

Table 2.5. Case-control studies of estrogen-only menopausal therapy and endometrial cancer

| Reference, study location and period | Characteristics of cases | Characteristics of controls | Exposure assessment | Exposure categories | No. of cases | Relative risk (95% CI)* | Adjustment for potential confounders | Comments |
|--|---|---|---|-----------------------------|--------------|-------------------------|--|------------------|
| Shields <i>et al.</i> (1999) Washington State, USA, 1985-91 | 553 (women) from The Cancer Surveillance System, aged 45-74 years; response rate 72.2%; 100% histologically confirmed | 752 population-based controls selected by random-digit-dialing, matched by age groups and county; response rate 75.4% | Interviewer-administered standardized questionnaire | Month of Estrogen use | | | Age, county of residence and body mass index | |
| | | | | None or <6 | | | | |
| | | | | Hypertension | | | | |
| | | | | No | 185 | 1.0 | | |
| | | | | Yes | 152 | 1.6 (1.2-2.2) | | |
| | | | | 6-84 | | | | |
| | | | | Hypertension | No | 23 | | 2.9 (1.6-5.3) |
| | | | | | Yes | 19 | | 4.1 (1.9-8.8) |
| | | | | ≥85 | | | | |
| | | | | Hypertension | No | 112 | | 18.3 (10.9-30.8) |
| | | | | | Yes | 61 | | 21.5 (10.3-45.1) |
| | | | | None or <6 | | | | |
| | | | | Quartile of body mass Index | 1-3 | 152 | | 1.0 |
| | | | | | 4 | 183 | | 2.9 (2.2-3.9) |
| | | | | 6-84 | | | | |
| | | | | Quartile of body mass Index | 1-3 | 25 | | 2.4 (1.4-4.1) |
| | 4 | 18 | 12.9 (4.3-39.0) | | | | | |
| ≥85 | | | | | | | | |
| Quartile of body mass Index | 1-3 | 27 | 17.1 (10.7-27.2) | | | | | |
| | 4 | 3 | 34.3 (10.3-114.1) | | | | | |
| None or <6 | | | | | | | | |
| Parity | 0 or 1 | 89 | 1.0 | | | | | |
| | 2+ | 248 | 0.7 (0.5-1.0) | | | | | |
| 6-84 | | | | | | | | |
| Parity | 0 or 1 | 9 | 1.4 (0.6-3.6) | | | | | |
| | 2+ | 34 | 2.6 (1.4-4.7) | | | | | |
| ≥85 | | | | | | | | |
| Parity | 0 or 1 | 53 | 15.4 (6.6-36.3) | | | | | |
| | 2+ | 120 | 11.5 (6.7-20.0) | | | | | |

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| Shields <i>et al.</i> (1999) (contd) | | | | Month of Estrogen use | | | | | |
| | | | | None or <6 | | | | | |
| | | | | Oral Contraceptive Use | 0-2 years | 283 | 1.0 | | |
| | | | | | >2 years | 54 | 0.7 (0.5-1.1) | | |
| | | | | 6-84 | | | | | |
| | | | | Oral Contraceptive Use | 0-2 years | 29 | 2.8 (1.5-5.1) | | |
| | | | | | >2 years | 14 | 2.6 (1.2-5.6) | | |
| | | | | ≥85 | | | | | |
| | | | | Oral Contraceptive Use | 0-2 years | 148 | 16.8 (10.4-27.3) | | |
| | | | | | >2 years | 25 | 12.1 (4.8-30.3) | | |
| | | | | None or <6 | | | | | |
| | | | | Smoking | Never | 196 | 1.0 | | |
| | | | | | Former/recent, light | 90 | 0.8 (0.6-1.2) | | |
| | | | | | Recent, heavy | 51 | 0.6 (0.4-0.8) | | |
| | | | | 6-84 | | | | | |
| | | | Smoking | Never | 26 | 3.1 (1.6-6.2) | | | |
| | | | | Former/recent, light | 9 | 1.3 (0.5-3.3) | | | |
| | | | | Recent, heavy | 8 | 2.9 (1.1-7.9) | | | |
| | | | ≥85 | | | | | | |
| | | | Smoking | Never | 84 | 16.2 (8.4-31.2) | | | |
| | | | | Former/recent, light | 47 | 12.1 (5.8-25.1) | | | |
| | | | | Recent, heavy | 42 | 12.7 (5.7-28.2) | | | |

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|---|---|--|---|----------------------------------|--------------|-------------------------|---|----------|
| Weiderpass <i>et al.</i> (1999) Sweden, 1994–95 | 789 (women) from six regional cancer registries, aged 50–74 years; response rate 75%; 100% histologically confirmed | 3128 population-based controls selected by random-digit-dialling, matched by age and sex; response rate 80% | Interviewer-administered standardized questionnaire | Endometrial cancer | | | Age, parity, age at menopause, body mass index, use of oral contraceptives, age at last birth, smoking, duration of use of estrogens without progestogens, estrogens with progestogens, progestogens without estrogens, and vaginal low-potency estrogen formulations | |
| | | | | Never use of oral oestriol | 534 | 1.0 | | |
| | | | | Ever use of oral oestriol | 137 | 2.0 (1.6–2.6) | | |
| | | | | Duration | | | | |
| | | | | <5 years | 86 | 1.7 (1.3–2.3) | | |
| | | | | ≥5 years | 51 | 3.0 (2.0–4.4) | | |
| | | | | Recency of use | | | | |
| | | | | <1 years | 116 | 2.4 (1.8–3.0) | | |
| | | | | ≥1 years | 21 | 1.2 (0.7–2.0) | | |
| | | | | Atypical endometrial hyperplasia | | | | |
| | | | | Never use of oral oestriol | 497 | 1.0 | | |
| | | | | Ever use of oral oestriol | 24 | 3.7 (2.1–6.5) | | |
| | | | | Duration | | | | |
| | | | | <5 years | 10 | 2.2 (1.0–4.6) | | |
| ≥5 years | 14 | 8.3 (4.0–17.4) | | | | | | |
| Recency of use | | | | | | | | |
| <1 years | 20 | 4.7 (2.6–8.5) | | | | | | |
| ≥1 years | 4 | 1.3 (0.3–4.9) | | | | | | |
| Beard <i>et al.</i> (2000) Minnesota, USA 1975–91 | 117 incident cases of endometrial cancer among women in Olmsted County, Minnesota; diagnosed between 1975–1991; mean age 65.4 years | 117 population-based controls within the same county, matched by age, gender and duration of medical records in the community; mean age 65.3 years | Medical records | Any estrogen use | [59] | 1.41 (0.76–2.63) | | |
| | | | | > 6 mo estrogen use | [31] | 2.18 (1.07–4.45) | | |
| | | | | > 6 mo steroidal estrogen | [20] | 2.38 (1.04–5.43) | | |
| | | | | > 6 mo conjugated estrogen | [20] | 2.71 (1.14–6.46) | | |
| | | | | | | | | |

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| Strom <i>et al</i> (2006), Philadelphia, USA, 1999–2002 | 511 cases of endometrial cancer, age 50–79 in Philadelphia area between 1999–2002 | 1412 controls selected by random digit dialing from the same area as cases, matched on age (5 year groups) and race | Telephone interviews | Never used any hormone therapy | 295 | 1.00 (reference) | BMI, education, number of full-term pregnancies, years of menses, type of menopause, smoking status, oral contraceptive use | |
| | | | | Ever used only estrogens | 35 | 1.40 (0.86–2.26) | | |
| | | | | Used only estrogens for ≥ 3 years | 13 | 3.40 (1.40–8.30) | | |
| Weiss <i>et al</i> (2006), Washington State, USA, 1985–1999 | 1304 cases of endometrial cancer, age 45–74, identified through cancer surveillance system/SEER program, diagnosed between 1985–1999 | 1779 controls selected by random digit dialing or Health Care Financing Administration files; age 45–74; frequency matched on 5 year age group and county of residence | In-person interviews | Low tumour aggressiveness | | | | |
| | | | | Non-user | 196 | 1.0 (reference) | | |
| | | | | 0.5–3.9 years use | 41 | 2.6 (1.7–3.9) | | |
| | | | | 4.0–7.9 years use | 27 | 4.9 (2.8–8.5) | | |
| | | | | ≥ 8 years use | 100 | 18.6 (12.2–28.6) | | |
| | | | | Moderate tumour aggressiveness | | | | |
| | | | | Non-user | 323 | 1.0 (reference) | | |
| | | | | 0.5–3.9 years use | 46 | 1.8 (1.2–2.7) | | |
| | | | | 4.0–7.9 years use | 22 | 2.5 (1.4–4.4) | | |
| | | | | ≥ 8 years use | 100 | 9.8 (6.6–14.7) | | |
| | | | | High tumour aggressiveness | | | | |
| | | | | Non-user | 65 | 1.0 (reference) | | |
| 0.5–3.9 years use | 13 | 2.4 (1.2–4.7) | | | | | | |
| 4.0–7.9 years use | 4 | 2.2 (0.7–6.5) | | | | | | |
| ≥ 8 years use | 15 | 7.1 (3.6–14.2) | | | | | | |