Studies on Breast Cancer with Hormone Therapy in Transfeminine People

Studies

# of trans women	# with breast cancer	Breast cancer risk	Duration of HRT	Age	HRT regimen	Country (clinic)	Study
303	0 (0%)	–	Median 4.4 years (range 0.5–13 years+)	Age at start of HRT: Median 32 years (range 16–67 years)	E: EE 100 µg/day (most; n = 258), DES 5–15 mg/day (pre-1980; "a few patients"), EU 200–800 mg/month (n = 45) AA: CPA 100 mg/day	Netherlands (VUMC)	Asscheman, Gooren, & Eklund (1989)
>500	0 (0%)	–	Median 6.5 years (range 0–20 years)	?	E: EE 100 µg/day (100 µg/day transdermal E2 patches instead in >40 years of age) AA: CPA 100 mg/day	Netherlands (VUMC)	Asscheman & Gooren (1993)
40 (all post-SRS)	0 (0%)	–	3 months–12 years	?	"Usually, in the beginning, I give weekly injections of 50 to 100 mg Delestrogen [estradiol valerate] (Squibb), a slowly absorbing and highly potent preparation. Later on, injections every two weeks or even less often, proved sufficient, provided an oral estrogen was taken at the same time. I found Schering's Estinyl [ethinylestradiol] (0.5 mg) the most useful tablet which, however, can be replaced with Stilbestrol [diethylstilbestrol] (25 to 50 mg), or 10 to 20 mg of Premarin [conjugated estrogens] (Ayerst), according to individual tolerance and response."	United States (NY)	Benjamin (1964); Orentreich & Durr (1974); Gooren et al. (2013)
141	0 (0%)	–	"some [treated] over several years"	?	"treated with medium to fairly large doses of estrogen"	United States (NY)	Benjamin (1966)
816	0 (0%)	–	Total person time: 7,734 PY	At time of study: mean 41 years (range 18–86 years)	E: EE 100 µg/day (transdermal E2 instead in >40 years of age)	Netherlands (VUMC)	van Kesteren, Asscheman,

			Mean person time: 9.5 years		AA: 100 mg/day CPA		Megens, & Gooren (1997)
60	0 (0%)	–	2 years	Age (at time of presentation?): 38.37 ± 11.36 years	E: EV 6 mg/day oral AA: Goserelin injections 3.8 mg/4 weeks	Germany (UKE)	Dittrich et al. (2005)
~2,200	1 (0.05%)	–	1–25 years	?	See other instances in this table of the VUMC clinic.	Netherlands (VUMC)	Mueller & Gooren (2008)
966	0 (0%)	–	Total person time: 18,678 PY Mean person time: 19.3 ± 7.7 years (median 18.6 years, range 0.7–44.5 years) Subgroups by time: <10 years: 72 (7.4%) 10–20 years: 481 (49.8%) 20–30 years: 321 (33.3%) >30 years: 92 (9.5%)	At start of HRT: mean 31.4 ± 11.4 years (range 16–76 years)	E: EE 100 µg/day (mostly pre-1989), transdermal E2 (mostly post-1989), small numbers of others (oral E (e.g., CEEs, EV 2–4 mg/day), E2 ester injections) AA: CPA 100 mg/day (usually), SPL 100–200 mg/day (<5%)	Netherlands (VUMC)	Asscheman, Giltay, Megens, de Ronde, van Trotsenburg, & Gooren (2011)
50 (all post-SRS)	0 (0%)	–	Mean person time: 11.4 years	At time of study: mean 43.0 ± 10.4 years At time of SRS: mean 36.7 ± 9.8 years	E: “different formulations” AA: CPA 50–100 mg/day (for maximum of 1 year, discontinued upon SRS)	Belgium (UZG)	Wierckx, Mueller, Weyers, van Caenegem, Roef, Heylens, & T'Sjoen (2012)
2,307	2 (0.09%)	Absolute risk: 4.1 per 100,000 PY (95% CI 0.8–13.0)	Total person time: 49,370–52,370 PY Mean person time: 21.4 ± 8.7 years (median 17.6, range 6.0–43.5 years)	At start of HRT: mean 29.3 ± 12.7 years (range 16–83 years)	Little information provided (“anti-androgens and estrogens or only estrogens”)	Netherlands (VUMC)	Gooren, van Trotsenburg, Giltay, & van Diest (2013)
3,556 (also included people with diagnosis of “transvestic fetishism”)	3 (0.08%)	SIR relative to cis men: 33.33 (95% CI 21.89–45.17) SIR relative to cis women: 0.70 (95% CI 0.03–5.57) Expected # cases (SEER data) of 0.09	Total person time (“VHA care”): 34,612 PY Mean person time (“VHA care”): 9.73 ± 4.62 years Subgroups by time (“VHA care”): <3 years: 601 (43.4%) 3–12 years: 613 (44.2%)	At time of study: Mean 55.80 ± 13.73 years At start of HRT (“VHA care” only; n = 1386): mean 48.69 ± 12.31 years At breast cancer diagnosis: mean 62 years (54–71 years)	The study was *irrespective of HRT* – some were on HRT, others were not; exact numbers unknown All people with a transgender or “transgender-related” diagnosis in the VHA system were included, notably including men with a “transvestic fetishism” diagnosis (most of whom presumably were	United States (VHA)	Brown & Jones (2015); Brown (2015)

		for cis men and 4.3 for cis women	>12 years: 172 (12.41%)		not on HRT) Since U.S., for those on HRT, probably E + SPL typically and no CPA or other progestogen Very confusing and unclear paper		
2,791	Unknown, but <5 (<0.18%); and: “One the largest studies examining cancer risk in transgender women in the United States used data from one large health care system (Kaiser Permanente: Georgia and Northern and Southern California (96). Using an electronic database method to identify transgender women in this cohort, they identified 2791 transgender women subjects. Based on ICD-9 codes, the investigators found no increased risk of breast cancer or any cancer when comparing transgender women to matched cisgender women. However, there was an increased risk of breast cancer and endocrine gland cancers in transgender women compared with matched cisgender men." (T'Sjoen et al., 2019)		Duration of follow up: mean 4 years	At index date: mean 39 years	No informed provided Since U.S., probably E + SPL typically and no CPA	United States (Kaiser; CA and GA)	Silverberg et al. (2017); T'Sjoen et al. (2019)
2,260	15 (0.66%)	SIR relative to cis men: 46.7 (95% CI 27.2–75.4) SIR relative to cis women: 0.3 (95% CI 0.2–0.4)	Total person time: 33,991 PY Median person time: 13 years (IQR 5–23 years) Median person time in those with breast cancer: 18 years (range 7–37 years)	At time of study: 51 years (IQR 38–60 years) At start of HRT: median 31 years (IQR 23–41 years) At breast cancer diagnosis: median 52 years	E: EE 25–100 µg/day, CEEs 0.625–1.25 mg/day, E2 patches 50–150 µg/day, E2 implants 20 mg/3–6 months, E2 ester injections 10–100 mg/2–4 weeks, EV 2–6 mg/day, E2 gel 0.75–3 mg/day AA: CPA 10–100 mg/day, SPL 100–200 mg/day (discontinued after orchiectomy)	Netherlands (nationwide by VUMC, using PALGA to retrieve breast cancer diagnoses)	de Blok, Wiepjes, Nota, van Engelen, Adank, Dreijerink, Barbé, Konings, & den Heijer (2019); de Blok et al., (2018)

Note: Normal *lifetime* breast cancer risks: 1 in 8 cisgender women (12.5%; mean age 60 years) and 1 in 1,000 cisgender men (0.1%; mean age 68 years).

Acronyms

SRS = Sex reassignment surgery; SIR = Standardized incidence ratio; PY = Person-years; CI = Confidence interval; IQR = Interquartile range; HRT = Hormone replacement therapy; E = Estrogen; E2 = Estradiol; EV = Estradiol valerate; EU = Estradiol undecylate; EE = Ethinylestradiol; CEEs = Conjugated estrogens; DES = Diethylstilbestrol; AA = Antiandrogen; CPA = Cyproterone acetate; SPL = Spironolactone; VUMC = Vrije Universiteit University Medical Center Amsterdam (treats 95% of transgender people in the Netherlands); PALGA = Nationwide Network and Registry of Histopathology and Cytopathology in the Netherlands; UKE = Universitätsklinikum Erlangen (University Hospital Erlangen); VHA = Veteran's Health Administration; UZG = University Hospital Ghent; SEER = Surveillance, Epidemiology, and End Results Program (of the National Cancer Institute)

Relevant Reviews

- Maglione, K. D., Margolies, L., Jaffer, S., Szabo, J., Schmidt, H., Weltz, C., & Sonnenblick, E. B. (2014). Breast cancer in male-to-female transsexuals: use of breast imaging for detection. *American Journal of Roentgenology*, *203*(6), W735–W740. [DOI:10.2214/AJR.14.12723]
- Braun, H., Nash, R., Tangpricha, V., Brockman, J., Ward, K., & Goodman, M. (2017). Cancer in transgender people: evidence and methodological considerations. *Epidemiologic Reviews*, *39*(1), 93–107. [DOI:10.1093/epirev/mxw003]
- Deutsch, M. B., Radix, A., & Wesp, L. (2017). Breast cancer screening, management, and a review of case study literature in transgender populations. *Seminars in Reproductive Medicine*, *35*(5), 34–441. [DOI:10.1055/s-0037-1606103]
- Hartley, R. L., Stone, J. P., & Temple-Oberle, C. (2018). Breast cancer in transgender patients: a systematic review. Part 1: male to female. *European Journal of Surgical Oncology*, *44*(10), 1455–1462. [DOI:10.1016/j.ejso.2018.06.035]
- Joint, R., Chen, Z. E., & Cameron, S. (2018). Breast and reproductive cancers in the transgender population: a systematic review. *BJOG: An International Journal of Obstetrics & Gynaecology*, *125*(12), 1505–1512. [DOI:10.1111/1471-0528.15258]
- McFarlane, T., Zajac, J. D., & Cheung, A. S. (2018). Gender-affirming hormone therapy and the risk of sex hormone-dependent tumours in transgender individuals—A systematic review. *Clinical Endocrinology*, *89*(6), 700–711. [DOI:10.1111/cen.13835]
- de Blok, C. J., Dreijerink, K. M., & den Heijer, M. (2019). Cancer risk in transgender people. *Endocrinology and Metabolism Clinics*, *48*(2), 441–452. [DOI:10.1016/j.ecl.2019.02.005]
- Dente, E., Farneth, R., Purks, J., & Torelli, S. (2019). Evaluating Risks, Reported Cases and Screening Recommendations for Breast Cancer in Transgender Patients. *Georgetown Medical Review*, *3*(1), 7774. [DOI:10.52504/001c.7774]
- Eismann, J., Heng, Y. J., Fleischmann-Rose, K., Tobias, A. M., Phillips, J., Wulf, G. M., & Kansal, K. J. (2019). Interdisciplinary management of transgender individuals at risk for breast cancer: case reports and review of the literature. *Clinical Breast Cancer*, *19*(1), e12–e19. [DOI:10.1016/j.clbc.2018.11.007]
- Meggetto, O., Peirson, L., Yakubu, M., Farid-Kapadia, M., Costa-Fagbemi, M., Baidoobonso, S., Moffatt, J., Chun, L., Chiarelli, A. M., & Muradali, D. (2019). Breast cancer risk and breast screening for trans people: an integration of 3 systematic reviews. *CMAJ Open*, *7*(3), E598. [DOI:10.9778/cmajo.20180028]

Additional Publications

Didn’t Distinguish Between AMABs and AFABs

- Nash, R., Ward, K. C., Jemal, A., Sandberg, D. E., Tangpricha, V., & Goodman, M. (2018). Frequency and distribution of primary site among gender minority cancer patients: An analysis of US national surveillance data. *Cancer Epidemiology*, *54*, 1–6. [DOI:10.1016/j.canep.2018.02.008]

Cisgender Men

- Sasco, A. J., Lowenfels, A. B., & Jong, P. P. D. (1993). Review article: Epidemiology of male breast cancer. A meta-analysis of published case-control studies and discussion of selected aetiological factors. *International Journal of Cancer*, *53*(4), 538–549. [DOI:10.1002/ijc.2910530403]
- Hultborn, R., Hanson, C., Köpf, I., Verbiene, I., Warnhammar, E., & Weimarck, A. (1997). Prevalence of Klinefelter's syndrome in male breast cancer patients. *Anticancer Research*, *17*(6D), 4293–4297. [PubMed]
- Thellenberg, C., Malmer, B., Tavelin, B., & Grönberg, H. (2003). Second primary cancers in men with prostate cancer: an increased risk of male breast cancer. *The Journal of Urology*, *169*(4), 1345–1348. [DOI:10.1097/01.ju.0000056706.88960.7c]
- Karlsson, C. T., Malmer, B., Wiklund, F., & Grönberg, H. (2006). Breast cancer as a second primary in patients with prostate cancer—estrogen treatment or association with family history of cancer? *The Journal of Urology*, *176*(2), 538–543. [DOI:10.1016/j.juro.2006.03.036]
- Brinton, L. A., Carreon, J. D., Gierach, G. L., McGlynn, K. A., & Gridley, G. (2010). Etiologic factors for male breast cancer in the US Veterans Affairs medical care system database. *Breast Cancer Research and Treatment*, *119*(1), 185–192. [DOI:10.1007/s10549-009-0379-0]
- Brinton, L. A. (2011). Breast cancer risk among patients with Klinefelter syndrome. *Acta Paediatrica*, *100*(6), 814–818. [DOI:10.1111/j.1651-2227.2010.02131.x]