referent subjects before and after adjusting for mental disorders

|   | Model 1 <sup>a</sup> | Model 2 <sup>a</sup> | Model 3 <sup>a</sup> |
|---|----------------------|----------------------|----------------------|
| <b>Hazard ratio of suicide in PD (95% CI)</b>   | 2.1(1.7-2.5)         | 1.9(1.5-2.3)         | 1.9(1.5-2.3)         |
| <i>Dementia (reference: no)</i>   | 0.9(0.6-1.4)         | -                    | 0.8(0.5-1.2)         |
| <i>Mental Disorders (reference: no mental disorder)</i>   |                      |                      |                      |
| Schizophrenia   | -                    | 4.1(1.5-11.2)        | 4.2(1.5-11.3)        |
| Bipolar disorder  | -                    | 6.3(3.1-12.7)        | 6.3(3.1-12.8)        |
| Depression  | -                    | 4.1(2.8-6.0)         | 4.1(2.8-6.0)         |
| Other mental disorders <sup>b</sup>   | -                    | 4.3(3.0-6.3)         | 4.4(3.1-6.5)         |
| Model 1: adjusted for age at index date, age <sup>2</sup> , sex, year of diagnosis, urbanization, insurance premium, medical comorbidities, and dementia (time-dependent).                                    |                      |                      |                      |
| Model 2: adjusted for age at index date, age <sup>2</sup> , sex, year of diagnosis, urbanization, insurance premium, medical comorbidities, and mental disorders (time-dependent).                            |                      |                      |                      |
| Model 3: adjusted for age at index date, age <sup>2</sup> , sex, year of diagnosis, urbanization, insurance premium, medical comorbidities, dementia (time-dependent), and mental disorders (time-dependent). |                      |                      |                      |
| <sup>a</sup> Time-dependent Cox model.  |                      |                      |                      |
| <sup>b</sup> Other mental disorders: mental disorder other than schizophrenia, bipolar disorder, and depression.  |                      |                      |                      |
| Note: age and age <sup>2</sup> were modelled in 10-year age bands   |                      |                      |                      |

eTable 5: Hazard ratios of suicide in Parkinson's disease patients compared to referent subjects from the general population stratified by their characteristics

|                                       | HR (95% CI) <sup>a</sup> | P-value for interaction |
|---------------------------------------|--------------------------|-------------------------|
| <b>Sex</b>                            |                          | 0.44                    |
| Men                                   | 1.9(1.5-2.5)             |                         |
| Women                                 | 2.3(1.7-3.2)             |                         |
| <b>Age (years)</b>                    |                          | 0.52                    |
| ≥75                                   | 1.9(1.5-2.6)             |                         |
| 65-74                                 | 2.1(1.5-2.9)             |                         |
| <65                                   | 2.5(1.6-3.8)             |                         |
| <b>Insurance premium (USD)</b>        |                          | 0.35                    |
| 0-36                                  | 1.8(1.2-2.8)             |                         |
| >36-650                               | 2.1(1.4-3.1)             |                         |
| >650                                  | 2.4(1.8-3.1)             |                         |
| <b>Level of urbanization</b>          |                          | 0.05                    |
| Low                                   | 2.4(1.5-3.8)             |                         |
| Medium                                | 1.4(1.0-2.0)             |                         |
| High                                  | 2.5(1.9-3.3)             |                         |
| <b>Dementia</b>                       |                          | --                      |
| Yes                                   | Not estimable            |                         |
| No                                    | 3.2(2.3-4.4)             |                         |
| <b>Mental disorders</b>               |                          | 0.67                    |
| No                                    | 2.9(2.0-4.3)             |                         |
| Depression                            | 1.8(0.6-5.9)             |                         |
| Mental disorder other than depression | 2.4(0.7-7.6)             |                         |

CCI, Charlson comorbidity index.

<sup>a</sup> Adjusted for age at index date, age<sup>2</sup>, sex, year of diagnosis, urbanization, insurance premium, and medical comorbidities.

eTable 6: Comparisons between socio-demographic and clinical characteristics of suicide and non-suicide in Parkinson's disease (PD) patient and referent subjects

|                                      | PD patients        |             |                           |             |             | Referent subjects  |              |                            |             |             |
|--------------------------------------|--------------------|-------------|---------------------------|-------------|-------------|--------------------|--------------|----------------------------|-------------|-------------|
| Baseline characteristics<br>n (%)    | Suicide<br>(n=151) |             | Non-Suicide<br>(n=35,704) |             | P-<br>value | Suicide<br>(n=300) |              | Non-Suicide<br>(n=143,257) |             | P-<br>value |
| <b>Matching Variables</b>            |                    |             |                           |             |             |                    |              |                            |             |             |
| <b>Age</b>                           |                    |             |                           |             | 0.51        |                    |              |                            |             | 0.73        |
| ≥75 years                            | 66                 | (43.7<br>1) | 16,986                    | (47.53<br>) |             | 14                 | (48.00<br>4) | 68,057                     | (47.51<br>) |             |
| 65-74 years                          | 49                 | (32.4<br>5) | 11,457                    | (32.06<br>) |             | 10                 | (33.33<br>0) | 45,924                     | (32.06<br>) |             |
| <65 years                            | 36                 | (23.8<br>4) | 7,297                     | (20.42<br>) |             | 56                 | (18.67<br>)  | 29,276                     | (20.44<br>) |             |
| <b>Sex</b>                           |                    |             |                           |             | 0.011       |                    |              |                            |             | <.000<br>1  |
| Male                                 | 93                 | (61.5<br>9) | 18,316                    | (51.25<br>) |             | 19                 | (65.67<br>7) | 73,432                     | (51.26<br>) |             |
| Female                               | 58                 | (38.4<br>1) | 17,424                    | (48.75<br>) |             | 10                 | (34.33<br>3) | 69,825                     | (48.74<br>) |             |
| <b>Demographic variables</b>         |                    |             |                           |             |             |                    |              |                            |             |             |
| <b>Insurance Premium (USD/month)</b> |                    |             |                           |             | 0.18        |                    |              |                            |             | <.000<br>1  |
| 0-36                                 | 31                 | (20.5<br>3) | 5,478                     | (15.33<br>) |             | 71                 | (23.67<br>)  | 20,192                     | (14.09<br>) |             |
| >36-650                              | 40                 | (26.4<br>9) | 9,323                     | (26.09<br>) |             | 85                 | (28.33<br>)  | 36,970                     | (25.81<br>) |             |

|  |     |         |        |         |        |     |         |         |         |        |
|--|-----|---------|--------|---------|--------|-----|---------|---------|---------|--------|
| >650                                     | 80  | (52.98) | 20,939 | (58.59) |        | 144 | (48.00) | 86,095  | (60.10) |        |
| Level of Urbanization                    |     |         |        |         | 0.29   |     |         |         |         | 0.02   |
| Low                                      | 28  | (18.54) | 5,408  | (15.13) |        | 49  | (16.33) | 21,654  | (15.12) |        |
| Medium                                   | 39  | (25.83) | 11,060 | (30.95) |        | 115 | (38.33) | 45,716  | (31.91) |        |
| High                                     | 84  | (55.63) | 19,272 | (53.92) |        | 136 | (45.33) | 75,887  | (52.97) |        |
| Medical comorbidities (CCI) <sup>a</sup> |     |         |        |         | 0.65   |     |         |         |         | 0.09   |
| 0  | 83  | (54.97) | 19,882 | (55.63) |        | 187 | (62.33) | 96,715  | (67.51) |        |
| 1  | 35  | (23.18) | 9,033  | (25.27) |        | 57  | (19.00) | 25,601  | (17.87) |        |
| ≥2                                       | 33  | (21.85) | 6,825  | (19.10) |        | 56  | (18.67) | 20,941  | (14.62) |        |
| Dementia <sup>a</sup>                    | 11  | (7.28)  | 5,840  | (16.34) | 0.0026 | 26  | (8.67)  | 13,961  | (9.75)  | 0.53   |
| Mental disorders <sup>b</sup>            |     |         |        |         | <.0001 |     |         |         |         | <.0001 |
| None                                     | 124 | (82.12) | 33,120 | (92.67) |        | 274 | (91.33) | 139,565 | (97.42) |        |
| Depression                               | 15  | (9.93)  | 1,254  | (3.51)  |        | 15  | (5.00)  | 1,616   | (1.13)  |        |
| Mental disorders other than depression   | 12  | (7.95)  | 1,366  | (3.82)  |        | 11  | (3.67)  | 2,076   | (1.45)  |        |

CCI, Charlson comorbidity index.

<sup>a</sup> Disease status from PD index date to 2016/12/31.

<sup>b</sup> Disease status within one year before the diagnosis of PD.

eTable 7: Characteristics of Parkinson's disease patients and referent subjects who died by suicide

| Characteristics<br>n (%)                         | Parkinson's<br>disease<br>(N=151) | Referent<br>subjects<br>(N=300) | P-value |
|--|-----------------------------------|---------------------------------|---------|
| <b>Gender</b>                                    |                                   |                                 | 0.39    |
| Male   | 93(61.6)                          | 197(65.7)                       |         |
| Female   | 58(38.4)                          | 103(34.3)                       |         |
| <b>Age at suicide, mean (standard deviation)</b> | 73.95(10.4)                       | 75.99(10.2)                     | 0.05    |
| <b>Urbanization</b>                              |                                   |                                 | 0.03    |
| Low  | 28(18.5)                          | 49(16.3)                        |         |
| Medium   | 39(25.8)                          | 115(38.3)                       |         |
| High   | 84(55.6)                          | 136(45.3)                       |         |
| <b>Insurance premium</b>                         |                                   |                                 | 0.59    |
| 0-36   | 31(20.5)                          | 71(23.7)                        |         |
| >36-650  | 40(26.5)                          | 85(28.3)                        |         |
| >650   | 80(53.0)                          | 144(48.0)                       |         |
| <b>Medical comorbidities (CCI)</b>               |                                   |                                 | 0.32    |
| 0  | 83(55.0)                          | 187(62.3)                       |         |
| 1  | 35(23.2)                          | 57(19.0)                        |         |
| ≥2   | 33(21.9)                          | 56(18.7)                        |         |
| <b>Dementia</b>                                  |                                   |                                 | 0.61    |
| Yes  | 11(7.3)                           | 26(8.7)                         |         |
| No   | 140(92.7)                         | 274(91.3)                       |         |
| <b>Mental disorders</b>                          |                                   |                                 | 0.02    |
| None   | 124(82.1)                         | 274(91.3)                       |         |
| Depression                                       | 15(9.9)                           | 15(5.0)                         |         |
| Mental disorders other than depression           | 12(8.0)                           | 11(3.7)                         |         |
| <b>Method of suicide</b>                         |                                   |                                 |         |
| Jumping  | 21(13.91)                         | 16(5.3)                         | <0.01   |
| Drowning   | 9(6.0)                            | 14(4.7)                         | 0.56    |
| Hanging/suffocation                              | 59(39.1)                          | 136(45.3)                       | 0.21    |
| Solid and Liquid poisoning                       | 35(23.2)                          | 85(28.3)                        | 0.24    |
| Charcoal burning                                 | 5(3.3)                            | 13(4.3)                         | 0.60    |
| Undetermined intent                              | 16(10.6)                          | 30(10.0)                        | 0.84    |
| Others   | 6(4.0)                            | 6(2.0)                          | 0.22    |

CCI, Charlson comorbidity index.