Supplementary Table S1. Patient clinical characteristics and IOTA Simple Rules results in premenopausal women (n=364)

| Parameters                      | Malignant (n=87) | Benign (n=277) | P-value |
|--------------------------------|-----------------|----------------|---------|
|                                | n   | (%)     | n   | (%)   |         |
| **Clinical characteristics**   |     |         |     |       |         |
| Age (year)*                    | 36.3 | ±10.3   | 37.6 | ±9.0  | 0.260   |
| Nulliparity                    | 53  | (60.9)  | 109 | (39.4)| 0.001   |
| **Biomarker**                  |     |         |     |       |         |
| Serum CA-125 (U/ml)**          | 384.9 | (123.4,708.2) | 40.5 | (24.0, 58.6) | <0.001 |
| Range (min-max)                | (16.4-1896.7) | (5.4-278.3) |         |         |         |
| **IOTA Simple Rules features** |     |         |     |       |         |
| Malignant tumor (M-features)   |     |         |     |       |         |
| M1                             | 46  | (52.9)  | 15  | (5.4) | <0.001  |
| M2                             | 23  | (26.4)  | 10  | (3.6) | <0.001  |
| M3                             | 22  | (25.3)  | 21  | (7.6) | <0.001  |
| M4                             | 51  | (58.6)  | 22  | (7.9) | <0.001  |
| M5                             | 60  | (69.0)  | 31  | (11.2)| <0.001  |
| Benign tumor (B-features)      |     |         |     |       |         |
| B1                             | 5   | (5.8)   | 145 | (52.4)| <0.001  |
| B2                             | 0   | (0)     | 13  | (4.7) | 0.044   |
| B3                             | 3   | (3.5)   | 56  | (20.2)| <0.001  |
| B4                             | 7   | (8.1)   | 60  | (21.7)| 0.004   |
| B5                             | 24  | (27.6)  | 244 | (88.1)| <0.001  |
| **IOTA Simple Rules diagnosis**|     |         |     |       |         |
| Benign                         | 6   | (6.9)   | 208 | (75.1)| NA      |
| Malignant                      | 59  | (67.8)  | 19  | (6.9) | NA      |
| Inconclusive                   | 22  | (25.3)  | 50  | (18.1)| NA      |

**Abbreviations:** IOTA, International Ovarian Tumor Analysis; SD, standard deviation; IQR, interquartile range; NA, not applicable.

*Mean±SD

**Median (IQR)
**Supplementary Table S2.** Patient clinical characteristics and IOTA Simple Rules results in postmenopausal women (n=115)

| Parameters                             | Malignant (n=58) | Benign (n=57) | P-value |
|----------------------------------------|------------------|---------------|---------|
| **Clinical characteristics**           |                  |               |         |
| Age (year)*                            | 59.0 ±8.7        | 55.3 ±7.8     | 0.018   |
| Nulliparity                            | 22 (37.9)        | 28 (49.1)     | 0.262   |
| **Biomarker**                          |                  |               |         |
| Serum CA-125, (U/ml)**                 | 492.8 (122.1, 732.1) | 33.4 (20.4, 47.4) | <0.001 |
| Range (min-max)                        | (13.7-2032.6)    | (8.4-269.4)   |         |
| **IOTA Simple Rules features**         |                  |               |         |
| Malignant tumor (M-features)           |                  |               |         |
| M1                                     | 27 (46.6)        | 1 (1.8)       | <0.001  |
| M2                                     | 11 (19.0)        | 1 (1.8)       | 0.004   |
| M3                                     | 10 (17.2)        | 5 (8.8)       | 0.268   |
| M4                                     | 23 (39.7)        | 4 (7.0)       | <0.001  |
| M5                                     | 36 (62.1)        | 4 (7.0)       | <0.001  |
| Benign tumor (B-features)              |                  |               |         |
| B1                                     | 4 (6.9)          | 24 (42.1)     | <0.001  |
| B2                                     | 1 (1.7)          | 4 (7.0)       | 0.206   |
| B3                                     | 2 (3.5)          | 10 (17.5)     | 0.016   |
| B4                                     | 10 (17.2)        | 18 (31.6)     | 0.085   |
| B5                                     | 18 (31.0)        | 53 (93.0)     | <0.001  |
| **IOTA Simple Rules diagnosis**        |                  |               |         |
| Benign                                 | 13 (22.4)        | 45 (79.0)     | NA      |
| Malignant                              | 39 (67.2)        | 3 (5.3)       | NA      |
| Inconclusive                           | 6 (10.3)         | 9 (15.8)      | NA      |

**Abbreviations:** IOTA, International Ovarian Tumor Analysis; SD, standard deviation; IQR, interquartile range; NA, not applicable.

*Mean±SD

**Median (IQR)
Supplementary Table S3. Histopathological classification of ovarian tumors in premenopausal and postmenopausal women

| Histopathological classification | Premenopausal (n=364) | Postmenopausal (n=115) | Overall (n=479) |
|----------------------------------|-----------------------|------------------------|-----------------|
|                                  | n (%) | n (%) | n (%) |
| Malignant tumors                 |        |        |        |
| Serous carcinoma                 | 19 (5.2) | 12 (10.4) | 31 (6.5) |
| Endometrioid carcinoma           | 20 (5.5) | 11 (9.6) | 31 (6.5) |
| Mucinous carcinoma               | 2 (0.5) | 15 (12.9) | 17 (3.5) |
| Clear cell carcinoma             | 7 (1.9) | 5 (4.4) | 12 (2.5) |
| Yolk sac tumor                   | 2 (0.5) | 1 (0.9) | 3 (0.6) |
| Dysgerminoma                     | 4 (1.1) | 0 (0) | 4 (0.8) |
| Sex-cord stromal tumor           | 6 (1.7) | 1 (0.9) | 7 (1.5) |
| Other tumors                     | 4 (1.1) | 3 (2.6) | 7 (1.5) |
| Metastatic carcinoma             | 12 (3.3) | 6 (5.2) | 18 (3.8) |
| Borderline tumors                | 11 (3.1) | 4 (3.5) | 15 (3.0) |
| Borderline serous tumor          | 5 (1.4) | 1 (0.9) | 6 (1.2) |
| Borderline mucinous tumor        | 6 (1.7) | 3 (2.6) | 9 (1.8) |
| Borderline endometrioid tumor    | 0 (0) | 0 (0) | 0 (0) |
| Benign tumors                    | 277 (76.1) | 87 (49.6) | 364 (69.8) |
| Endometriotic cyst               | 95 (26.1) | 11 (9.6) | 106 (22.1) |
| Mature cystic teratoma           | 52 (14.3) | 13 (11.3) | 65 (13.6) |
| Mucinous cystadenoma             | 19 (5.2) | 12 (10.4) | 31 (6.5) |
| Serous cystadenoma               | 27 (7.4) | 7 (6.1) | 34 (7.1) |
| Pseudocyst                       | 25 (6.9) | 5 (4.4) | 30 (6.3) |
| Leiomyoma                        | 25 (6.9) | 3 (2.6) | 28 (5.8) |
| Other tumors                     | 34 (9.3) | 6 (5.2) | 40 (8.4) |
**Supplementary Table S4.** Results of internal validation with bootstrap resampling procedures

| Parameters or statistics | Mean       | SD          | Min        | Max        |
|--------------------------|------------|-------------|------------|------------|
| **Premenopausal model**  |            |             |            |            |
| Apparent AuROC           | 0.948113   | 0.017543    | 0.877739   | 0.991503   |
| Apparent CITL            | -0.00969   | 0.10411     | -0.38092   | 0.276765   |
| Apparent slope           | 8.354806   | 0.777098    | 6.58501    | 11.35269   |
| Test AuROC               | 0.944209   | 0.0013      | 0.939541   | 0.947633   |
| Test CITL                | 0.006266   | 0.101979    | -0.28934   | 0.343617   |
| Test slope               | 0.982131   | 0.066177    | 0.81173    | 1.220379   |
| Optimism AuROC           | 0.003904   | 0.017454    | -0.06898   | 0.046568   |
| Optimism CITL            | -0.01595   | 0.205918    | -0.72454   | 0.566104   |
| Optimism slope           | 0.017869   | 0.066177    | -0.22038   | 0.18827    |
| **Postmenopausal model** |            |             |            |            |
| Apparent AuROC           | 0.977092   | 0.014082    | 0.919048   | 0.999455   |
| Apparent CITL            | 0.009766   | 0.208748    | -0.5625    | 0.566503   |
| Apparent slope           | 9.995468   | 25.09239    | 5.428964   | 512.292    |
| Test AuROC               | 0.976059   | 0.001861    | 0.968845   | 0.980944   |
| Test CITL                | -0.00614   | 0.213661    | -0.52381   | 0.593935   |
| Test slope               | 0.97512    | 0.087469    | 0.773721   | 1.262725   |
| Optimism AuROC           | 0.001033   | 0.014131    | -0.05645   | 0.024802   |
| Optimism CITL            | 0.015903   | 0.421316    | -1.15643   | 1.025843   |
| Optimism slope           | 0.02488    | 0.087469    | -0.26273   | 0.226279   |

**Abbreviations:** SD, standard deviation; Min, minimum; Max, maximum; AuROC, area under the receiver operating characteristic curve; CITL, calibration-in-the-large.