Supplemental Online Content

Rocca WA, Smith CY, Gazzuola Rocca L, Savica R, Mielke MM. Association of premenopausal bilateral oophorectomy with parkinsonism and Parkinson disease. JAMA Netw Open. 2022;5(10):e2238663. doi:10.1001/jamanetworkopen.2022.38663

eTable 1. Diagnostic Codes for Parkinsonism Used to Screen Medical Records

eTable 2. Associations of Bilateral Oophorectomy Performed in 1950-1987 With Incident Parkinsonism (MOA-1 Study)

eTable 3. Associations of Bilateral Oophorectomy Performed in 1988-2007 With Incident Parkinsonism (MOA-2 Study)

eFigure 1. Balance of Characteristics at Baseline Obtained Using Inverse Probability Weights

eFigure 2. Flowchart of the Study Groups

eFigure 3. Cumulative Incidence of Parkinsonism and Parkinson Disease by Age at Oophorectomy in Tertiles

This supplemental material has been provided by the authors to give readers additional information about their work.
**eTable 1. Diagnostic Codes for Parkinsonism Used to Screen Medical Records**

| Diagnostic code | Code type | Description |
|-----------------|-----------|-------------|
| 331.82          | ICD-9     | Dementia with Lewy bodies |
| 331.9           | ICD-9     | Cerebral degeneration, unspecified |
| 332.0           | ICD-9     | Paralysis agitans |
| 332.1           | ICD-9     | Secondary parkinsonism |
| 333.0           | ICD-9     | Other degenerative diseases of the basal ganglia |
| 333.1           | ICD-9     | Essential and other specified forms of tremor |
| G20             | ICD-10    | Parkinson disease |
| G21.0           | ICD-10    | Malignant neuroleptic syndrome |
| G21.11          | ICD-10    | Neuroleptic induced parkinsonism |
| G21.19          | ICD-10    | Other drug induced secondary parkinsonism |
| G21.2           | ICD-10    | Secondary parkinsonism due to other external agents |
| G21.3           | ICD-10    | Postencephalitic parkinsonism |
| G21.4           | ICD-10    | Vascular parkinsonism |
| G21.8           | ICD-10    | Other secondary parkinsonism |
| G21.9           | ICD-10    | Secondary parkinsonism, unspecified |
| G23.0           | ICD-10    | Hallervorden-Spatz disease |
| G23.1           | ICD-10    | Progressive supranuclear ophthalmoplegia |
| G23.2           | ICD-10    | Striatonigral degeneration |
| G23.8           | ICD-10    | Other specified degenerative diseases of basal ganglia |
| G23.9           | ICD-10    | Degenerative disease of basal ganglia, unspecified |
| G25.0           | ICD-10    | Essential tremor |
| G25.1           | ICD-10    | Drug-induced tremor |
| G25.2           | ICD-10    | Other specified forms of tremor |
| G31.83          | ICD-10    | Dementia with Lewy bodies |
| G31.9           | ICD-10    | Degenerative disease of nervous system, unspecified |

Abbreviation: ICD, International Classification of Diseases.
### eTable 2. Associations of Bilateral Oophorectomy Performed in 1950-1987 With Incident Parkinsonism (MOA-1 Study)

| Characteristic                | Women with bilateral oophorectomy<sup>a</sup> | Women without bilateral oophorectomy | Unweighted models<sup>b</sup> | Weighted models<sup>c</sup> |
|-------------------------------|---------------------------------------------|-------------------------------------|-------------------------------|------------------------------|
|                               | No. at risk | Person-years | Events, No. | Cumulative incidence at 50 y, % (95% CI)<sup>d</sup> | No. at risk | Person-years | Events, No. | Cumulative incidence at 50 y, % (95% CI)<sup>d</sup> | HR (95% CI) | P value | HR (95% CI) | P value |
| **Any parkinsonism**          |            |              |             |                                                |            |              |             |                                                |              |         |              |         |
| Age tertiles<sup>f</sup>, y   | 1097       | 35 903       | 38          | 4.5 (3.3-6.3)                                  | 1096       | 36 029       | 26          | 2.7 (1.8-4.1)                                  | 1.50 (0.91-2.46) | .11     | 1.51 (0.92-2.49) | .11     |
| <43                           | 365        | 12 994       | 10          | 4.0 (2.1-7.4)                                  | 365        | 12 824       | 2           | 0.7 (0.1-5.0)                                  | 5.22 (1.20-22.79) | .03     | 5.26 (1.20-22.95) | .03     |
| 43-47                         | 332        | 11 024       | 14          | 5.6 (3.3-9.5)                                  | 332        | 11 179       | 14          | 5.0 (3.0-8.4)                                  | 1.04 (0.50-2.18) | .92     | 1.02 (0.49-2.14) | .96     |
| ≥48                           | 400        | 11 885       | 14          | 4.0 (2.3-6.8)                                  | 399        | 12 026       | 10          | 2.7 (1.4-4.9)                                  | 1.41 (0.63-3.17) | .41     | 1.40 (0.62-3.15) | .42     |
| **Age group<sup>i</sup>, y**  |            |              |             |                                                |            |              |             |                                                |              |         |              |         |
| <40                           | 238        | 8536         | 4           | 2.7 (1.0-7.4)                                  | 238        | 8280         | 1           | 1.2 (0.2-8.2)                                  | 4.03 (0.47-34.90) | .21     | 4.38 (0.51-37.83) | .18     |
| 40-45                         | 315        | 10 829       | 15          | 6.1 (3.7-10.1)                                 | 315        | 11 023       | 12          | 4.0 (2.2-7.3)                                  | 1.29 (0.60-2.76) | .51     | 1.29 (0.60-2.76) | .51     |
| 46-49                         | 295        | 9329         | 11          | 4.8 (2.6-8.8)                                  | 295        | 9534         | 7           | 2.7 (1.3-5.6)                                  | 1.64 (0.63-4.24) | .31     | 1.57 (0.60-4.07) | .36     |
| ≥50                           | 249        | 7209         | 8           | 3.4 (1.7-6.7)                                  | 248        | 7192         | 6           | 2.5 (1.1-5.4)                                  | 1.33 (0.46-3.83) | .60     | 1.43 (0.50-4.15) | .51     |
| **Benign indication**<sup>g</sup> | 557      | 18 961       | 19          | 4.4 (2.8-6.9)                                  | 557        | 18 772       | 10          | 2.4 (1.3-4.5)                                  | 1.94 (0.90-4.14) | .09     | 1.96 (0.92-4.21) | .08     |
| No ovarian indication<sup>h</sup> | 540    | 16 943       | 19          | 4.6 (2.9-7.4)                                  | 539        | 17 257       | 16          | 3.0 (1.8-5.0)                                  | 1.23 (0.63-2.38) | .55     | 1.22 (0.63-2.37) | .56     |
| Years 1950-1969               | 334        | 11 616       | 14          | 4.6 (2.7-7.7)                                  | 334        | 11 602       | 8           | 2.2 (1.1-4.7)                                  | 1.78 (0.75-4.26) | .19     | 1.86 (0.78-4.45) | .16     |
| Years 1970-1987               | 763        | 24 288       | 24          | 4.3 (2.8-6.5)                                  | 762        | 24 427       | 18          | 2.9 (1.8-4.6)                                  | 1.36 (0.74-2.50) | .32     | 1.36 (0.74-2.50) | .32     |
| **Parkinson disease**         | 1097       | 35 977       | 24          | 2.8 (1.8-4.2)                                  | 1096       | 36 064       | 18          | 1.8 (1.1-3.0)                                  | 1.36 (0.74-2.49) | .33     | 1.38 (0.75-2.54) | .30     |
| Age tertiles<sup>f</sup>, y   | 1097       | 35 903       | 38          | 4.5 (3.3-6.3)                                  | 1096       | 36 029       | 26          | 2.7 (1.8-4.1)                                  | 1.50 (0.91-2.46) | .11     | 1.51 (0.92-2.49) | .11     |
| <43                           | 365        | 13 019       | 6           | 2.6 (1.2-5.9)                                  | 365        | 12 824       | 2           | 0.7 (0.1-5.0)                                  | 3.17 (0.67-14.92) | .14     | 3.36 (0.72-15.80) | .12     |
| 43-47                         | 332        | 11 040       | 10          | 3.6 (1.9-6.8)                                  | 332        | 11 208       | 8           | 2.7 (1.3-5.3)                                  | 1.30 (0.52-3.26) | .58     | 1.29 (0.51-3.24) | .59     |
| ≥48                           | 400        | 11 918       | 8           | 2.1 (1.1-4.3)                                  | 399        | 12 032       | 8           | 2.1 (1.1-4.3)                                  | 0.99 (0.37-2.64) | .99     | 0.98 (0.37-2.61) | .97     |
| **Age group<sup>i</sup>, y**  |            |              |             |                                                |            |              |             |                                                |              |         |              |         |
| <40                           | 238        | 8546         | 2           | 1.6 (0.4-6.8)                                  | 238        | 8280         | 1           | 1.2 (0.2-8.2)                                  | 2.03 (0.19-21.54) | .56     | 2.36 (0.23-24.71) | .97     |
| 40-45                         | 315        | 10 856       | 10          | 4.0 (2.1-7.4)                                  | 315        | 11 051       | 7           | 2.0 (0.9-4.5)                                  | 1.45 (0.55-3.83) | .45     | 1.46 (0.55-3.84) | .45     |
| 46-49                         | 295        | 9346         | 7           | 2.8 (1.3-6.0)                                  | 295        | 9539         | 5           | 1.9 (0.8-4.7)                                  | 1.45 (0.46-4.61) | .53     | 1.40 (0.44-4.46) | .53     |
| ≥50                           | 249        | 7228         | 5           | 2.1 (0.9-5.1)                                  | 248        | 7193         | 5           | 2.0 (0.8-4.8)                                  | 0.99 (0.29-3.41) | .99     | 1.10 (0.32-3.76) | .97     |

© 2022 Rocca WA et al. JAMA Network Open.
**Table 2. Continued**

| Characteristic          | Women with bilateral oophorectomy<sup>a</sup> | Women without bilateral oophorectomy | Unweighted models<sup>b</sup> | Weighted models<sup>c</sup> |
|-------------------------|-----------------------------------------------|-------------------------------------|-------------------------------|-------------------------------|
|                         | No. at risk Person-years Events, No.          | Cumulative incidence at 50 y, % (95% CI)<sup>d</sup> | No. at risk Person-years Events, No. | Cumulative incidence at 50 y, % (95% CI)<sup>d</sup> | HR (95% CI) | P value | HR (95% CI) | P value |
| Benign indication<sup>g</sup> | 557 18 999 12 | 2.7 (1.5-4.9) | 557 18 794 5 | 1.2 (0.5-3.1) | 2.42 (0.86-6.82) | .09 | 2.54 (0.90-7.19) | .08 |
| No ovarian indication<sup>h</sup> | 540 16 977 12 | 2.8 (1.6-5.0) | 539 17 270 13 | 2.4 (1.4-4.3) | 0.94 (0.43-2.06) | .89 | 0.95 (0.43-2.07) | .89 |
| Years 1950-1969         | 334 11 638 9  | 3.0 (1.6-5.7) | 334 11 619 7 | 1.9 (0.9-4.3) | 1.30 (0.48-3.48) | .61 | 1.37 (0.51-3.67) | .54 |
| Years 1970-1987         | 763 24 339 15 | 2.6 (1.5-4.4) | 762 24 444 11 | 1.6 (0.9-3.0) | 1.38 (0.63-2.99) | .42 | 1.39 (0.64-3.01) | .41 |

Abbreviation: CI, confidence interval; HR, hazard ratio; MOA-1, Mayo Clinic Cohort Study of Oophorectomy and Aging - 1.

- **<sup>a</sup>** Almost all 1097 women were premenopausal at the time of bilateral oophorectomy as determined by medical records abstraction. However, 158 women had unknown age at menopause and were presumed to be premenopausal because the surgery was performed at age ≤55 years. Menopause was defined as ≥12 months of continuous amenorrhea.
- **<sup>b</sup>** HRs were calculated using Cox proportional hazards models with age as the time scale.
- **<sup>c</sup>** HRs were calculated using Cox proportional hazards models with age as the time scale and including inverse probability weights derived from a logistic regression model including years of education (unknown, ≤12, 13-16, >16), race (white vs the combined group of Asian, Black, and other), age at index date (continuous), and calendar year at index date (continuous). The inverse probability weights were calculated separately within each stratum to maximize the balance of the variables. After balancing the two cohorts using inverse probability weights, the standardized differences for all of the conditions or characteristics considered were below the recommended threshold of .10 (ie, negligible imbalance between the two cohorts; eFigure 1). Interactions by age, indication, and calendar year were assessed using stratified analyses. No significant overall interactions were found.
- **<sup>d</sup>** Cumulative risk of parkinsonism at 50 years after bilateral oophorectomy (or index) calculated using the cumulative incidence function and accounting for the competing risk of death. The models included inverse probability weights derived from a logistic regression model including years of education (unknown, ≤12, 13-16, >16), race (white vs the combined group of Asian, Black, and other), age at index date (continuous), and calendar year at index date (continuous).
- **<sup>e</sup>** A total of 39 women with Parkinsonism (27 among women with oophorectomy and 12 among referent women) had been included in the initial MOA-1 report (Rocca et al., Neurology 2008) and 25 women (11 among women with oophorectomy and 14 among referent women) were newly detected during the extension of follow-up.
- **<sup>f</sup>** Linear trends by age tertiles and by conventional age groups were assessed using separate models comparing age at oophorectomy strata to all referent women combined and including inverse probability weights. No significant linear trends for Parkinsonism were found by age tertiles (P = .26) or by age groups (P = .06). No significant linear trends were found for Parkinson disease by age tertiles (P = .53) or by age groups (P = .24).
- **<sup>g</sup>** The benign condition (eg, benign tumor, cyst, or endometriosis) was listed by the gynecologist in the medical record at the time of bilateral oophorectomy, but may not have been the sole indication for the surgery.
- **<sup>h</sup>** Women without an ovarian condition. Historically, the terms *prophylactic, elective, or incidental* bilateral oophorectomy were used; however, we did not use these terms.

© 2022 Rocca WA et al. *JAMA Network Open.*
### eTable 3. Associations of Bilateral Oophorectomy Performed in 1988-2007 With Incident Parkinsonism (MOA-2 Study)

| Characteristic | Women with bilateral oophorectomy<sup>a</sup> | Women without bilateral oophorectomy | Unweighted models<sup>b</sup> | Weighted models<sup>c</sup> |
|----------------|-----------------------------------------------|-------------------------------------|------------------------------|-------------------------------|
|                | No. at risk Person-years Events, No. | Cumulative incidence at 25 y, % (95% CI)<sup>d</sup> | No. at risk Person-years Events, No. | Cumulative incidence at 25 y, % (95% CI)<sup>d</sup> | HR (95% CI) | P value | HR (95% CI) | P value |
| **Any parkinsonism** | | | | | | | | |
| Age tertiles<sup>e</sup>, y | | | | | | | | |
| <42 | 521 10 525 2 | 0.4 (0.1-1.7) | 521 9970 0 | 0.0 (0.0-0.0) | NA | NA | NA | NA |
| 42-45 | 510 10 096 1 | 0.0 (0.0-0.0) | 510 10 007 0 | 0.0 (0.0-0.0) | NA | NA | NA | NA |
| 46-49 | 622 12 048 9 | 1.9 (0.9-4.0) | 622 12 328 6 | 1.3 (0.5-3.3) | 1.56 (0.60-4.08) | .36 | 1.49 (0.55-3.99) | .43 |
| Age group<sup>e</sup>, y | | | | | | | | |
| <40 | 344 6962 2 | 0.6 (0.1-2.3) | 344 6511 0 | 0.0 (0.0-0.0) | NA | NA | NA | NA |
| 40-45 | 687 13 659 1 | 0.0 (0.0-0.0) | 687 13 466 0 | 0.0 (0.0-0.0) | NA | NA | NA | NA |
| 46-49 | 622 12 048 9 | 1.9 (0.9-4.0) | 622 12 328 6 | 1.3 (0.5-3.3) | 1.56 (0.60-4.08) | .36 | 1.49 (0.55-3.99) | .43 |
| Benign indication<sup>f</sup> | 675 13 370 3 | 0.4 (0.1-1.4) | 675 13 130 1 | 0.4 (0.1-2.5) | 3.07 (0.60-15.74) | .18 | 2.36 (0.39-14.43) | .35 |
| No ovarian indication<sup>g</sup> | 978 19 299 9 | 1.2 (0.5-2.6) | 978 19 175 5 | 0.6 (0.2-1.7) | 1.81 (0.61-5.38) | .29 | 1.76 (0.58-5.36) | .32 |
| Years 1988-1997 | 723 17 248 10 | 1.1 (0.5-2.3) | 723 17 252 2 | 0.2 (0.0-1.2) | 5.06 (1.11-23.02) | .04 | 4.90 (1.07-22.39) | .04 |
| Years 1998-2007 | 930 15 421 2 | NA | 930 15 053 4 | NA | 0.50 (0.12-2.02) | .33 | 0.51 (0.11-2.33) | .39 |
| Ever smokers | 756 14 901 6 | 0.8 (0.3-2.3) | 696 13 764 3 | 0.4 (0.1-1.9) | 2.18 (0.64-7.43) | .21 | 2.09 (0.61-7.20) | .24 |
| Never smokers | 897 17 768 6 | 0.8 (0.3-2.2) | 957 18 541 3 | 0.6 (0.2-2.0) | 2.01 (0.51-8.03) | .32 | 1.69 (0.40-7.21) | .48 |
| **Parkinson disease** | 1653 32 681 8 | 0.7 (0.3-1.5) | 1653 32 314 3 | 0.2 (0.1-0.6) | 2.67 (0.71-10.07) | .15 | 2.81 (0.73-10.85) | .13 |
| Age tertiles<sup>e</sup>, y | | | | | | | | |
| <42 | 521 10 525 2 | 0.4 (0.1-1.7) | 521 9970 0 | 0.0 (0.0-0.0) | NA | NA | NA | NA |
| 42-45 | 510 10 096 0 | 0.0 (0.0-0.0) | 510 10 007 0 | 0.0 (0.0-0.0) | NA | NA | NA | NA |
| 46-49 | 622 12 060 6 | 1.2 (0.5-3.1) | 622 12 337 3 | 0.6 (0.2-2.0) | 2.07 (0.52-8.28) | .31 | 1.88 (0.45-7.82) | .39 |
| Age group<sup>e</sup>, y | | | | | | | | |
| <40 | 344 6962 2 | 0.6 (0.1-2.3) | 344 6511 0 | 0.0 (0.0-0.0) | NA | NA | NA | NA |
| 40-45 | 687 13 659 0 | 0.0 (0.0-0.0) | 687 13 466 0 | 0.0 (0.0-0.0) | NA | NA | NA | NA |
| 46-49 | 622 12 060 6 | 1.2 (0.5-3.1) | 622 12 337 3 | 0.6 (0.2-2.0) | 2.07 (0.52-8.28) | .31 | 1.88 (0.45-7.82) | .39 |

© 2022 Rocca WA et al. JAMA Network Open.
### eTable 3. Continued

| Characteristic | Women with bilateral oophorectomy<sup>a</sup> | Women without bilateral oophorectomy | Unweighted models<sup>b</sup> | Weighted models<sup>c</sup> |
|----------------|---------------------------------------------|-------------------------------------|-----------------------------|-----------------------------|
|                | No. at risk | Person-years | Events, No. | Cumulative incidence at 25 y, % (95% CI)<sup>d</sup> | No. at risk | Person-years | Events, No. | Cumulative incidence at 25 y, % (95% CI)<sup>d</sup> | HR (95% CI) | P value | HR (95% CI) | P value |
| Age group<sup>e</sup>, y |                      |                        |             |                         |                      |                        |             |                         |                    |        |                    |        |
| <40            | 344         | 6962        | 2           | 0.6 (0.1-2.3)           | 344         | 6511        | 0           | 0.0 (0.0-0.0)           | NA         | NA      | NA         | NA      |
| 40-45          | 687         | 13 659      | 0           | 0.0 (0.0-0.0)           | 687         | 13 466      | 0           | 0.0 (0.0-0.0)           | NA         | NA      | NA         | NA      |
| 46-49          | 622         | 12 060      | 6           | 1.2 (0.5-3.1)           | 622         | 12 337      | 3           | 0.6 (0.2-2.0)           | 2.07 (0.52-8.28) | .31 | 1.88 (0.45-7.82) | .39 |
| Benign indication<sup>f</sup> | 675         | 13 378      | 1           | 0.2 (0.0-1.2)           | 675         | 13 132      | 0           | 0.0 (0.0-0.0)           | NA         | NA      | NA         | NA      |
| No ovarian indication<sup>g</sup> | 978         | 19 303      | 7           | 0.9 (0.4-2.3)           | 978         | 19 182      | 3           | 0.4 (0.1-1.1)           | 2.33 (0.60-8.99) | .22 | 2.35 (0.59-9.38) | .23 |
| Years 1988-1997 | 723         | 17 258      | 7           | 1.0 (0.4-2.2)           | 723         | 17 259      | 0           | 0.0 (0.0-0.0)           | NA         | NA      | NA         | NA      |
| Years 1998-2007 | 930         | 15 423      | 1           | NA                      | 930         | 15 055      | 3           | NA                      | 0.34 (0.03-3.28) | .35 | 0.47 (0.05-4.65) | .52 |
| Ever smokers   | 756         | 14 913      | 2           | 0.4 (0.1-1.7)           | 696         | 13 768      | 1           | 0.1 (0.0-0.9)           | 1.90 (0.17-21.16) | .60 | 2.17 (0.19-24.21) | .53 |
| Never smokers  | 897         | 17 768      | 6           | 0.8 (0.3-2.2)           | 957         | 18 547      | 2           | 0.3 (0.1-1.4)           | 3.04 (0.62-14.92) | .17 | 2.38 (0.43-13.07) | .32 |

**Abbreviation:** BMI, body mass index; CI, confidence interval; HR, hazard ratio; MOA-2, Mayo Clinic Cohort Study of Oophorectomy and Aging – 2; NA, not applicable.

<sup>a</sup> All 1653 women were premenopausal at the time of bilateral oophorectomy as determined by medical records abstraction. Menopause was defined as ≥12 months of continuous amenorrhea.

<sup>b</sup> HRs were calculated using Cox proportional hazards models with age as the time scale.

<sup>c</sup> HRs were calculated using Cox proportional hazards models with age as the time scale and including inverse probability weights derived from a logistic regression model including 18 chronic conditions present at baseline, years of education (unknown, ≤12, 13-16, >16), quartiles of household income (<$42 000, $42 000-56 999, $57 000-71 999, ≥$72 000), race (white vs the combined group of Asian, Black, and other), BMI (<30 vs ≥30 kg/m²), cigarette smoking (current or former vs never), age at index date (continuous), and calendar year at index date (continuous). The 18 chronic conditions included depression, anxiety, substance abuse disorders (drugs and alcohol), dementia, schizophrenia and psychosis, hyperlipidemia, hypertension, diabetes, cardiac arrhythmias, coronary artery disease, congestive heart failure, stroke, arthritis, cancer (all types), asthma, chronic obstructive pulmonary disease, osteoporosis, and chronic kidney disease. Each condition required the presence of two or more related diagnostic codes, separated by >30 days to reduce the risk of false-positive diagnoses. A finer dating of diagnostic codes was not available before 1994; therefore, a 1-year separation of codes was required before 1994. The inverse probability weights were calculated separately within each stratum to maximize the balance of the variables. After balancing the two cohorts using inverse probability weights, the standardized differences for all of the conditions or characteristics considered were below the recommended threshold of .10 (ie, negligible imbalance between the two cohorts; eFigure 1). Interactions by indication, calendar year, and cigarette smoking were assessed using stratified analyses. The interaction by calendar year was significant for parkinsonism (P = .04), however, no other significant interactions were found.

<sup>d</sup> Cumulative risk of parkinsonism at 25 years after bilateral oophorectomy (or index) calculated using the cumulative incidence function and accounting for the competing risk of death. The models included inverse probability weights derived from a logistic regression model including 18 chronic conditions present at baseline, years of education (unknown, ≤12, 13-16, >16), quartiles of household income (<$42 000, $42 000-56 999, $57 000-71 999, ≥$72 000), race (white vs the combined group of Asian, Black, and other), BMI (<30 vs ≥30 kg/m²), cigarette smoking (current or former vs never), age at index date (continuous), and calendar year at index date (continuous).

<sup>e</sup> Linear trends by age tertiles and by conventional age groups could not be assessed.

<sup>f</sup> Women without an ovarian condition. Historically, the terms prophylactic, elective, or incidental bilateral oophorectomy were used; however, we did not use these terms.

© 2022 Rocca WA et al. JAMA Network Open.
eFigure 1. Balance of Characteristics at Baseline Obtained Using Inverse Probability Weights

Abbreviations: COPD, chronic obstructive pulmonary disease; IPW, inverse probability weights; MOA, Mayo Clinic Cohort Study of Oophorectomy and Aging.

The red circles indicate the absolute standardized differences before balancing and the black diamonds indicate these differences after balancing using IPW for all women overall (Panel A), for women from the MOA-1 study only (Panel B), and for women from the MOA-2 study only (Panel C). After the IPW balancing, all of the standardized differences were at or below the

© 2022 Rocca WA et al. JAMA Network Open.
recommended threshold of .10, denoting negligible imbalance of these characteristics between the women with and without bilateral oophorectomy. For each condition or characteristic, the absolute standardized difference is defined as the absolute value of the difference in means for that characteristic between women in the 2 groups, divided by the pooled standard deviation for that characteristic. The weights were derived from propensity scores estimated from logistic regression models including years of education (≤12, 13 to 16, >16, unknown), race (white vs the combined group of Asian, Black and other), age at index date (continuous), and calendar year at index date (continuous). Additional data were available for the women in the MOA-2 study, so those propensity models also included 18 chronic conditions present at baseline, quartiles of household income (<$42 000, $42 000-56 999, $57 000-71 999, ≥$72 000), body mass index (<30 vs ≥30 kg/m²), and cigarette smoking (current or former vs never). These models were fit overall and separately in each stratum to maximize the balance at the index date. Weights greater than 10 were trimmed by setting these weights to the value of the 99th percentile for their respective group (with or without bilateral oophorectomy). The weights were then stabilized to reduce variability by dividing each weight by the mean weight for their respective group. After stabilization, the IPW ranged between 0.9 and 1.6 for the overall bilateral oophorectomy group and between 0.7 and 1.1 for the overall reference group. Among women from the MOA-1 study, the stabilized IPW ranged between 0.9 and 1.2 for the oophorectomy group and between 0.9 and 1.1 for the reference group. Among women from the MOA-2 study, the stabilized IPW ranged between 0.6 and 3.4 for the oophorectomy group and between 0.5 and 3.0 for the reference group.
eFigure 2. Flowchart of the Study Groups

Abbreviations: MOA, Mayo Clinic Cohort Study of Oophorectomy and Aging.

Women from both the MOA-1 (1950-1987) and MOA-2 (1988-2007) studies were combined for this study. As part of MOA-1 and MOA-2, the oophorectomy cohorts were identified by reviewing the medical records for women with a procedure code for bilateral oophorectomy (including second unilateral oophorectomy). Women in the bilateral oophorectomy groups

© 2022 Rocca WA et al. JAMA Network Open.
were matched to reference groups of women without bilateral oophorectomy from the same population. Some women in the MOA-1 study were screened for parkinsonism using a direct interview or an interview of a proxy informant if the woman was already deceased or incapacitated. Women who screened positive via interview were offered an examination by a movement disorders specialist. In addition, and independent from the direct contact, all women in both MOA-1 and MOA-2 were screened for one or more diagnostic codes for parkinsonism at any time in life through the end of the study period (December 31, 2020). For women who screened positive, we reviewed the complete medical records to confirm the diagnosis and type of parkinsonism. Only one referent woman was found to have developed parkinsonism before the index date, and was excluded from the analyses. The source of the screening (direct interview, proxy interview, diagnostic code only) and the source of clinical diagnostic confirmation of parkinsonism are provided in Table 2.
eFigure 3. Cumulative Incidence of Parkinsonism and Parkinson Disease by Age at Oophorectomy in Tertiles

Weighted cumulative incidence of parkinsonism (Panels A-C) and Parkinson disease (Panel D-F) in women with bilateral oophorectomy compared to referent women by age at surgery in tertiles, accounting for the competing risk of death.

© 2022 Rocca WA et al. JAMA Network Open.