Hormone Replacement Therapy Drug Costs Study – 2022

As Required by Senate Bill 711 (2021)

About DCBS:
The Department of Consumer and Business Services is Oregon's largest business regulatory and consumer protection agency. For more information, visit https://www.oregon.gov/dcbs/.

About Oregon DFR:
The Division of Financial Regulation protects consumers and regulates insurance, depository institutions, trust companies, securities, and consumer financial products and services and is part of the Department of Consumer and Business Services. Visit: dfr.oregon.gov.

Additional report information:
This report is based on information and data collected by DFR from the Oregon All Payer All Claims Reporting Program (APAC).

Throughout this report, we also reference therapeutic class information extracted from the Medi-Span drug database.

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1. Overview

Senate Bill 711 (2021) directs the Department of Consumer and Business Services (DCBS) to conduct a study of disparities in the cost of hormone replacement drugs between those for men and those for women.

The Oregon Drug Price Transparency Program within DCBS carried out this study by analyzing the expected patient costs (co-pay, co-insurance, and deductibles) recorded in retail pharmacy insurance claims for hormone replacement drugs from the Oregon All Payer All Claims Reporting Program (APAC) from the years 2018, 2019, and 2020.

1.1 Findings and recommendations

Claimants who were exclusively identified as female in the pharmacy claims data (F claimants) paid an average of $5 more per claim than claimants who were exclusively identified as male (M claimants). On average, F claimants paid $32.45 per claim and M claimants paid $27.76 per claim. Further, F claimants were responsible for paying 31 percent of their claim costs, compared to 20 percent for M claimants, with the rest paid by insurance.

Our analysis suggests that most of the $5 difference in the average costs per claim between F claimants and M claimants can be explained by the top 5 percent highest cost claims. These claims cost $134 or more to the claimant. Many of these high-cost claims were for estradiol, conjugated estrogens, and testosterone. F claimants were disproportionately

represented in these highest-cost claims. Further, the difference in cost sharing between F claimants and M claimants (31 percent vs. 20 percent) was primarily due to the fact that claimants paid a higher share of the claim costs for commonly prescribed estrogens and progestins than for commonly prescribed testosterone.

Though their average costs per claim and the average cost sharing percentages were lower, M claimants made more claims on average, leading to a slightly higher average total cost per claimant over the three-year period from 2018 to 2020. On average, an M claimant had 9.5 claims and paid a total of $262.43, while an F claimant had 7.8 claims and paid a total of $252.94.

The data collected for this study is insufficient to directly tie this apparent disparity solely to a patient's gender. These differences could be due to other factors such as the medical condition being treated, the relative list price of the drug, the delivery mechanism of the drug (such as intravenous versus oral), or the benefit design of the patient's insurance (for example, formulary placement). Due to this, it is difficult to make specific legislative recommendations to address disparities based solely on the conclusions of this study. Additional research and analysis would be needed to be able to identify the cost drivers that create this apparent disparity, and to make legislative recommendations to address any disparity in the cost of prescription drugs due to gender.

We recommend additional research into the following questions:

- What is driving the disparities in cost sharing? Why do claimants pay a higher share of the cost of claims for estrogens and progestins than for testosterone?

- Why do M claimants make more claims than F claimants? Are there barriers preventing F claimants from getting the drugs they need?

- Why are drugs used by F claimants, such as estradiol and conjugated estrogens, so often the highest-cost claims?

- Why do some claimants have multiple gender flags in their APAC claims data? How should those gender flags be interpreted?

We would also recommend a broader survey of prescription drug claims spanning all therapeutic classes, without limiting our query to claims for hormone replacement drugs. This could help identify whether the apparent disparity is present for nonhormone replacement drugs.

1.2 APAC claims

This study is based on expected patient costs (copay, coinsurance, and deductibles) recorded in retail pharmacy insurance claims for hormone replacement drugs from the Oregon All Payer All Claims Reporting Program (APAC). APAC is part of the Oregon Health Authority.

APAC claims data does not include the actual dollar amount that a patient ended up paying for a claim. Instead, APAC claims record the expected payments from patients. "Costs" in this study refers to expected patient costs.

For additional information on APAC, we recommend reading the program's published documentation, available on the APAC program webpage. We especially recommend the section "What APAC Is and What APAC Is Not" in the APAC Data User Guide.

The Drug Price Transparency Program (DPT) obtained the claims data for the study through APAC's official data request process.

First, DPT compiled a list of National Drug Codes (NDCs) for hormone replacement drugs with the help of Andrew Gibler, PharmD at the Oregon Health Authority. See Section 5 of this report for the details of this work.

DPT provided APAC with this list of hormone replacement NDCs and requested all matching paid retail pharmacy claims from the years 2018, 2019, and 2020.[1] We did ask that Medicaid claims and claims by out-of-state people be excluded, but otherwise set no restrictions on the claims.

1.3 Analysis and presentation of data

This study is an exploratory analysis of the APAC claims data. Its primary objective is to identify and measure possible differences between gender groups in average patient costs for hormone replacement drugs.

This report includes many different statistical summaries of the claims data, with written analyses to highlight and interpret their most important aspects. Additionally, for analysts who wish to make comparisons beyond the ones that are highlighted, standard errors and confidence intervals are included for many of the averages in the report.[2] These are statistical measures of precision which can help analysts understand the reliability of an estimate. Typically, a standard error will be large or a confidence interval will be wide when its corresponding average is based on a small number of claims.

To protect the privacy of the claimants in the data, statistics such as counts, percentages, and averages are not shown for any group with fewer than 10 claimants. When a count or percentage is hidden for this reason, the statistic for the next-smallest claimant group is also hidden.[3]

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[1] Claims from the year 2020 are the most recent claims available for analysis.

[2] Confidence intervals and margins of error in this report have not been adjusted for multiple comparisons.

[3] Table 27 is the only exception to these data suppression rules.

2. Claims breakdown

APAC contains records for 2,796,687 insurance claims for retail pharmacy drugs for Hormone Replacement Therapy (HRT) drugs in 2018, 2019, and 2020. We analyzed 2,612,444 of those claims in this study, excluding the rest due to data quality issues.

In this section we will describe these 2.6 million claims in the study.

2.1 Classes of HRT drugs

The HRT drugs included in the study are split into five main classes: androgens/anabolic drugs, contraceptives, estrogens, progestins, and vaginal and related products.[4]

Contraceptives: Contraceptives are oral, injectable, and patch and ring devices that combine an estrogen and a progestin or a contraceptive can be a progestin alone. Combination hormonal contraceptives inhibit ovulation by changing the cervical mucus, rendering it unfavorable for sperm penetration, or changing the endometrium, producing an unfavorable environment for implantation of the ovum.

Estrogens: Estrogens (e.g., estradiol products) are responsible for the development and maintenance of the female reproductive system and secondary sexual characteristics. Estradiol is the principal human estrogen and is the primary estrogen secreted prior to menopause. Estrogen replacement helps manage vasomotor symptoms (hot flashes), insomnia (sleep difficulties), vaginal atrophy (vaginal wall thinning and dryness), and sexual dysfunction (decreased libido, painful intercourse) associated with menopause. Estrogens are also used as cross-sex hormone therapy for transgender females with persistent gender dysphoria/gender incongruence.

Progestins: Progesterone primarily acts on the uterus and is balanced with estrogen to prepare the uterus for pregnancy, either inducing menstruation if there is no pregnancy or preventing menstruation and contraction of the uterus if pregnancy occurs. Progesterone and progestins (synthetic progesterone) medicines are used to manage several conditions. Some progestins are used in combination or alone as a contraceptive in females. They are also used for endometrial hyperplasia (abnormal thickening of the lining of the uterus), which raises the risk of developing endometrial cancer (a type of uterine cancer). Some progesterone and progestin products are also used to manage uterine bleeding unrelated to the menstrual cycle, to manage amenorrhea (absence of periods in menstruating women), to treat female infertility, and to prevent the preterm labor and birth of a newborn. These medicines can also be used to manage advanced endometrial cancer and advance breast cancer, and to manage cachexia (body wasting) associated with some cancers and AIDS.

Androgens: Androgens (e.g., testosterone products) are used to treat hypogonadism (lack of testosterone production) in males, either due to congenital causes or acquired causes (e.g., radiation, medications, autoimmune, obesity, age). Androgens are also used as cross-sex hormone therapy for transgender males with persistent gender dysphoria/gender incongruence.

Most of the claims were for contraceptive drugs. The most common contraceptives were oral contraceptives containing combinations of hormones such as ethinyl estradiol, levonorgestrel, and norethindrone.

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[4] These drug classes come from the Medi-Span Therapeutic Classification System hierarchy.

Drug Class	Claims		
Contraceptives	1,321,992	51%	
Estrogens	568,862	22%	
Progestins	272,234	10%	
Vaginal and related products	227,427	9%	
Androgens/anabolic	221,929	8%	

Table 1: Numbers of HRT drug claims in the study in each drug class.

Vaginal and related products	Claims
Vaginal estrogens	225,791
Vaginal progestins	1,295
Prasterone	341

Table 2: Numbers of HRT drug claims for drugs in the "Vaginal and Related Products" drug class.

Nine percent of the claims fell into the class "Vaginal and Related Products." This class included vaginal estrogens, vaginal progestins, and prasterone.

In the data, claims for contraceptives tended to have very different patient costs compared to the other drug classes. About 95 percent of claims for contraceptives cost $0 for the patient, while the proportions of $0 claims in the other drug classes ranged from 9 percent to 12 percent. This difference is likely attributable to the federal Affordable Care Act and Oregon's Reproductive Health Equity Act (ORS 743A.067), which require coverage of contraceptive drugs without cost-sharing for most insured Oregonians. Further, claims for contraceptives were far more common for some gender groups than others. For these reasons, claims for contraceptives have a large effect on analyses of overall cost differences between gender groups.

In this study, claims for contraceptives will not be included in the main analyses. All claim counts, all claimant counts, and all analyses of claim costs from this point on will not include claims for contraceptives. Instead we will analyze the claims for contraceptives and their effects on costs separately in Section 4 (Costs of Contraceptives).

2.2 Claimants and genders

Claims from a total of 159,932 different claimants are included in the study. This is the number of unique person IDs in the data, assigned by the organization that maintains the APAC database. As discussed in the previous section, this count does not include claimants who only had claims for contraceptives.

Each claim includes a variable called "member gender."[5] This information is taken from the contract that the individual has with their insurer. It is not entered by a physician or a pharmacist involved with the specific prescription. The variable allows "F" for female, "M" for male, or "U" when the information is missing or unknown.

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[5] "Member gender" refers to data element ME013 in the APAC data.

During our initial analysis of the data, we found that several claimants had multiple different values in the gender fields of their claims. This could be because they had contracts with multiple insurers or because their contracts for different years contained different information. See Section 5 (Appendix: Discussion of Gender Groups) for additional discussion of these findings.

In our analyses, we will split the claims into three groups:

- Claims submitted by claimants with only "F" claims
- Claims submitted by claimants with only "M" claims
- Claims submitted by claimants with only "U" claims or with multiple recorded gender values – we will refer to these as "UV" for "Unknown or Various."

Across all three years of data, an F claimant had 7.8 claims, on average, compared to 9.5 claims for an M claimant and 15.8 claims for a UV claimant.

Claims for a single claimant

	Median	Mean	Std Dev	Maximum	Claimants
F claimant	4	7.8	10.3	158	135,611
M claimant	7	9.5	9.5	142	23,758
UV claimant	12	15.8	14.9	132	563

Table 3: Statistics for the total number of claims for a single claimant over the three years 2018, 2019, and 2020.

In the tables below, we break down the numbers of claimants and claims in each drug class by the recorded genders of the claimants.

	F claimants		M claimantss		UV claimants	
Drug Class	Claimants	Claims	Claimants	Claims	Claimants	Claims
Androgens/ anabolic	1,823	12,365	21,993	206,245	269	3,319
Estrogens	56,717	550,187	1,626	14,770	265	3,905
Progestins	42,085	267,375	496	3,310	142	1,549
Vaginal and related products	61,542	227,028	129	304	35	95

Table 4: Numbers of claimants and claims in each drug class by gender group of claimant.

Vaginal and related products	F claimants		M claimants		UV claimants	
	Claimants	Claims	Claimants	Claims	Claimants	Claims
Prasterone	109	341	0	0	0	0
Vaginal estrogens	61,053	225,392	129	304	35	95
Vaginal progestins	429	1,295	0	0	0	0

Table 5: Numbers of claimants and claims in the "Vaginal and Related Products" drug class by gender group of claimant.

The vast majority of the claims from M claimants were for androgens and anabolic steroids.

Prasterone and vaginal estrogens are medications applied directly into the vagina via an applicator to help alleviate vaginal atrophy associated with menopause (vaginal dryness, discharge, itching, painful sexual intercourse) and sexual dysfunction (decreased libido). In contrast, vaginal progestins are used to help treat female infertility, to prevent premature birth of a newborn, and is used for secondary amenorrhea (absence of periods in menstruating women).

Note that several M claimants and UV claimants had claims for drugs in the "Vaginal and Related Products" drug class. All of those claims were for vaginal estrogens. It is possible that those claims may be from transgender males receiving treatment for post-transition conditions.

APAC's member gender field generally reflects a member's sex rather than their gender, but the presence of claims for vaginal estrogens by M claimants shows that is not always the case.

2.3 Types of insurance coverage and payers

About two-thirds of the claims in the study were commercial health insurance claims. The other third were Medicare claims.

F claimants and M claimants had similar proportions of commercial claims vs. Medicare claims, while UV claimants tended to have more commercial claims.

	F claimants		M claimants		UV claimants	
Payer line of business	Claims	Percent	Claims	Percent	Claims	Percent
Commercial	673,417	64%	141,334	63%	7,579	85%
Medicare	383,519	36%	83,295	37%	1,289	15%
(Unknown)	19	< 1%	0	0%	0	0%

Table 6: Number of claims for each payer line of business by gender group of claimant.

The most common type of insurance coverage for F and M claimants was Medicare Part D only coverage, followed by pharmacy benefits only coverage. For UV claimants, the most common type was commercial HMO coverage, followed by commercial PPO coverage.

	F claimants		M claimants		UV claimants	
Type of insurance coverage	Claims	Percent	Claims	Percent	Claims	Percent
Medicare Part D only	226,105	22%	51,884	22%	1,084	12%
Pharmacy benefits only	195,699	19%	45,128	20%	1,570	18%
Commercial PPO	158,111	15%	31,960	14%	1,696	19%
Commercial HMO	110,420	11%	17,284	8%	2,227	25%
Medicare Advantage HMO	85,214	8%	14,312	6%	63	1%
Self-insured POS	68,113	6%	15,377	7%	721	8%
Commercial EPO	64,091	6%	11,070	5%	481	5%
Commercial POS	57,297	5%	15,170	7%	703	8%
Medicare Advantage PPO	55,748	5%	13,142	6%		
Self-insured PPO	15,238	1%	4,485	2%	133	1%
Special needs plan – dual eligible	12,751	1%	3,629	2%		
Other	8,168	1%	1,188	1%	51	1%

Table 7: Number of claims for each type of insurance coverage by gender group of claimant. Counts and percents have been suppressed to protect the privacy of groups with fewer than 10 claimants.

Types of insurance coverage in the "Other" category include self-insured HMO plans and dental HMO plans, among others.
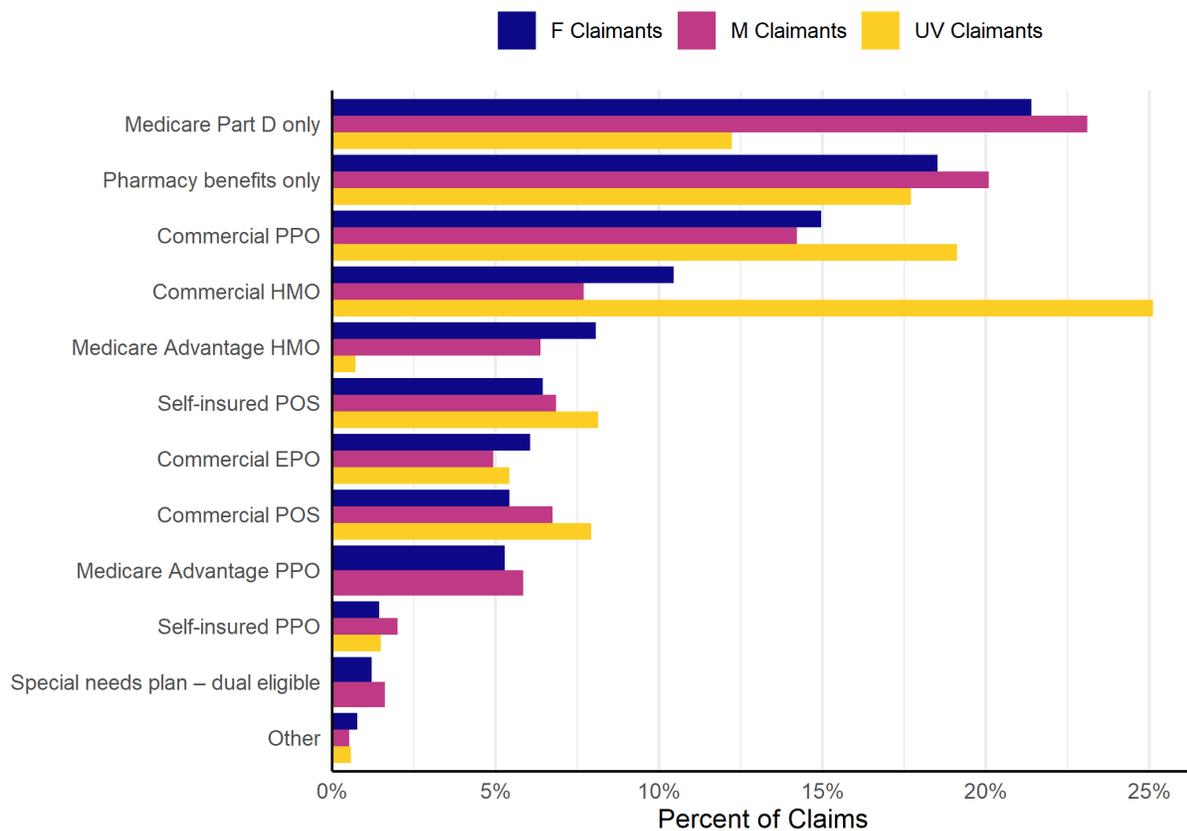
Figure 1: Percent of claims for each type of insurance coverage within each gender group. Percents have been suppressed to protect the privacy of groups with fewer than 10 claimants.

Health insurance carriers were the most common payers, accounting for about two-thirds of the claims. One-third of the claims were paid by pharmacy benefits managers. Third-party administrators and government agencies paid for about 1 percent of the claims, each.

Claims paid by pharmacy benefits managers were slightly more common for M claimants than for F claimants. Claims paid by carriers were more common for UV claimants than for the other groups.

Payer type	F claimants		M claimants		UV claimants	
	Claims	Percent	Claims	Percent	Claims	Percent
Carrier	695,147	65%	139,232	62%	6,270	70%
Pharmacy benefits manager	348,156	33%	81,476	36%	2,474	28%
Other government agency	6,929	1%	2,340	1%		
Third-party administrator	6,723	1%	1,581	1%		

Table 8: Numbers of claims for each payer type by gender group of claimant. Counts and percents have been suppressed to protect the privacy of groups with fewer than 10 claimants.

3. Claim costs

On average, F claimants paid $5 more per claim than M claimants.

	Average	Std Err	95% Conf Int
Average cost per claim			
F claimants	$32.45	$0.06	(32.34 to 32.57)
M claimants	$27.76	$0.14	(27.48 to 28.03)
UV claimants	$16.96	$0.27	(16.42 to 17.50)

	Average	Std Err	95% Conf Int
Average total cost to claimant			
F claimants	$252.94	$1.32	(250.37 to 255.52)
M claimants	$262.43	$3.57	(255.44 to 269.42)
UV claimants	$267.15	$13.11	(241.39 to 292.91)

Table 9: Average cost per claim and average total cost per claimant by gender group. The total costs are over the three year span from 2018 to 2020. Standard errors and 95% confidence intervals for each mean are shown to help make comparisons.

The average cost per claim for F claimants was higher than for M claimants, but M claimants made more claims on average (9.5 claims per M claimant vs. 7.8 claims per F claimant), leading to slightly higher average total costs in the end ($262.43 per M claimant vs. $252.94 per F claimant).

Because claimants in different gender groups will generally be receiving different treatments using different drugs, comparing their average claim costs may not be an appropriate comparison. Instead, the average total cost to a claimant gives a better sense of the overall financial impact of the different HRT therapies commonly used by each gender group.

We can still investigate the source of the $5 difference in average cost per claim between F claimants and M claimants. Our analysis suggests that most of that difference can be explained by the top 5 percent highest cost claims. These claims cost $134 or more to the claimant.

If we exclude the top 5 percent highest cost claims, the difference in average costs per claim between F claimants and M claimants falls from $5 to $1.

Averages after removing top 5 percent highest cost claims

	Average cost per claim	Average total cost to claimant
F claimants	$21.15	$164.49
M claimants	$19.67	$183.49
UV claimants	$15.60	$244.10

Table 10: Average cost per claim and average total cost per claimant by gender group. The total costs are over the three year span from 2018 to 2020. The top 5 percent highest cost claims in the data were excluded before splitting the claims by gender group.

This suggests that F claimants were disproportionately represented in the top 5 percent highest cost claims. A small number of very expensive claims for F claimants raised their overall average cost per claim.

In total there were 64,597 claims in the top 5 percent by highest cost ($134 or more). Of those, 90 percent were made by F claimants, compared to 82 percent by F claimants in the full dataset.

For four of the five most common drugs in those 64,597 highest cost claims, nearly all of the claims were made by F claimants.

Most common drugs in the top 5 percent highest cost claims

	Claims in top 5%	Average cost per claim in top 5%	Percent of claims by F claimants in top 5%
Estradiol vaginal	24,392	$226.53	> 99%
Estrogens, conjugated vaginal	8,389	$250.71	> 99%
Estradiol	8,292	$195.92	> 99%
Estrogens, conjugated	7,289	$230.46	> 99%
Testosterone	5,680	$310.61	1%

Table 11: Most common drugs in the top 5 percent highest cost claims. Average costs are calculated across the drug's claims in the top 5 percent. Percent of claims by F claimants are calculated across the drug's claims in the top 5 percent.

Vaginal estradiol and vaginal conjugated estrogens are medications applied directly into the vagina to help alleviate vaginal atrophy associated with menopause (vaginal dryness, discharge, itching, painful sexual intercourse) and sexual dysfunction (decreased libido).

Estradiol and conjugated estrogens (i.e., Premarin) are oral medications most commonly used by females to treat vasomotor symptoms (hot flashes) and vaginal atrophy (vaginal wall thinning and dryness) associated with menopause. Estradiol products can also be used as cross-sex hormone therapy for transgender females with persistent gender dysphoria/gender incongruence. They may be used to prevent osteoporosis in post-menopausal women and used in palliative care for advanced androgen-dependent prostate cancer in males and metastatic breast cancer in females and males.

Testosterone medications are most commonly used to treat hypogonadism (lack of testosterone production) in males, either due to congenital causes or acquired causes (e.g., radiation, medications, autoimmune, obesity, age). Testosterone products can also be used as cross-sex hormone therapy for transgender males with persistent gender dysphoria/gender incongruence.

All of these most common drugs, except estradiol, are overrepresented among high-cost claims. About 28 percent of the claims for vaginal conjugated estrogens, 21 percent of the claims for conjugated estrogens, 13 percent of the claims for vaginal estradiol, and 12 percent of the claims for testosterone are in the top 5 percent highest cost claims.

Estradiol is actually underrepresented among high-cost claims. Only about 2 percent of the claims for estradiol are in the top 5 percent highest cost claims.

Some drugs were even more overrepresented among the top 5 percent highest cost claims.

Most overrepresented drugs in the top 5 percent highest cost claims

	Claims in top 5%	Claims overall	Average cost per claim overall	Percent of claims by F claimants overall
Estradiol-norgestimate	55	108	$110.23	100%
Estradiol acetate vaginal	747	1,469	$172.91	> 99%
Hydroxyprogesterone caproate	221	710	$187.97	100%
Drospirenone-estradiol	81	280	$108.61	100%
Estrogens, conjugated vaginal	8,389	30,482	$103.58	> 99%

Table 12: Drugs most overrepresented in the top 5 percent highest cost claims. Average costs and percents of claims by F claimants are calcualted across all claims. Drugs with fewer than 10 claimants are excluded.

The most overrepresented drug among high-cost claims was estradiol-norgestimate, with 55 of its 108 claims appearing in the top 5 percent highest cost claims. The average cost per claim for this drug was $110.23, and all of its claims were made by F claimants.

In summary, our analysis suggests that the differences between average costs per claim for F claimants and M claimants can be attributed to a small number of very high-cost claims, among which F claimants were disproportionately represented. Overall, the average total costs over the three years of claims data to an F claimant and an M claimant were similar.

In the sections below we will highlight other differences in various aspects of the claims data.

3.1 Differences in drugs claimed

Estradiol (or vaginal estradiol) was the most common HRT drug claimed by F claimants, with a total of 653,484 claims accounting for just under 62 percent of claims by F claimants.

Most Common Drugs for F Claimants

Drug	Class of drug	Claims	Avg claim cost	Std err
Estradiol	Estrogens	459,992	$17.78	$0.05
Estradiol vaginal	Vaginal and related products	193,492	$58.12	$0.18
Progesterone	Progestins	188,449	$20.30	$0.05
Medroxyprogesterone acetate	Progestins	65,585	$7.28	$0.03
Estrogens, conjugated	Estrogens	35,181	$84.02	$0.51

Table 13: Claim counts and average costs per claim for the most common drugs for F claimants. Standard errors for each mean are shown to help make comparisons.

For M claimants, the most common HRT drug was testosterone cypionate, with a total of 157,501 claims accounting for over 70 percent of claims by M claimants.

Most Common Drugs for M Claimants

Drug	Class of drug	Claims	Avg claim cost	Std err
Testosterone cypionate	Androgens/anabolic	157,501	$19.19	$0.06
Testosterone	Androgens/anabolic	46,459	$61.70	$0.62
Estradiol	Estrogens	13,498	$10.57	$0.16
Progesterone	Progestins	2,453	$13.67	$0.36
Testosterone Enanthate	Androgens/anabolic	1,934	$40.33	$2.28

Table 14: Claim counts and average costs per claim for the most common drugs for M claimants. Standard errors for the each mean are shown to help make comparisons.

For UV claimants, the most common HRT drug was estradiol, followed closely by testosterone cypionate. These drugs accounted for 38 percent and 33 percent of claims, respectively, by UV claimants.

Most Common Drugs for UV Claimants

Drug	Class of drug	Claims	Avg claim cost	Std err
Estradiol	Estrogens	3,339	$12.63	$0.23
Testosterone Cypionate	Androgens/ anabolic	2,956	$15.54	$0.27
Progesterone	Progestins	1,219	$16.76	$0.50
Estradiol Valerate	Estrogens	321	$41.25	$3.10
Medroxyprogesterone Acetate	Progestins	283	$8.87	$0.53

Table 15: Claim counts and average costs per claim for the most common drugs for UV claimants. Standard errors for each mean are shown to help make comparisons.

Estradiol is available as tablets taken orally, as patches applied to the skin, and as creams, tablets, capsules, and inserts applied vaginally. These products are used in females to treat vasomotor symptoms (hot flashes) and vaginal atrophy (vaginal wall thinning and dryness) associated with menopause. Estradiol may also be used to prevent osteoporosis in post-menopausal women and may be used in palliative care for advanced androgen-dependent prostate cancer in males and metastatic breast cancer in females and males. Estradiol products can also be used as cross-sex hormone therapy for transgender females with persistent gender dysphoria/gender incongruence.

Progesterone is available as capsules taken orally, as intramuscular injection and as vaginal tablets and jelly. These products are used in females to prevent endometrial hyperplasia (abnormal thickening of the lining of the uterus), which raises the risk of developing endometrial cancer (a type of uterine cancer), to manage abnormal uterine bleeding unrelated to the menstrual cycle, to manage amenorrhea (absence of periods in menstruating women), to treat female infertility, and to prevent the preterm labor and birth of a newborn. Use in males is very uncommon, although some synthetic progesterone products (progestin) may be used in males with advanced prostate cancer.

Figure 2 shows the average cost per claim for each HRT drug and gender group. A table of the information plotted in Figure 2 can be found in .
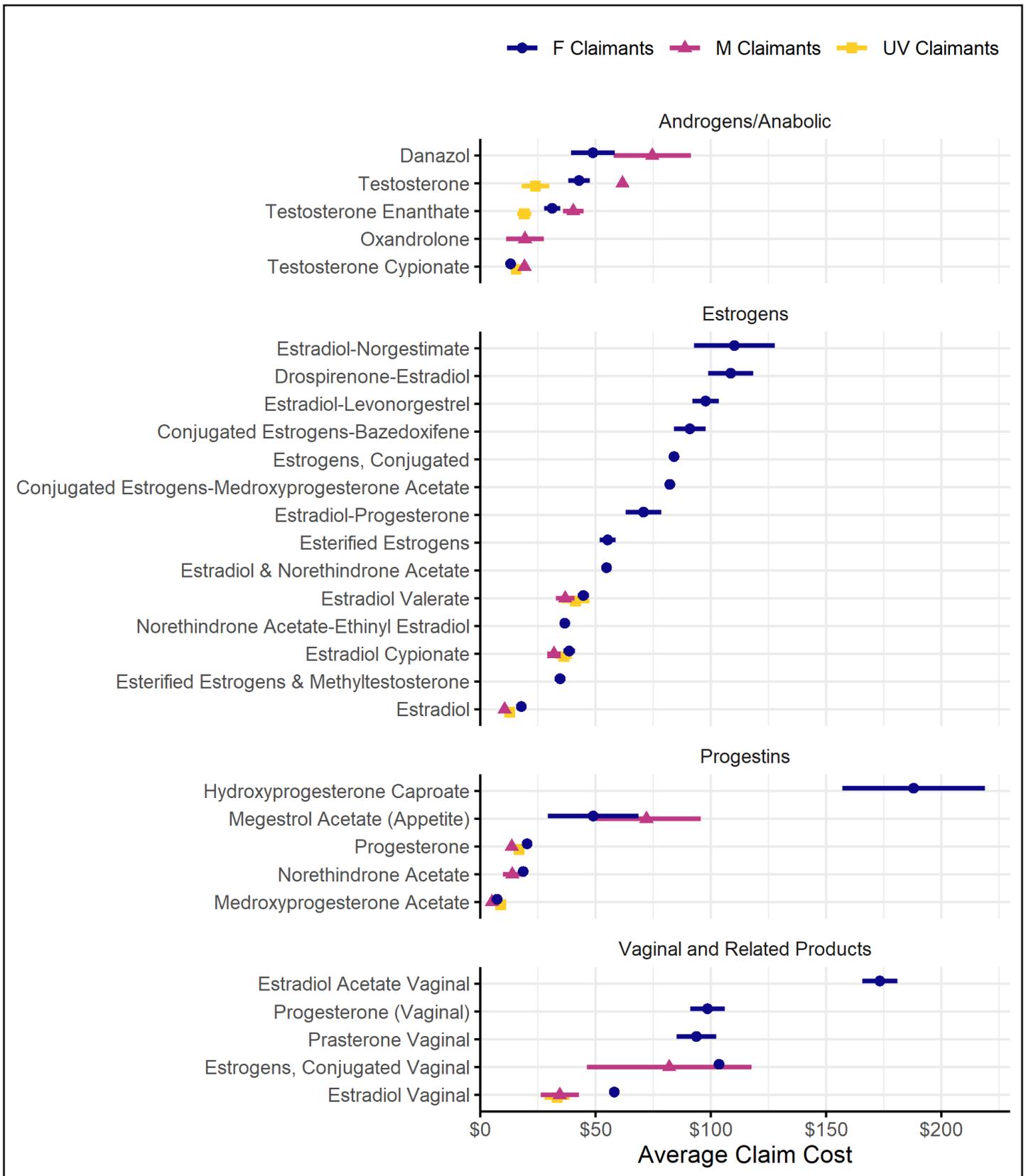
Figure 2: Average cost per claim for each HRT drug and gender group. Dots represent means and flat lines represent 95% confidence intervals. An average for a gender group is only shown if there were at least 10 claimants in that gender group who claimed the drug.

We can also calculate each drug's average total cost per claimant over the three-year span from 2018 to 2020.

An F claimant who made claims for drospirenone-estradiol, a drug combining the estrogen estradiol and the progestin drospirenone, paid a total of $844.75 for this drug, on average, over the three years 2018-20. This drug had the highest average total cost per claimant out of all drugs in the study. However, please note that the estimate for this drug's average total cost is not very precise, with a standard error of $165.19, primarily due to the relatively small number of claimants for it.

Drugs with the highest total cost for F claimants

Drug	Class of drug	Avg total cost	Std err
Drospirenone-estradiol	Estrogens	$844.75	$165.19
Estrogens, conjugated	Estrogens	$837.16	$16.14
Conjugated estrogens-medroxyprogesterone acetate	Estrogens	$828.83	$24.71
Estradiol acetate vaginal	Vaginal and related products	$814.22	$47.62
Conjugated estrogens-Bazedoxifene	Estrogens	$744.83	$83.54

Table 16: Average total cost per claimant for F claimants. The total costs are over the three year span from 2018 to 2020. Standard errors for each mean are shown to help make comparisons.

Danazol had the highest average total cost for M claimants, at $626.70 per claimant. However, as with drospirenone-estradiol above, this estimate is not very precise due to the relatively small number of claimants for the drug.

Drugs with the highest total cost for M claimants

Drug	Class of drug	Avg total cost	Std err
Danazol	Androgens/anabolic	$626.70	$221.41
Testosterone	Androgens/anabolic	$563.19	$14.70
Testosterone enanthate	Androgens/anabolic	$248.39	$28.19
Estradiol cypionate	Estrogens	$191.27	$41.48
Testosterone cypionate	Androgens/anabolic	$171.99	$1.49

Table 17: Average total cost per claimant for M claimants. The total costs are over the three year span from 2018 to 2020. Standard errors for each mean are shown to help make comparisons.

Estradiol Cypionate had the highest average total cost for UV claimants, at $266.27 per claimant.

Drugs with the highest total cost for UV claimants

Drug	Class of drug	Avg total cost	Std err
Estradiol cypionate	Estrogens	$266.27	$62.12
Estradiol valerate	Estrogens	$259.61	$50.31
Progesterone	Progestins	$189.16	$19.94
Testosterone cypionate	Androgens/anabolic	$180.85	$9.93
Estradiol	Estrogens	$178.00	$11.40

Table 18: Average total cost per claimant for UV claimants. The total costs are over the three year span from 2018 to 2020. Standard errors for each mean are shown to help make comparisons.

This figure shows the average total cost per claimant for each HRT drug and gender group. A table of the information can be found in Section 9 (Appendix: Additional Tables).
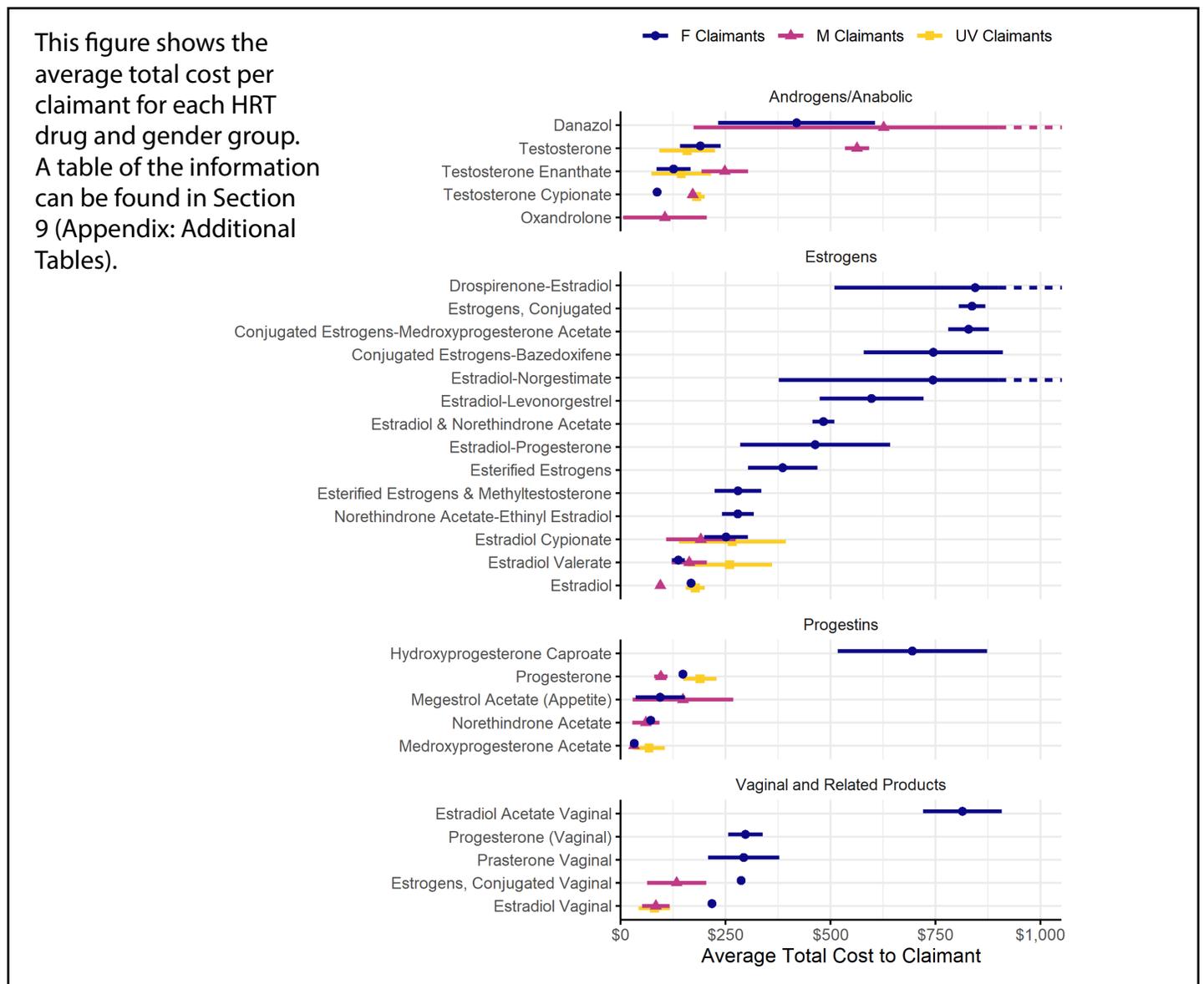
Figure 3: Average total cost per claimant for each HRT drug and gender group. Dots represent means and flat lines represent 95% confidence intervals. An average for a gender group is only shown if there were at least 10 claimants in that gender group who claimed the drug. The confidence interval for Danazol for M claimants and the intervals for Drospirenone-Estradiol and Estradiol-Norgestimate for F claimants have been truncated since they extend so far to the right. Those confidence intervals are ($174 to $1,080), ($509 to $1,180), and ($377 to $1,111), respectively.

3.2 Cost sharing between claimants and payers

Claimants paid a total of $40,687,239 for the claims in the study, while payers (health insurance carriers, pharmacy benefit managers, third-party administrators, and other governmental agencies) paid a total of $102,499,654.[6] Combining those two amounts, the total cost for the claims was $143,186,893.

On average, F claimants paid a higher share of their claim costs than M claimants (31 percent vs. 20 percent). UV claimants paid a similar share to F claimants.[7]

	Total paid combined	Total paid by payers	Total paid by claimants	Percent paid by claimants	Std Err
F claimants	$111,567,872	$77,265,830	$34,302,042	30.7%	0.05%
M claimants	$31,116,861	$24,882,069	$6,234,792	20.0%	0.10%
UV claimants	$502,160	$351,755	$150,405	30.0%	0.55%

Table 19: Total dollars paid by payers and claimants, and the percentage of the combined costs paid by claimants, by gender group. Standard errors for the percentages are shown to help make comparisons.

The combined cost (claimant cost plus payer cost) per claim, on average, was highest for M claimants, at $138.53 per claim. Claims for F claimants had an average combined cost of $105.55 per claim, and claims for UV claimants had an average combined cost of $56.63 per claim.

	Claimant cost		Payer cost		Combined cost	
	Average	Std err	Average	Std err	Average	Std err
F claimants	$32.45	$0.06	$73.10	$0.13	$105.55	$0.15
M claimants	$27.76	$0.14	$110.77	$0.58	$138.53	$0.62
UV claimants	$16.96	$0.27	$39.67	$0.89	$56.63	$0.97

Table 20: Average cost per claim for claimants, payers, and both combined by gender group. Standard errors for each mean are shown to help make comparisons.

Generally, claimants paid a higher share of the claim costs for commonly prescribed estrogens and progestins than for commonly prescribed testosterone. This difference is the primary reason that F claimants paid a higher share of their claim costs than M claimants (31 percent vs. 20 percent).

Overall, cost sharing is similar between gender groups for each drug, though there are some exceptions. For example, F claimants paid 36.4 percent of their claim costs for testosterone enanthate, while M claimants paid 23.5 percent of their claim costs. A large difference was also seen for medroxyprogesterone acetate: F claimants paid 71.5 percent of their claim costs, while M claimants paid 43.4 percent of their claim costs.

Figure 4 shows the average total cost per claimant for each HRT drug and gender group. A table of the information plotted in Figure 4 can be found in Section 9 (Appendix: Additional Tables).

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[6] Dollar amount paid by payer refers to data element PC036 in the APAC data.

[7] APAC does not include data on patient assistance programs (PAPs), but does report the consumers expected final cost. There is not enough information to determine if PAP information is a factor or affects the findings.
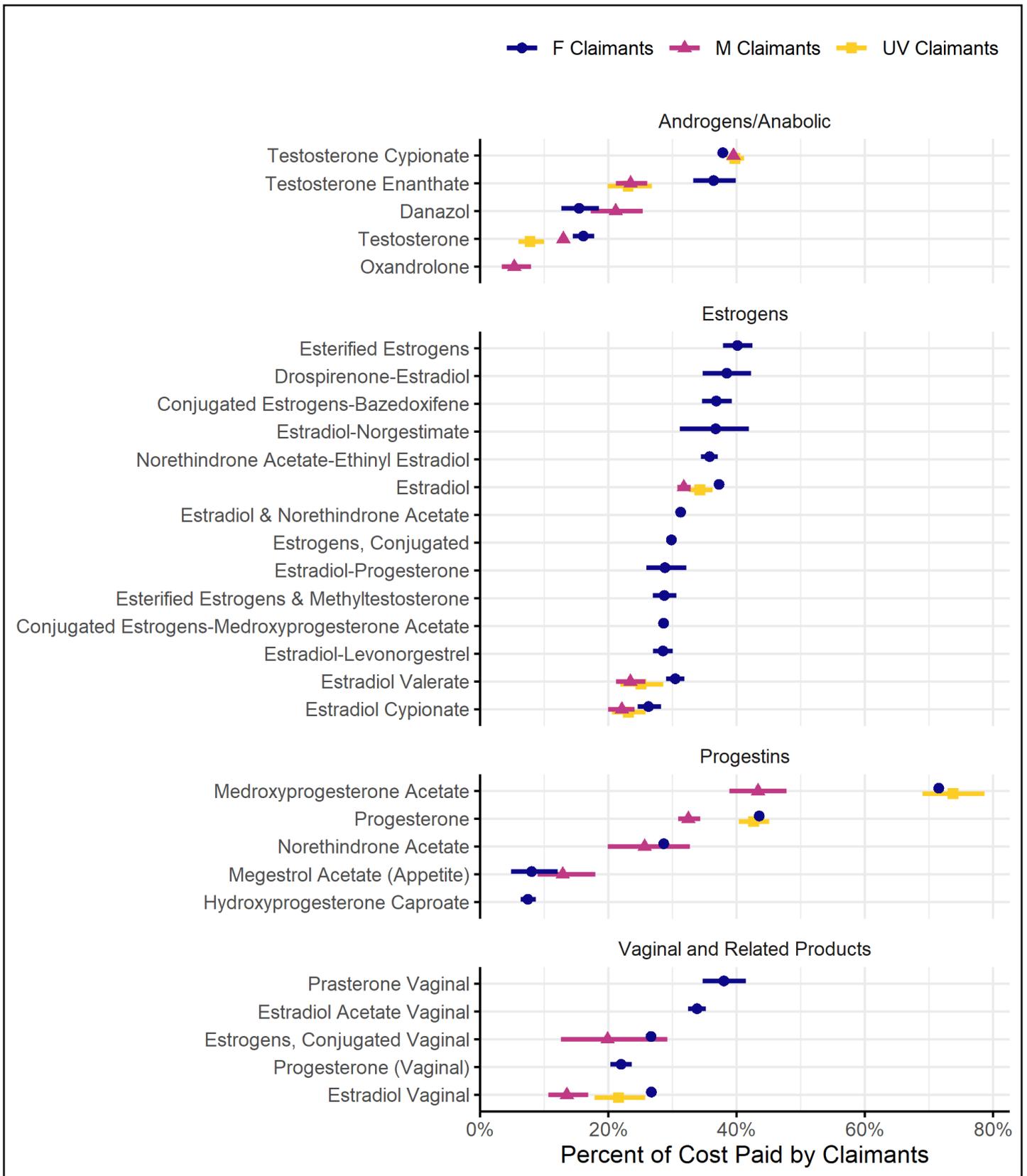
Figure 4: Percentages of combined costs paid by claimants for each HRT drug and gender group. Dots represent raw percentages and flat lines represent 95% confidence intervals. A percentage for a gender group is only shown if there were at least 10 claimants in that gender group who claimed the drug.

3.3 Differences in types of insurance coverage

Generally, F claimants tended to pay more per claim, on average, regardless of what type of insurance coverage was used for a claim.
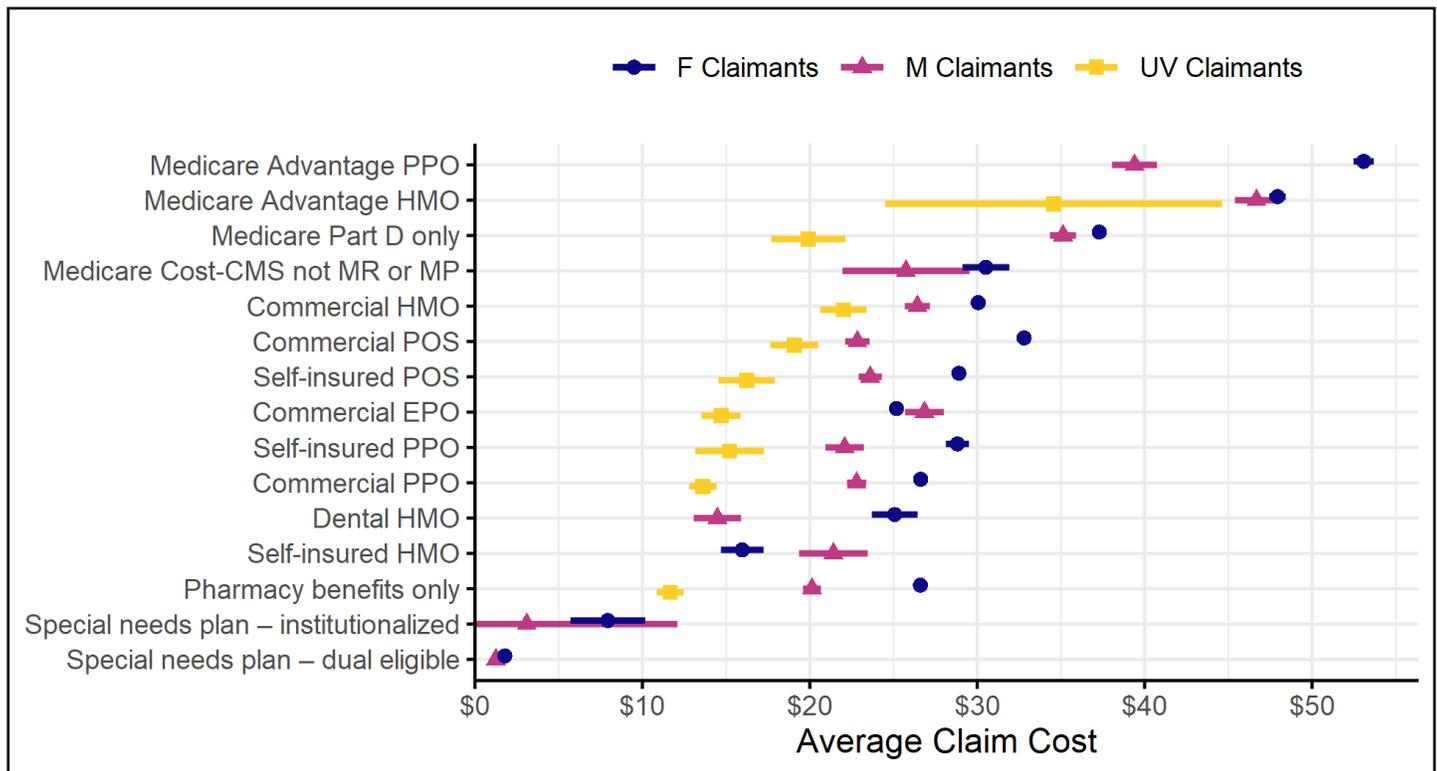
Figure 5: Average cost per claim for each type of insurance and gender group. Dots represent means and flat lines represent 95% confidence intervals. An average for a gender group is only shown if there were at least 10 claimants in that gender group with claims of that type of insurance.

A table of the information plotted in Figure 5 can be found in Section 9 (Appendix: Additional Tables).

3.4 Differences in payer type

F claimants tended to pay more per claim, on average, regardless of what type of payer paid the remainder of the claim's cost.
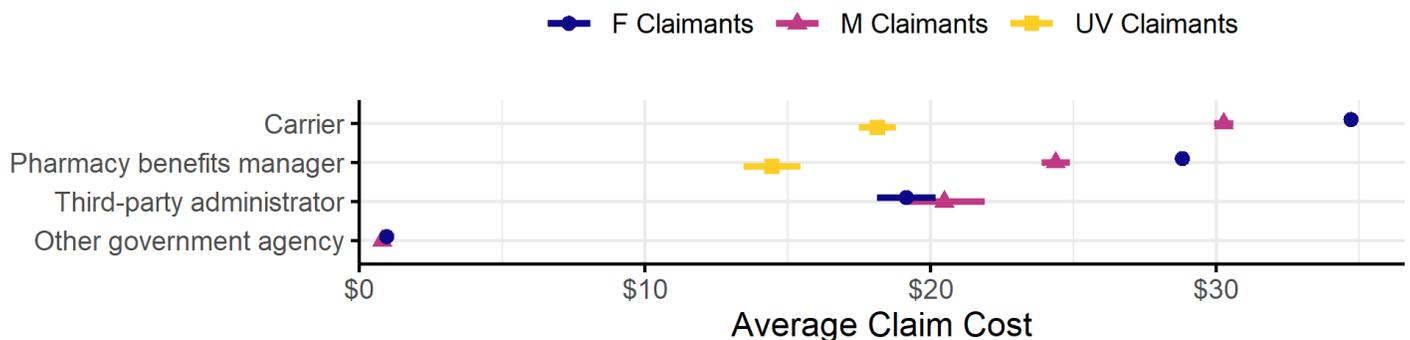

Figure 6: Average cost per claim for each payer type and gender group. Dots represent means and flat lines represent 95% confidence intervals. An average for a gender group is only shown if there were at least 10 claimants in that gender group with claims of paid by that type of payer.

A table of the information plotted in Figure 6 can be found in Section 9 (Appendix: Additional Tables).

4. Costs of contraceptives

Contraceptive HRT drugs were excluded from the main analyses in this study because claim costs for contraceptives were very different from claim costs for the other drug groups.

Over 95 percent of claims for contraceptives cost $0 to the claimant. Percentages of zero-cost claims in the other drug classes ranged from 9 percent to 12 percent.

Drug class	Percent of claims
Contraceptives	95.4%
Androgens/anabolic	12.1%
Estrogens	10.8%
Progestins	9.9%
Vaginal and related products	9.1%

Table 21: Percentage of claims in each drug class that cost $0 to the claimant.

Because there were so many zero-cost claims, the average costs for contraceptives were much lower than the averages for other drug classes.

Costs of contraceptive drugs

Average cost per claim	Average	Std err	95% conf int
F claimants	$1.33	$0.01	(1.31 to 1.35)
M claimants	$2.87	$0.57	(1.75 to 3.99)
UV claimants	$0.61	$0.10	(0.42 to 0.80)

Average total cost to claimant	Average	Std err	95% conf int
F claimants	$9.84	$0.20	(9.44 to 10.23)
M claimants	$14.97	$3.49	(8.11 to 21.84)
UV claimants	$5.62	$1.75	(2.18 to 9.06)

Table 22: Average cost per claim and average total cost per claimant for contraceptives by gender group. The total costs are over the three year span from 2018 to 2020. Standard errors and 95% confidence intervals for each mean are shown to help make comparisons.

Almost all (over 99 percent) of contraceptive claims were by F claimants. If we were to include contraceptives when calculating overall average costs, that would greatly lower the average costs for F claimants. For example, compare the average costs in Table 23, which include all contraceptive and non-contraceptive drugs, to the averages in Table 9, which exclude contraceptive drugs.

Average costs overall (all drugs, including contraceptives)

Average cost per claim	Average	Std err	95% conf int
F claimants	$15.18	$0.03	(15.12 to 15.24)
M claimants	$27.56	$0.14	(27.29 to 27.84)
UV claimants	$13.95	$0.23	(13.50 to 14.41)

Average total cost to claimant	Average	Std err	95% conf int
F claimants	$118.67	$0.64	(117.42 to 119.92)
M claimants	$259.52	$3.53	(252.61 to 266.43)
UV claimants	$207.13	$10.88	(185.76 to 228.50)

Table 23: Average cost per claim and average total cost per claimant across all drugs (contraceptives and non-contraceptives) by gender group. The total costs are over the three year span from 2018 to 2020. Standard errors and 95% confidence intervals for each mean are shown to help make comparisons.

The average cost per claim for F claimants decreases from $32.45 to $15.18 when claims for contraceptive drugs are included, while the average for M claimants decreases from $27.76 to $27.56.

4.1 Differences in contracpetive drugs claimed

Table 24, Table 25, and Table 26 show the five most commonly claimed contraceptive drugs for each gender group.

Most common contraceptives for F claimants			
Drug	Claims	Avg claim cost	Std err
Levonorgestrel & ethinyl estradiol	194,140	$0.53	$0.01
Norethindrone acetate & estradiol-fe	180,555	$0.89	$0.02
Norgestimate-ethinyl estradiol	125,428	$0.52	$0.01
Norgestimate-ethinyl estradiol (Triphasic)	110,959	$0.59	$0.01
Drospirenone-ethinyl estradiol	108,924	$2.11	$0.04

Table 24: Claim counts and average costs per claim for the most common contraceptives for F claimants. Standard errors for each mean are shown to help make comparisons.

Most common contraceptives for M claimants			
Drug	**Claims**	**Avg claim cost**	**Std err**
Norgestimate-ethinyl estradiol	244	$1.50	$0.58
Levonorgestrel & ethinyl estradiol	221	$2.97	$0.43
Norgestimate-ethinyl estradiol (Triphasic)	188	$1.04	$0.37
Norethindrone acetate & estradiol-fe	185	$1.16	$0.95
Drospirenone-ethinyl estradiol	173	$0.82	$0.82

Table 25: Claim counts and average costs per claim for the most common contraceptives for M claimants. Standard errors for each mean are shown to help make comparisons.

Most common contraceptives for UV claimants			
Drug	**Claims**	**Avg claim cost**	**Std err**
Levonorgestrel & ethinyl estradiol	324	$0.56	$0.18
Drospirenone-ethinyl estradiol	322	$1.21	$0.37
Norethindrone acetate & estradiol-fe	197	$0.00	$0.00
Norgestimate-ethinyl estradiol	197	$0.00	$0.00
Norgestimate-ethinyl estradiol (Triphasic)	177	$0.95	$0.28

Table 26: Claim counts and average costs per claim for the most common contraceptives for UV claimants. Standard errors for each mean are shown to help make comparisons.

Contraceptive hormones are generally only prescribed to females. Contraceptive claims for M claimants may be for transgender males who have a uterus.

Common brand names for some of the most claimed contraceptives:

- Levonorgestrel & Ethinyl Estradiol
    - Portia-28
    - Lessina
    - Aviane
    - Kurvelo
    - Vienva
- Norethindrone Acetate & Estradiol-Fe
    - Junel FE 1/20
    - Larin Fe 1/20
    - Blisovi FE 1/20
    - Microgestin FE 1/20
    - Blisovi Fe 1.5/30
- Norgestimate-Ethinyl Estradiol
    - Sprintec 28
    - Mono-Linyah
    - Estarylla
    - Femynor
    - Previfem
- Norgestimate-Ethinyl Estradiol (Triphasic)
    - Tri-Sprintec
    - Tri-Linyah
    - Tri-Lo-Marzia
    - Tri-Lo-Sprintec
    - Tri-Lo-Mili
- Drospirenone-Ethinyl Estradiol
    - Syeda
    - Nikki
    - Gianvi
    - Ocella
    - Loryna

5. Appendix: Discussion of gender groups

As described in Section 2.2, we found that several claimants had multiple different values in the gender fields of their claims. For example, we found 457 claimants in the data who had some claims where the gender marker was "F" and other claims where the gender marker was "M." We also found claimants who had only "U" claims, or both "F" and "U" claims, or "M" and "U" claims, or claims with all three values.

Recorded Genders	Claimants	Claims
F	135,611	1,056,955
M	23,758	224,629
F+M	457	8,076
U	55	223
F+U	35	361
M+U	10	110
F+M+U	6	98

Table 27: Numbers of claimants and claims, by gender. Multiple recorded values for gender are separated by a plus + sign. The "F," "M," and "U" rows only include claimants with that one recorded gender value.

Because there are claimants with both "F" and "M" claims, it would not be appropriate to assign claimants with "F" and "U" claims to the "F" group, or to assign claimants with "M" and "U" claims to the "M" group. In other words, the existence of "F+M" claimants suggests that any "U" could be an "F" or an "M." Further, this variable does not have a value that signifies that a claimant is intersex or identifies as nonbinary or agender.

Because we did not want to exclude these claimants from the study, and because there were so few claimants with certain combinations of gender values, we combined all claimants who do not just have "M" or "F" values into a third group. This allowed us to include statistics describing these claimants' data while often avoiding the need to hide it due to privacy concerns.

Some claimants in both the "M" or "F" category were likely incorrectly categorized due to limitations and differences in how information is collected or updated in the APAC or insurer systems. We can infer this from the presence of claims for drugs that would not be or rarely be prescribed for a particular gender.

While it's possible that diagnosis coding or other information associated with particular claims could potentially be used to appropriately recategorize some claimants to the correct gender, this goes beyond the data we have available. For the purposes of this study, we will present findings that compare the "M" and "F" categories, recognizing that a minority of claims are likely identified with an incorrect gender.

6. Appendix: How HRT drugs were selected

The process for selecting the drugs to include in this study had two parts: First we extracted a list of hormone drugs from Medi-Span, then we enlisted an external expert to narrow that list down to HRT drugs.

6.1 Extracting hormone drugs from Medi-Span

We began for searching for all NDCs in Medi-Span for which any of these word segments matched any part of their Medi-Span Therapeutic Classification System (TCS) hierarchy or their Medi-Span drug name:

- "hormon" (to include hormone and hormonal)
- "estrogen"
- "progestin"
- "androgen"
- "estradiol"

We excluded any NDCs that were classified as chemicals, diagnostic products, pharmaceutical adjuvants, alternative medicines, nutritional supplements, or multivitamins with minerals.

The list of all remaining TCS drug groups, classes, subclasses, and names was sent to an external expert to identify which ones contained HRT drugs.

6.2 Identification of HRT drugs

We sent the therapeutic classes we identified in Medi-Span to Andrew Gibler, PharmD at the Oregon Health Authority, for review.

We asked Dr. Gibler to exclude any of the therapeutic classes that were not relevant, to add any unlisted classes that may have been relevant to the goals of the study, and to identify any classes that may have been problematic (if, for example, they could contain more than just hormone replacement drugs). We asked them to cast as wide a net as possible to include any drug that could fall under the umbrella of "hormone replacement."

Dr. Gibler returned our list with the HRT drug classes identified.

6.3 Extracting the final list of HRT NDCs

We extracted all NDCs in Medi-Span whose TCS matched the classes identified as HRT drugs by Dr. Gibler.

In addition to the NDCs we identified in our first pass, this final step added vaginal prasterone drugs to the final list of HRT NDCs.

When requesting claims data from the Oregon Health Authority's All Payer All Claims (APAC) database, we requested all claims for NDCs on this final list of HRT drugs.

7. Appendix: Sensitivity analysis of the 5 percent cutoff for highest cost claims

In Section 3: Claim Costs we calculated that, on average, F claimants paid $32.45 per claim and M claimants paid $27.76 per claim, which is a difference of $4.69.

After we excluded the top 5 percent highest-cost claims, we found that this difference dropped to $1.48 ($21.15 for F claimants vs. $19.67 for M claimants). We concluded that most of the original $5 difference could be accounted for by those top 5 percent highest-cost claims.

Because this is an exploratory study, we wanted to check how reliable this finding is. If we had picked a different cutoff than 5 percent, would we see a similar reduction in the difference in costs per claim?

To explore this question, we calculated the average difference using many different cutoffs. Table 28 shows some of these calculations. Its first column shows which percentile of highest-cost claims was excluded before calculating the averages – so, for example, excluding the 95th percentile means excluding the top 5 percent highest-cost claims. We saw that, when we excluded more and more of the highest-cost claims, the difference between the F claimants' average and the M claimants' average fell to less than one dollar and stayed there.

Average costs per claim after excluding highest-cost claims			
Percentile excluded	**F avg per claim**	**M avg per claim**	**Difference**
60th	$6.93	$7.28	-$0.35
70th	$8.89	$9.48	-$0.59
80th	$11.61	$12.44	-$0.83
90th	$16.17	$16.46	-$0.29
95th	$21.15	$19.67	$1.48
99th	$28.51	$23.26	$5.25

Table 28: Average costs per claim for F claimants and M claimants after excluding different percentiles of the highest-cost claims. Claims were excluded prior to splitting the data by gender.

As stated at the start of this section, when the averages were calculated using all of the claims, the difference between them was $4.69. When we excluded only the 99th percentile of highest-cost claims before calculating the averages, the difference between them increased to $5.25. But when we excluded more high-cost claims, everything in the 95th percentile, the difference fell to $1.48. Then, when we excluded even more, everything in the 90th percentile, the difference fell to $0.29. Beyond that, it did not matter how much more of the highest-cost claims we excluded before calculating the averages, the difference between the averages was always less than one dollar.

Figure 7 plots the differences for every percentile cutoff between the 60th and the 99th, filling in the gaps between the rows in Table 28.
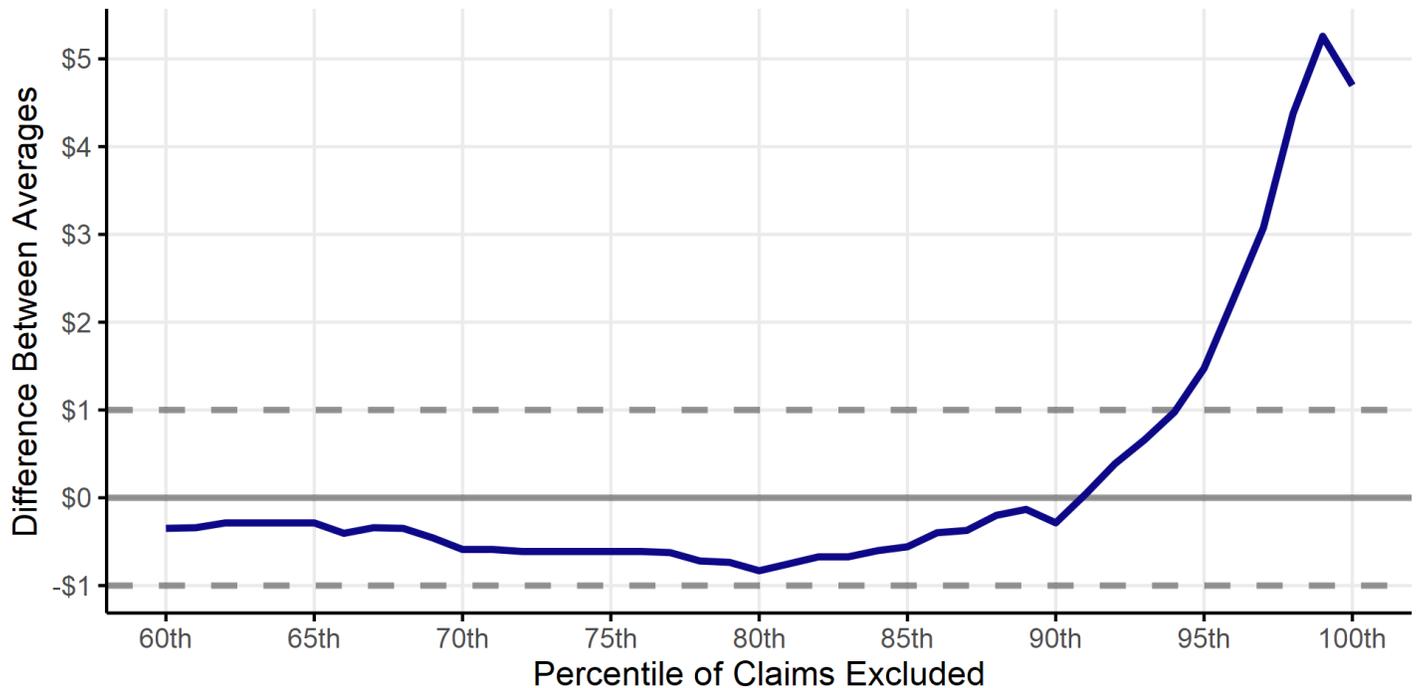

Figure 7: Average costs per claim for F claimants and M claimants after excluding different percentiles of the highest-cost claims. Claims were excluded prior to splitting the data by gender.

Finally, we also checked the precision of the cost gap accounted for the top 5 percent highest cost claims. In our original analysis, we found that excluding that 5 percent of claims reduced the difference between the F average and the M average from $4.69 to $1.48, a reduction of $3.21. To measure the precision of this calculation of the reduction, we used a bootstrapping approach (a statistical procedure that resamples the same data into multiple simulations):

1. Bootstrap resample the entire claims dataset. Then, using the resampled data.

2. Calculate the average costs per claim for F

claimants and for M claimants, then subtract them. Call this difference "A." In the original dataset, A = 4.69.

3. Exclude the top 5 percent highest cost claims, then calculate the average costs per claim for F claimants and for M claimants, then subtract them. Call this difference "B." In the original dataset, B = 1.48.

4. Calculate the difference between A and B. In the original dataset, A - B = 3.21.

5. Also calculate the proportion of A explained by the top 5 percent of claims: (A - B)/A. In the original dataset, (A - B)/A = 68.4 percent.

We performed this bootstrapping procedure 100 times. Across all iterations:

- A ranged from $4.41 to $5.08.

- B ranged from $1.37 to $1.65.

- The difference between A and B ranged from $2.96 to $3.54.

- The ratio (A - B)/A ranged from 65.8 percent to 70.4 percent.

In other words, we estimate that the overall difference between the average cost per claim for F claimants and the average for M claimants is between $4.40 and $5.10. Further, we estimate that excluding the top 5 percent of claims reduces that difference by 66 percent to 70 percent ($3 to $3.50).

These intervals help us understand the precision of our original observation that the overall difference between the averages was $4.69, and that excluding the top 5 percent of claims reduced that difference by 68.4 percent ($3.21).

This sensitivity analysis supported our original inference that the highest-cost claims in the data, the most common of which were made by F claimants and in which F claimants were overrepresented overall, could explain most of the difference between the average cost per claims for F claimants and the average cost per claim for M claimants.

8. Appendex: Data quality and cleaning

Each APAC claim record contains these four fields relating to expected payments from patients:

- Expected patient copay paid (data element PC040)

- Expected patient coinsurance paid (data element PC041)

- Expected patient deductible paid (data element PC042)

- Expected amount paid by patient (data element PC043)

According to the APAC data submission guidelines, PC043 is required if any of PC040, PC041, or PC042 is missing. It should be 0 if the amount equals zero, and it should be blank if it is missing.

Most of our data cleaning was motivated by apparent disagreements between these fields.

This appendix is intended for analysts who are familiar with APAC claims data. Each section below describes a step in our data cleaning process. Later sections assume the cleaning described in earlier sections has already been done.

8.1 Negative values

A single claim in APAC may span multiple records, with each record representing a single claim line. Negative values in the payment fields indicate that a claim line has been reversed.

We excluded all records with negative payment fields.

8.2 Missing payment fields

When any of the fields PC040 (copay), PC041 (coinsurance), or PC042 (deductible) are missing, PC043 (total patient paid) should be present. We found that PC040 and PC042 were never missing. However, in 6.5 percent of the records (180,814 records), PC041 and PC043 were both missing.

Since our study is based on total patient costs, we excluded all records where both PC041 and PC043 were missing.

8.3 Creating a new "total paid" field

In general, PC043 matches the sum of PC040, PC041, and PC042. PC043 matches that sum in 93.2 percent of the records where all of the

fields are present (2,176,065 out of 2,335,379 records). Seeing this, we began a careful analysis of the values in the payment fields in an effort to understand which value to use when they did not match.

To combine the information contained in PC040 through PC043, we created a new "total paid" field. The main cost analyses in this study used the values in this new field.

For the purposes of this writeup, we will call this new field "PAID."

The sections below describe the data quality issues we discovered in the payment fields and the final set of rules we used to define PAID.

8.3.1 Missing coinsurance

The data submission guidelines state that PC043 is required if any of PC040, PC041, or PC042 is missing. PC040 and PC042 were never missing, but PC041 was missing in 0.3 percent of the records (7,919 records).

For those records where PC041 was missing:

- In 95.8 percent of the records (7,584 records), PC043 matched the sum of PC040 and PC042. It seemed that PC041 should have been zero in these cases, not missing. Still, PC043 seemed reliable in this case.

- There were only three records where PC043 was larger than PC040 + PC042. In all of those records, PC040 matched PC042. PC043 seemed reliable in this case, but it was unclear how to interpret PC040 and PC042.

- The records where PC043 was smaller than PC040 + PC042 could be split into two groups:
  - PC043 > 0. In all of these records, it turned out that PC040, PC042, and PC043 had identical values. Presumably the total amount paid by the patient had been repeatedly entered in every field and PC043 was reliable.
  - PC043 = 0. In all of these records, either PC040 or PC042 was positive. This seemed to violate the APAC data submission guidelines, suggesting that PC043 was unreliable for these records. Further, since PC041 was missing, we could not interpret PC040 + PC042 as the amount paid by the patient.

8.3.2 Both coinsurance (PC041) and PC043 present

These 2,335,379 records can be split into groups similar to the ones above:

- In 93.2 percent of these records (2,176,065 records), PC043 matched the sum of PC040, PC041, and PC042. PC043 seemed reliable in this case.

- In 1.1 percent of these records (26,072 records), PC043 was larger than PC040 + PC041 + PC042. A visual inspection of these records did not reveal any obvious relationship between PC043 and the other fields. However, it was still plausible that PC043 was reliable in this case.

- The remaining 133,242 records, where PC043 was smaller than PC040 + PC041 + PC042, could be split again:

Record #	PC040	PC041	PC042	PC043
1	$3	$1	$0	$3
2	$2	$4	$4	$6

- PC043 > 0 (58,436 records). In 95.5 percent of these records (55,829 records), either PC043 matched at least one of the other fields or PC043 matched the sum of the unique values in the other fields. Consider the example records at the bottom of the previous page.

  For those records, the presence of duplicate entries suggests that we should use the sum of the unique values in PC040, PC041, and PC042. In the other 4.5 percent of the records with PC043 > 0 (2,607 records), visual inspection did not reveal any obvious relation between PC043 and the other price fields. Nine of those records had identical values for PC040, PC041, and PC042, in which case we might as well use PC043, but we should use PC040 + PC041 + PC042 otherwise.

- PC043 = 0 (74,806 records). As before, PC043 seemed unreliable for these records. For three of these records, PC040, PC041, and PC042 were all identical, so we should use their common value. Otherwise, we should use the sum PC040 + PC041 + PC042 since we do not have PC043 available to further suggest duplication occurring.

8.3.3 PC043 missing

The cases above cover 89.5 percent of the records in the data (2,343,298 out of 2,617,070 records). In this last group of 273,772 records, we no longer have PC043 available to help us identify likely duplication in the other cost fields.

We can only identify the most obvious case, where PC040, PC041, and PC042 are all equal, which was true in 60.1 percent of these records (164,618 records). Actually, when PC040, PC041, and PC042 were equal, it turned out that they were all zero.

For the other 39.9 percent of these records (109,154 records), we should just use PC040 + PC041 + PC042.

8.3.4 Final definition of the PAID field

To define the new PAID field, we excluded records where PC041 (coinsurance) was missing and PC043 was zero, then defined PAID to have the following values, guided by the data quality issues

we observed above:

- PC043 when PC041 was missing. Otherwise,

- PC043 when PC043 was larger than PC040 + PC041 + PC042. Otherwise,

- The sum of the unique values in PC040, PC041, and PC042 when PC043 was positive and PC043 matched any of those values or the sum of those unique values. Otherwise,

- PC043 when PC043 was positive and PC040, PC041, and PC042 were identical. Otherwise,

- PC040 when PC040, PC041, and PC042 were identical. Otherwise,

- PC040 + PC041 + PC042.

8.3.5 Comparison to a simpler definition

Instead of the relatively complex definition above, we could have used a simpler definition for PAID. For example, we could have defined it to equal PC043 when PC043 was present, and PC040 + PC041 + PC042 otherwise. Let's call this simpler definition PAID2.

This simpler PAID2 differs from PAID in 3.4 percent of the records (88,418 records). Across those records where they differ, the average of PAID was $55.94 and the average of PAID2 was $7.85.

Based on our data quality analysis, we believe that PAID should be more accurate than the simpler PAID2. Further, it seems that basing this study on PAID2 could have led to underestimates of the average costs of hormone replacement drugs.

8.4 Missing person IDs

Records for 113 claims in the data were missing their "person ID" field.

This field is assigned by the organization that maintains the APAC database. According to the APAC Data Dictionary, it is intended to be a unique identifier for a person across payers and time. There is also a related field, "member ID,"

which is intended to be a payer and plan specific unique identifier for a person.

Those 113 claims with missing person IDs were associated with eight member IDs. All claims associated with these eight member IDs were missing their person IDs.

For those 113 claims with missing person IDs, we used their associated member ID as their person ID.

8.5 Filtering multiple claim lines

Each record in APAC is one line of an insurance claim. As such, multiple records may be associated with a single claim. This could happen if, for example, a claim was billed, reversed, and billed again.

There were 823 claims in the data associated with multiple records.

For each claim, we selected the record with the latest fill date to be used in the study based on guidance from APAC.

9. Appendix: Additional tables

The tables in this section contain the raw data plotted in the figures in Section 3: Claim Costs.

Average cost per claim by HRT drug and gender group			
Androgens/Anabolic	**F claimants**	**M claimants**	**UV claimants**
Danazol	$48.85 ± $9.50	$74.61 ± $16.76	
Testosterone	$42.84 ± $4.67	$61.70 ± $1.21	$23.93 ± $5.99
Testosterone enanthate	$31.19 ± $3.50	$40.33 ± $4.47	$19.05 ± $3.05
Oxandrolone		$19.38 ± $8.19	
Testosterone cypionate	$13.14 ± $0.27	$19.19 ± $0.11	$15.54 ± $0.54

Estrogens	**F claimants**	**M claimants**	**UV claimants**
Estradiol-norgestimate	$110.23 ± $17.54		
Drospirenone-estradiol	$108.61 ± $9.78		
Estradiol-levonorgestrel	$97.74 ± $5.74		
Conjugated estrogens-bazedoxifene	$90.87 ± $6.88		
Estrogens, conjugated	$84.02 ± $0.99		
Conjugated estrogens-medroxyprogesterone acetate	$82.21 ± $1.30		
Estradiol-progesterone	$70.78 ± $7.73		
Esterified estrogens	$55.24 ± $3.45		
Estradiol & norethindrone acetate	$54.76 ± $0.90		
Estradiol valerate	$44.71 ± $2.44	$36.84 ± $4.03	$41.25 ± $6.10

	F claimants	M claimants	UV claimants
Norethindrone acetate-ethinyl estradiol	$36.66 ± $1.60		
Estradiol cypionate	$38.56 ± $2.51	$31.95 ± $2.93	$36.19 ± $3.55
Esterified estrogens & methyltestosterone	$34.59 ± $2.36		
Estradiol	$17.78 ± $0.09	$10.57 ± $0.31	$12.63 ± $0.44

Progestins	F claimants	M claimants	UV claimants
Hydroxyprogesterone caproate	$187.97 ± $30.92		
Megestrol acetate (appetite)	$48.96 ± $19.68	$72.09 ± $23.53	
Progesterone	$20.30 ± $0.11	$13.67 ± $0.70	$16.76 ± $0.98
Norethindrone acetate	$18.60 ± $0.41	$13.87 ± $4.06	
Medroxyprogesterone acetate	$7.28 ± $0.05	$5.04 ± $0.46	$8.87 ± $1.05

Vaginal and related products	F claimants	M claimants	UV claimants
Estradiol acetate vaginal	$173.32 ± $7.62		
Progesterone (vaginal)	$98.56 ± $7.49		
Prasterone vaginal	$93.75 ± $8.60		
Estrogens, conjugated vaginal	$103.56 ± $1.28	$81.96 ± $35.71	
Estradiol vaginal	$58.12 ± $0.36	$34.50 ± $8.28	$33.30 ± $5.43

Table 29: Average cost per claim for each HRT drug and gender group, plus or minus its margin of error. Margins of error represent 95% confidence intervals for the means. An average for a gender group is only shown if there were at least 10 claimants in that gender group who claimed the drug.

Average total cost per claimant by HRT drug and gender group			
Androgens/Anabolic	F claimants	M claimants	UV claimants
Danazol	$419.27 ± $186.72	$626.70 ± $452.84	
Testosterone	$190.12 ± $48.45	$563.19 ± $28.81	$158.75 ± $66.36
Testosterone enanthate	$126.36 ± $40.60	$248.39 ± $55.46	$144.49 ± $71.01
Testosterone cypionate	$87.16 ± $5.38	$171.99 ± $2.91	$180.85 ± $19.56
Oxandrolone		$105.73 ± $99.63	

Estrogens	F claimants	M claimants	UV claimants
Drospirenone-estradiol	$844.75 ± $335.35		
Estrogens, conjugated	$837.16 ± $31.65		
Conjugated estrogens-medroxyprogesterone acetate	$828.83 ± $48.46		
Conjugated estrogens-bazedoxifene	$744.83 ± $165.64		
Estradiol-norgestimate	$744.07 ± $367.21		
Estradiol-levonorgestrel	$597.92 ± $123.70		
Estradiol & norethindrone acetate	$483.19 ± $26.10		
Estradiol-progesterone	$463.55 ± $178.61		
Esterified estrogens	$386.30 ± $82.69		
Esterified estrogens & methyltestosterone	$279.71 ± $55.66		
Norethindrone acetate-ethinyl estradiol	$279.44 ± $37.92		
Estradiol cypionate	$251.24 ± $52.08	$191.27 ± $82.65	$266.27 ± $127.47
Estradiol valerate	$137.66 ± $15.53	$163.69 ± $41.73	$259.61 ± $101.05
Estradiol	$168.02 ± $2.95	$94.82 ± $7.45	$178.00 ± $22.45

Progestins	F claimants	M claimants	UV claimants
Hydroxyprogesterone caproate	$695.11 ± $177.81		
Progesterone	$148.51 ± $2.44	$96.05 ± $15.93	$189.16 ± $39.53
Megestrol acetate (appetite)	$94.35 ± $58.59	$148.69 ± $119.85	
Norethindrone acetate	$71.76 ± $5.46	$60.43 ± $32.35	
Medroxyprogesterone acetate	$32.76 ± $0.85	$31.98 ± $9.89	$67.87 ± $37.64

Vaginal and related products	F claimants	M claimants	UV claimants
Estradiol acetate vaginal	$814.22 ± $93.70		
Progesterone (vaginal)	$297.51 ± $41.03		
Prasterone vaginal	$293.28 ± $84.77		
Estrogens, conjugated vaginal	$287.32 ± $7.40	$133.72 ± $70.46	
Estradiol vaginal	$217.75 ± $3.67	$84.08 ± $32.75	$80.57 ± $37.67

Table 30: Average total cost per claimant for each HRT drug and gender group, plus or minus its margin of error. Margins of error represent 95% confidence intervals for the means. An average for a gender group is only shown if there were at least 10 claimants in that gender group who claimed the drug.

Percentages of claim costs paid by claimants			
Androgens/Anabolic	**F claimants**	**M claimants**	**UV claimants**
Testosterone cypionate	37.9% ± 0.8%	39.5% ± 0.2%	39.8% ± 1.4%
Testosterone enanthate	36.4% ± 3.3%	23.5% ± 2.3%	23.1% ± 3.5%
Danazol	15.5% ± 2.9%	21.2% ± 4.0%	
Testosterone	16.1% ± 1.7%	13.0% ± 0.2%	7.8% ± 1.9%
Oxandrolone		5.3% ± 2.4%	

Estrogens	**F claimants**	**M claimants**	**UV claimants**
Esterified estrogens	40.1% ± 2.3%		
Drospirenone-estradiol	38.5% ± 3.6%		
Conjugated estrogens-bazedoxifene	36.8% ± 2.4%		
Estradiol-norgestimate	36.7% ± 5.5%		
Norethindrone acetate-ethinyl estradiol	35.8% ± 1.3%		
Estradiol	37.3% ± 0.2%	31.8% ± 1.1%	34.3% ± 1.8%
Estradiol & norethindrone acetate	31.3% ± 0.4%		
Estrogens, conjugated	29.8% ± 0.3%		
Estradiol-progesterone	28.8% ± 3.1%		
Esterified estrogens & methyltestosterone	28.7% ± 2.0%		
Conjugated estrogens-medroxyprogesterone acetate	28.6% ± 0.4%		
Estradiol-levonorgestrel	28.5% ± 1.6%		
Estradiol valerate	30.4% ± 1.5%	23.4% ± 2.3%	25.1% ± 3.3%
Estradiol cypionate	26.3% ± 1.8%	22.1% ± 2.1%	23.1% ± 2.7%

Progestins	**F claimants**	**M claimants**	**UV claimants**
Medroxyprogesterone acetate	71.5% ± 0.4%	43.4% ± 4.5%	73.7% ± 5.2%
Progesterone	43.5% ± 0.2%	32.5% ± 1.7%	42.7% ± 2.2%
Norethindrone acetate	28.6% ± 0.6%	25.7% ± 6.5%	
Megestrol acetate (appetite)	8.0% ± 3.6%	12.9% ± 4.5%	
Hydroxyprogesterone caproate	7.4% ± 1.2%		

Vaginal and related products	F claimants	M claimants	UV claimants
Prasterone vaginal	38.0% ± 3.4%		
Estradiol acetate vaginal	33.8% ± 1.4%		
Estrogens, conjugated vaginal	26.7% ± 0.3%	19.9% ± 8.1%	
Progesterone (vaginal)	22.0% ± 1.6%		
Estradiol vaginal	26.7% ± 0.2%	13.5% ± 3.2%	21.6% ± 3.9%

Table 31: Percentage of combined costs paid by claimants for each HRT drug and gender group, plus or minus its margin of error. Margins of error represent 95% confidence intervals for the percentages. A percentage for a gender group is only shown if there were at least 10 claimants in that gender group who claimed the drug.

Average cost per claim by type of insurance coverage and gender group			
Androgens/Anabolic	**F claimants**	**M claimants**	**UV claimants**
Medicare Advantage PPO	$53.08 ± $0.60	$39.40 ± $1.35	
Medicare Advantage HMO	$47.94 ± $0.49	$46.68 ± $1.29	$34.56 ± $10.06
Medicare Part D only	$37.29 ± $0.30	$35.12 ± $0.78	$19.91 ± $2.21
Medicare Cost-CMS not MR or MP	$30.52 ± $1.40	$25.74 ± $3.79	
Commercial HMO	$30.06 ± $0.31	$26.43 ± $0.75	$22.01 ± $1.38
Commercial POS	$32.80 ± $0.43	$22.84 ± $0.73	$19.08 ± $1.43
Self-insured POS	$28.91 ± $0.38	$23.61 ± $0.69	$16.22 ± $1.68
Commercial EPO	$25.18 ± $0.33	$26.85 ± $1.16	$14.69 ± $1.17
Self-insured PPO	$28.82 ± $0.69	$22.08 ± $1.15	$15.21 ± $2.05
Commercial PPO	$26.62 ± $0.22	$22.80 ± $0.57	$13.61 ± $0.82
Dental HMO	$25.07 ± $1.37	$14.48 ± $1.41	
(Unknown)	$17.78 ± $1.36	$20.36 ± $2.82	
Self-insured HMO	$15.97 ± $1.27	$21.41 ± $2.05	
Pharmacy benefits only	$26.61 ± $0.25	$20.13 ± $0.53	$11.66 ± $0.80
Special needs plan – institutionalized	$7.94 ± $2.24	$3.09 ± $6.05	
Special needs plan – dual eligible	$1.79 ± $0.07	$1.26 ± $0.14	

Table 32: Average cost per claim for each type of insurance and gender group, plus or minus its margin of error. Margins of error represent 95% confidence intervals for the means. An average for a gender group is only shown if there were at least 10 claimants in that gender group with claims of that type of insurance.

Average cost per claim by payer type and gender group			
Androgens/Anabolic	**F claimants**	**M claimants**	**UV claimants**
Carrier	$34.72 ± $0.14	$30.26 ± $0.34	$18.14 ± $0.65
Pharmacy benefits manager	$28.81 ± $0.20	$24.38 ± $0.50	$14.45 ± $1.00
Third-party administrator	$19.15 ± $1.03	$20.49 ± $1.41	
Other government agency	$0.96 ± $0.04	$0.81 ± $0.14	

Table 33: Average cost per claim for each payer type and gender group, plus or minus its margin of error. Margins of error represent 95% confidence intervals for the means. An average for a gender group is only shown if there were at least 10 claimants in that gender group with claims of paid by that type of payer.