

Supplementary Table 1. Disease free survival and overall survival outcomes by sex hormone level at time of endometrial cancer diagnosis in the Alberta Endometrial Cancer Cohort among post-menopausal women

| | Disease Free Survival | | | Overall Survival | | |
|---------------------------|-----------------------|---------------------------------------|------------------------------------|------------------|---------------------------------------|------------------------------------|
| | Events/ Cases | Minimally Adjusted* HR (95% CI) | Fully Adjusted** HR (95% CI) | Events/ Cases | Minimally Adjusted* HR (95% CI) | Fully Adjusted** HR (95% CI) |
| Androstenedione | | | | | | |
| <1.16 ng/mL | 56/144 | 1.00 | 1.00 | 51/144 | 1.00 | 1.00 |
| 1.16-1.59 ng/mL | 38/136 | 0.83 (0.54, 1.27) | 0.83 (0.54, 1.27) | 35/136 | 0.88 (0.56, 1.34) | 0.88 (0.56, 1.37) |
| >1.59 ng/mL | 34/119 | 0.88 (0.57, 1.36) | 0.88 (0.57, 1.36) | 33/119 | 0.99 (0.64, 1.56) | 0.99 (0.63, 1.56) |
| Per 1 ng/mL | 128/399 | 0.83 (0.54, 1.27) | 0.97 (0.66, 1.41) | 124/415 | 1.04 (0.71, 1.53) | 1.04 (0.71, 1.53) |
| Estradiol | | | | | | |
| <3.37 pg/mL | 44/143 | 1.00 | 1.00 | 51/144 | 1.00 | 1.00 |
| 3.37-12.41 pg/mL | 42/127 | 1.21 (0.79, 1.86) | 1.21 (0.78, 1.86) | 35/136 | 1.08 (0.69, 1.69) | 1.01 (0.69, 1.69) |
| >12.41 pg/mL | 42/129 | 1.44 (0.92, 2.25) | 1.44 (0.92, 2.24) | 33/119 | 1.45 (0.92, 1.12) | 1.45 (0.92, 2.31) |
| Per 1 pg/mL | 128/399 | 1.00 (0.99, 1.01) | 1.00 (0.99, 1.01) | 119/399 | 1.00 (0.99, 1.01) | 1.00 (0.99, 1.01) |
| Estrone | | | | | | |
| <48.61 pg/mL | 38/134 | 1.00 | 1.00 | 34/134 | 1.00 | 1.00 |
| 48.61-123.86 pg/mL | 42/133 | 1.31 (0.83, 2.05) | 1.30 (0.83, 2.05) | 38/133 | 1.21 (0.75, 1.95) | 1.21 (0.75, 1.96) |
| >123.86 pg/mL | 48/132 | 1.42 (0.83, 2.05) | 1.42 (0.92, 2.18) | 47/132 | 1.63 (1.04, 2.55) | 1.64 (1.05, 2.56) |
| Per 1 pg/mL | 128/399 | 1.00 (0.99, 1.00) | 1.00 (0.99, 1.00) | 119/399 | 1.00 (0.99, 1.00) | 1.00 (0.99, 1.00) |
| SHBG | | | | | | |
| <34.30 nmol/L | 38/125 | 1.00 | 1.00 | 36/125 | 1.00 | 1.00 |
| 34.30-77.42 nmol/L | 44/137 | 0.94 (0.60, 1.46) | 0.94 (0.60, 1.47) | 43/137 | 1.03 (0.65, 1.61) | 1.02 (0.65, 1.61) |
| >77.42 nmol/L | 46/137 | 0.92 (0.59, 1.43) | 0.92 (0.59, 1.43) | 40/137 | 0.81 (0.51, 1.29) | 0.81 (0.51, 1.29) |
| Per 1 nmol/L | 128/399 | 1.00 (0.99, 1.00) | 1.00 (0.99, 1.00) | 119/399 | 1.00 (0.99, 1.00) | 0.99 (0.99, 1.00) |
| Total Testosterone | | | | | | |
| <1.54 ng/mL | 54/145 | 1.00 | 1.00 | 51/145 | 1.00 | 1.00 |
| 1.54-2.35 ng/mL | 37/130 | 0.94 (0.62, 1.44) | 0.94 (0.61, 1.44) | 33/130 | 0.87 (0.56, 1.36) | 0.87 (0.56, 1.36) |
| >2.35 ng/mL | 37/124 | 1.01 (0.67, 1.56) | 1.02 (0.67, 1.56) | 35/124 | 1.03 (0.66, 1.61) | 1.03 (0.66, 1.61) |
| Per 1 ng/mL | 128/399 | 0.98 (0.90, 1.07) | 0.99 (0.90, 1.07) | 119/399 | 0.99 (0.91, 1.08) | 0.99 (0.91, 1.08) |

SHBG = sex hormone binding globulin; *Adjusted for grade, stage, treatment, and age; **Adjusted for grade, stage, treatment, age, and parity

Supplementary Table 2. Disease free survival outcomes by sex hormone level at time of endometrial cancer diagnosis in the Alberta Endometrial Cancer Cohort among participants who completed labs pre-operatively compared with post-operatively.

| | Pre-Operative Blood Collection | | | Post-Operative Blood Collection | | |
|---------------------------|--------------------------------|--------------------------------------|-----------------------------------|---------------------------------|--------------------------------------|-----------------------------------|
| | Events/ Cases | Minimally Adjusted* HR (95%CI) | Fully Adjusted** HR (95%CI) | Events/ Cases | Minimally Adjusted* HR (95%CI) | Fully Adjusted** HR (95%CI) |
| Androstenedione | | | | | | |
| <1.16 ng/mL | 38/82 | 1.00 | 1.00 | 21/90 | 1.00 | 1.00 |
| 1.16-1.59 ng/mL | 22/70 | 0.84 (0.48, 1.45) | 0.84 (0.48, 1.45) | 22/99 | 1.42 (0.76, 2.68) | 1.41 (0.75, 2.65) |
| >1.59 ng/mL | 18/80 | 0.61 (0.34, 1.10) | 0.61 (0.34, 1.10) | 22/93 | 1.40 (0.76, 2.58) | 1.39 (0.75, 2.56) |
| Per 1 ng/mL | 78/232 | 0.85 (0.52, 1.40) | 0.85 (0.52, 1.41) | 65/282 | 1.18 (0.88, 1.59) | 1.22 (0.74, 2.03) |
| Estradiol | | | | | | |
| <3.37 pg/mL | 20/66 | 1.00 | 1.00 | 24/102 | 1.00 | 1.00 |
| 3.37-12.41 pg/mL | 31/81 | 1.66 (0.94, 2.96) | 1.71 (0.95, 3.06) | 17/92 | 0.78 (0.41, 1.48) | 0.77 (0.41, 1.47) |
| >12.41 pg/mL | 27/85 | 1.53 (0.83, 2.85) | 1.55 (0.83, 2.89) | 24/88 | 1.34 (0.74, 2.42) | 1.34 (0.74, 2.41) |
| Per 1 pg/mL | 78/232 | 1.00 (0.99, 1.01) | 1.01 (0.99, 1.02) | 65/282 | 0.99 (0.98, 1.01) | 0.99 (0.99, 1.01) |
| Estrone | | | | | | |
| <48.61 pg/mL | 22/73 | 1.00 | 1.00 | 19/101 | 1.00 | 1.00 |
| 48.61-123.86 pg/mL | 27/68 | 1.53 (0.85, 2.75) | 1.53 (0.85, 2.76) | 20/100 | 1.02 (0.53, 1.9) | 1.02 (0.53, 1.97) |
| >123.86 pg/mL | 29/91 | 1.20 (0.68, 2.12) | 1.06 (0.59, 1.90) | 26/81 | 1.92 (1.04, 3.57) | 1.91 (1.02, 3.55) |
| Per 1 pg/mL | 78/232 | 1.00 (0.99, 1.00) | 1.00 (0.99, 1.00) | 65/282 | 1.00 (0.99, 1.00) | 1.00 (0.99, 1.00) |
| SHBG | | | | | | |
| <34.30 nmol/L | 23/74 | 1.00 | 1.00 | 23/95 | 1.00 | 1.00 |
| 34.30-77.42 nmol/L | 27/73 | 0.85 (0.47, 1.53) | 0.85 (0.47, 1.53) | 21/99 | 1.11 (0.60, 2.08) | 1.12 (0.60, 2.08) |
| >77.42 nmol/L | 28/85 | 1.06 (0.59, 1.90) | 1.06 (0.59, 1.90) | 21/88 | 0.83 (0.45, 1.52) | 0.85 (0.60, 2.08) |
| Per 1 nmol/L | 78/232 | 0.99 (0.99, 1.00) | 0.99 (0.99, 1.00) | 65/282 | 0.99 (0.99, 1.00) | 0.99 (0.99, 1.00) |
| Total Testosterone | | | | | | |
| <1.54 ng/mL | 40/90 | 1.00 | 1.00 | 20/80 | 1.00 | 1.00 |
| 1.54-2.35 ng/mL | 21/71 | 0.92 (0.53, 1.60) | 0.93 (0.53, 1.61) | 19/102 | 1.07 (0.56, 2.03) | 1.07 (0.56, 2.03) |
| >2.35 ng/mL | 17/71 | 0.63 (0.35, 1.13) | 0.63 (0.35, 1.61) | 26/100 | 1.51 (0.83, 2.77) | 1.49 (0.81, 2.74) |
| Per 1 ng/mL | 78/232 | 0.98 (0.85, 1.12) | 0.99 (0.86, 1.14) | 65/282 | 0.96 (0.85, 1.09) | 0.96 (0.85, 1.09) |

SHBG = sex hormone binding globulin; *Adjusted for grade, stage, treatment, and age; **Adjusted for grade, stage, treatment, age, and parity

Supplementary Table 3. Overall survival outcomes by sex hormone level at time of endometrial cancer diagnosis in the Alberta Endometrial Cancer Cohort among participants who completed labs pre-operatively compared with post-operatively

| | Pre-Operative Blood Collection | | | Post-Operative Blood Collection | | |
|---------------------------|--------------------------------|--------------------------------------|-----------------------------------|---------------------------------|--------------------------------------|-----------------------------------|
| | Events/ Cases | Minimally Adjusted* HR (95%CI) | Fully Adjusted** HR (95%CI) | Events/ Cases | Minimally Adjusted* HR (95%CI) | Fully Adjusted** HR (95%CI) |
| Androstenedione | | | | | | |
| <1.16 ng/mL | 34/82 | 1.00 | 1.00 | 19/90 | 1.00 | 1.00 |
| 1.16-1.59 ng/mL | 18/70 | 0.72 (0.39, 1.32) | 0.72 (0.39, 1.32) | 20/99 | 1.44 (0.74, 2.81) | 1.42 (0.72, 2.79) |
| >1.59 ng/mL | 15/80 | 0.64 (0.34, 1.22) | 0.65 (0.34, 1.22) | 21/93 | 1.51 (0.80, 2.86) | 1.49 (0.79, 2.83) |
| Per 1 ng/mL | 67/232 | 0.87 (0.51, 1.48) | 0.87 (0.51, 1.48) | 60/282 | 1.14 (0.67, 1.94) | 1.13 (0.66, 21.92) |
| Estradiol | | | | | | |
| <3.37 pg/mL | 19/66 | 1.00 | 1.00 | 23/102 | 1.00 | 1.00 |
| 3.37-12.41 pg/mL | 25/81 | 1.23 (0.67, 2.26) | 1.24 (0.67, 2.29) | 15/92 | 0.70 (0.36, 1.36) | 0.69 (0.35, 1.35) |
| >12.41 pg/mL | 23/85 | 1.31 (0.68, 2.52) | 1.33 (0.69, 2.55) | 22/88 | 1.20 (0.66, 2.20) | 1.20 (0.66, 2.19) |
| Per 1 pg/mL | 67/232 | 1.00 (0.99, 1.01) | 1.01 (0.99, 1.02) | 60/282 | 0.99 (0.98, 1.01) | 0.99 (0.98, 1.01) |
| Estrone | | | | | | |
| <48.61 pg/mL | 18/73 | 1.00 | 1.00 | 18/101 | 1.00 | 1.00 |
| 48.61-123.86 pg/mL | 21/68 | 1.36 (0.70, 2.62) | 1.36 (0.71, 2.63) | 19/100 | 1.01 (0.51, 1.97) | 1.01 (0.52, 1.99) |
| >123.86 pg/mL | 28/91 | 1.46 (0.81, 2.65) | 1.65 (0.89, 3.06) | 23/81 | 1.68 (0.88, 3.19) | 1.65 (0.86, 3.16) |
| Per 1 pg/mL | 67/232 | 1.00 (0.99, 1.00) | 1.00 (0.99, 1.00) | 60/282 | 1.00 (0.99, 1.00) | 1.00 (0.99, 1.00) |
| SHBG | | | | | | |
| <34.30 nmol/L | 20/74 | 1.00 | 1.00 | 20/95 | 1.00 | 1.00 |
| 34.30-77.42 nmol/L | 27/73 | 1.01 (0.55, 1.84) | 1.00 (0.55, 1.83) | 20/99 | 1.20 (0.63, 2.31) | 1.21 (0.63, 2.32) |
| >77.42 nmol/L | 20/85 | 0.73 (0.38, 1.40) | 0.73 (0.38, 1.40) | 20/88 | 1.02 (0.54, 1.94) | 1.05 (0.55, 2.01) |
| Per 1 nmol/L | 67/232 | 0.99 (0.99, 1.00) | 0.99 (0.99, 1.00) | 60/282 | 1.00 (0.99, 1.00) | 1.00 (0.99, 1.00) |
| Total Testosterone | | | | | | |
| <1.54 ng/mL | 37/90 | 1.00 | 1.00 | 18/80 | 1.00 | 1.00 |
| 1.54-2.35 ng/mL | 16/71 | 0.69 (0.38, 1.26) | 0.69 (0.37, 1.27) | 18/102 | 1.29 (0.65, 2.53) | 1.29 (0.65, 2.55) |
| >2.35 ng/mL | 14/71 | 0.60 (0.31, 1.13) | 0.60 (0.37, 1.27) | 24/100 | 1.77 (0.93, 3.34) | 1.74 (0.92, 3.30) |
| Per 1 ng/mL | 67/232 | 1.03 (0.89, 1.18) | 1.03 (0.89, 1.18) | 60/282 | 0.96 (0.85, 1.09) | 0.96 (0.85, 1.09) |

SHBG = sex hormone binding globulin; *Adjusted for grade, stage, treatment, and age; **Adjusted for grade, stage, treatment, age, and parity

Supplementary Table 4. Duration of hormonal contraception use and menopausal hormone therapy use for Alberta Endometrial Cancer Cohort participants by vital status, 2002-2022

| Characteristic | All Participants Median (IQR)/N (%) N=540 | Alive Median (IQR)/N (%) N=406 | Disease-Free Survival Events^a Median (IQR)/N (%) N=152 | Overall Deaths Median (IQR)/N (%) N=134 |
|--------------------------------------------------------------------------------|--------------------------------------------------------|---------------------------------------------|--------------------------------------------------------------------------------|------------------------------------------------------|
| Duration of Hormonal Contraception Use | | | | |
| Never or <6 months | 212 (39) | 140 (35) | 81 (53) | 72 (54) |
| 6 to 35 months | 128 (24) | 105 (26) | 29 (19) | 23 (17) |
| 36 to 59 months | 58 (11) | 46 (11) | 13 (9) | 12 (9) |
| 60+ months | 142 (26) | 115 (28) | 29 (19) | 27 (20) |
| Duration of Estrogen + Progesterone Use in Post-Menopausal Participants | | | | |
| 6 to 59 months | 33 (8) | 27 (9) | 8 (6) | 6 (5) |
| 60+ months | 50 (12) | 41 (15) | 10 (7) | 9 (7) |

^a Participants who experienced endometrial cancer recurrence and/or death from any cause.

Supplementary Table 5. Endogenous hormone levels for Alberta Endometrial Cancer Cohort participants by vital status, 2002-2022

| Endogenous Hormone Levels | All Participants Median (IQR)/N (%) N=540 | Alive Median (IQR)/N (%) N=406 | Disease-Free Survival Events^a Median (IQR)/N (%) N=152 | Overall Deaths Median (IQR)/N (%) N=134 |
|----------------------------------|--------------------------------------------------------|---------------------------------------------|--------------------------------------------------------------------------------|------------------------------------------------------|
| Androstenedione (ng/mL) | 1.32 (1.07-1.67) | 1.35 (1.10-1.74) | 1.19 (0.97-1.62) | 1.19 (0.97-1.62) |
| Estradiol (pg/mL) | 5.86 (2.22-16.47) | 5.28 (2.20-15.5) | 7.14 (2.65-18.11) | 7.13 (2.31-17.60) |
| Estrone (pg/mL) | 80.77 (34.72-153.41) | 78.71 (32.70-143.43) | 96.98 (40.92-175.74) | 96.98 (41.68-175.74) |
| SHBG (nmol/L) | 51.30 (25.32-114.60) | 50.74 (25.51-113.41) | 53.78 (25.39-121.12) | 52.04 (25.00-118.64) |
| Total Testosterone (ng/mL) | 1.92 (1.34-2.61) | 1.97 (1.37-2.64) | 1.73 (1.18-2.52) | 1.72 (1.16-2.47) |

^a Participants who experienced endometrial cancer recurrence and/or death from any cause.