Hormone Therapy for Transfeminine Non-Binary Individuals and Femboys 101

In the last few years there has been increasing interest in transfeminine hormone therapy for non-binary individuals. The goal of this form of hormone therapy is often to induce some but not all aspects of demasculinization and/or feminization. Sometimes the aim is to achieve a more androgynous or completely androgynous appearance. Other times it's to achieve a partially or fully feminine body with the sole exception of breast development.

In some cases, the person may not even identify as "transgender" but rather as, e.g., a femboy. These are cisgender males who don't want genital reassignment surgery nor generally want decreased sexual function but nonetheless want to have more feminine bodies. See r/femboy, r/femineboys, and r/femboytransition for relevant subreddits. Whatever the goal, these non-conventional transfeminine non-binary and even cisgender individuals are increasingly deciding to act on their feelings and pursue hormonal changes.

I am a transgender woman, but I totally sympathize with these individuals, whether transgender or cisgender. Since this approach is very new and there is very little available that's written on this topic (including close to nothing in the published literature), I thought that I would do a write up on the topic. In this thread, I'll go over the various possibilities for non-conventional feminizing hormone therapy for non-binary individuals and femboys.

It should be noted that the content in this thread is experimental and preliminary. There have been no studies of non-conventional hormone therapy for non-binary individuals as of present, and there are no standards or guidelines to inform this kind of hormone therapy. Instead, all of the information in this thread is extrapolated from theory and from research in other patient populations, such as cisgender men with prostate cancer and/or gynecomastia and transgender women. The content of this thread should be considered an exploratory "white paper" of sorts rather than as therapeutic recommendations or anything of the sort.

Conventional feminizing hormone therapy

In conventional hormone therapy for transgender women, otherwise known as male-to-female hormone replacement therapy (MtF HRT), the goal is to produce complete demasculinization and feminization. This is achieved by suppressing testosterone levels into the normal female range and increasing estrogen levels into the normal female range. It's generally done by administration of estrogens, which induce feminization and suppress testosterone levels (thereby providing demasculinization and permitting full feminization), and optionally by administration of antiandrogens or progestogens, which block or suppress any remaining testosterone that persists even with estrogen therapy.

Medications used in MtF HRT include estrogens like estradiol and estradiol esters such as estradiol valerate; antiandrogens like bicalutamide, spironolactone, and GnRH agonists/antagonists; and progestogens like cyproterone acetate and progesterone. 5α-Reductase inhibitors like finasteride and dutasteride have been used as targeted antiandrogens that inhibit only specific androgenic effects, namely in skin and hair follicles.

For a thorough introduction to feminizing hormone therapy for transgender women that covers the effects, medications, routes, and dosages, see Hormone Therapy for Transgender Women 101. In addition, see the Medications section of the Transgender hormone therapy (male-to-female) article on Wikipedia.

If a non-binary transfeminine person or a femboy doesn't mind complete demasculinization and feminization, including breast development, then conventional feminizing hormone therapy can be employed. If this is not the case however and prevention or minimization of feminization or breast development are desired, things become more complex...

Achieving androgen deprivation

If the goal of non-binary hormone therapy is simply to achieve an androgynous appearance with minimal or no feminization, this can be achieved via deprivation of testosterone without concomitant administration of an estrogen. There are a number of ways to achieve androgen deprivation or testosterone suppression in people assigned male at birth. These include high-dose progestogen therapy, medical and surgical castration with GnRH agonists/antagonists or orchiectomy, high-dose androgen receptor antagonist therapy, and a few other miscellaneous possibilities. In this section, I'll discuss androgen deprivation largely from the standpoint of efficacy. There are issues with androgen deprivation alone in terms of tolerability and safety due to the co-consequence of estrogen deficiency however, which I'll discuss in the subsequent section.

Testosterone suppression with high-dose progestogens

Androgen deprivation can be achieved with high doses of progestogens, which suppress testosterone levels by up to 70 to 80%. This is a substantial decrease in testosterone levels, but isn't quite into the female range. Androgen receptor antagonists can additionally be included to block the remaining 20 to 30% of testosterone that isn't suppressed if desired. For these purposes, low-dose cyproterone acetate (e.g., 5.0–12.5 mg/day; link) plus bicalutamide (e.g., 12.5–50 mg/day) or spironolactone (e.g., 200–400 mg/day) is likely to be an effective regimen. As an alternative to cyproterone acetate, high doses of other progestogens, such as just about any other progestin, or alternatively rectal progesterone (link), can be used instead.

Testosterone suppression with medical or surgical castration

Another option for androgen deprivation is the use of a GnRH agonist or antagonist. These medications suppress testosterone levels by about 95%, or into the normal female range or male castrate range (<50 ng/dL). However, GnRH agonists and antagonists are very expensive, although there may be some viable options for obtaining them more cheaply (e.g., purchasing from certain online pharmacies/vendors).

Alternatively, a gonadectomy, or surgical removal of the gonads, can be performed. However, this is expensive (a few thousand dollars USD), requires minor surgery, can be difficult to obtain. Most surgeons require letters from gender therapists and real-life experience; informed-consent surgeons do exist however. It's also irreversible, notably resulting in permanent loss of testes and sterility. With that said however, gonadectomy is far less expensive and much more convenient than GnRH agonists and antagonists in the long run.

Testosterone blockade with androgen receptor antagonists

High-dose bicalutamide monotherapy (e.g., 150–300 mg/day) is an option for androgen deprivation therapy (link). However, bicalutamide monotherapy increases testosterone and hence estradiol levels. The testosterone will be blocked by bicalutamide and will not have effects, but estradiol is increased to a concentration range that allows for marked or full feminization, including breast development. In addition, bicalutamide alone, even at very high doses, might not be enough to completely block male-range testosterone (link). With these considerations, if the goal is full demasculinization with no feminization or breast development, bicalutamide monotherapy is not something that, at least alone, can achieve this.

High-dose bicalutamide is expensive and potentially cost-prohibitive. High-dose spironolactone monotherapy is not a good option for this route as it is a relatively weak antiandrogen and likely falls far short of being able to handle male-range levels of testosterone (at least 200 mg/day appears to be required to fully block *female* testosterone levels; source; sixth paragraph specifically). Concomitant partial suppression of testosterone and estrogen levels via additional use of a progestogen (e.g., cyproterone acetate) may be a more feasible option than an androgen receptor antagonist alone.

Some potentially major advantages of high-dose bicalutamide monotherapy are that in contrast to marked or full suppression of testosterone levels, bicalutamide monotherapy largely preserves sexual desire and erectile function and likely does not result in infertility.

Other options: lower doses, 5α-reductase inhibitors, and nandrolone decanoate

Another option is only partial demasculinization, which can be achieved essentially by using lower dosages of the medications discussed above (e.g., cyproterone acetate, bicalutamide). If desired, 5α-reductase inhibitors can be added in this context to more substantially decrease scalp hair loss and body hair growth. Note that if testosterone is more fully suppressed or blocked however, there is likely to be little or no benefit with 5α-reductase inhibitors.

Yet another possibility could be to incorporate low-dose nandrolone decanoate, an androgen receptor agonist and anabolic–androgenic steroid (AAS) with much less masculinizing/androgenic effect in skin and hair follicles (link). This drug will help to suppress and hence replace testosterone levels. Nandrolone decanoate might also have the benefit of helping to maintain sexual desire and function. However, nandrolone decanoate was recently discontinued in the United States. Oxandrolone is another, similar AAS, but has been associated with liver toxicity.

Avoiding estrogen deficiency

While androgen deprivation therapy is effective for achieving the desired changes – specifically demasculinization without feminization – it is *not recommended by itself*. This is because estradiol is produced from testosterone and hence androgen deprivation results in estrogen deficiency as well. Estrogens are essential for maintaining bone density in both men and women, and without them, a person will quickly lose bone mass, eventually develop osteoporosis, and be at a high risk for bone fractures. Skeletal/postural disfigurement will also eventually occur (image, image). In addition, the person is likely to experience other menopause-like symptoms, such as hot flashes, mood and sleep issues, sexual dysfunction (e.g., low sexual desire, erectile dysfunction), and accelerated aging of the skin (link). An increased risk of weight gain, type 2 diabetes, cardiovascular disease, and dementia is associated with androgen/estrogen deficiency as well. As such, extended deprivation of both androgens and estrogens with no estrogenic supplementation is not advisable in the slightest.

With that said, a couple of clarifications should be made. Due to preservation of estradiol levels, high-dose bicalutamide monotherapy has minimal to no risk of bone density loss or most other menopausal symptoms. In addition, the low-dose cyproterone acetate plus low-dose bicalutamide option may have less of a risk of menopausal symptoms and possibly osteoporosis as well. This is because high-dose progestogens (of which "low-dose" cyproterone acetate certainly qualifies) can help treat certain menopausal symptoms such as hot flashes and possibly bone density loss, and also because some estradiol will be preserved (since testosterone will only be suppressed by 70 to 80% rather than more fully). With that said however, in the latter case, it's probably best not to take any risks.

Selective estrogen receptor modulators (SERMs)

Instead of only androgen and estrogen deprivation, the inclusion of so-called partial estrogens, or selective estrogen receptor modulators (SERMs), can be employed. These medications are partial agonists of the estrogen receptor, and have mixed estrogenic and antiestrogenic effects depending on the tissue. For example, the SERM raloxifene has estrogenic effects in bone, fat tissue, and the liver, but antiestrogenic effects in the breasts. In general, SERMs reduce bone density loss and osteoporosis risk while not causing breast development (and actually blocking it). A full list of SERMs can be found here. However, practically speaking, only raloxifene (Evista), tamoxifen (Nolvadex), and toremifene (Fareston) are available, inexpensive, and commonly used. For an overview of the estrogenic and antiestrogenic effects of the different SERMs in different tissues, see here. In general, SERMs have a fairly similar pattern of effects. Although we have some idea of the differential tissue effects of SERMs, in many cases we do not know how they behave in specific tissues. For example, only a single clinical study has shown that a SERM, specifically raloxifene, has estrogenic effects in fat tissue (link). In addition, it's less clear how SERMs behave in, for example, skin, or in most of the brain.

SERMs also have various side effects. For instance, SERMs commonly produce hot flashes as an adverse effect. However, the fairly recently introduced combination of bazedoxifene/conjugated estrogens (Duavee) has been found to *reduce* the incidence of hot flashes in postmenopausal women (source). It is still on-patent and hence is expensive however. In any case, SERMs are also likely to produce other menopause-like symptoms. Additionally, SERMs have estrogenic effects in the liver and therefore increase production of coagulation factors and decrease production of insulin-like growth factor-1, among other potentially undesirable changes. Due to the increase in coagulation with SERMs, they have a notable risk of blood clots and cardiovascular complications like stroke. Some SERMs, like tamoxifen, also have unique off-target actions and risks, like rare liver toxicity. Raloxifene is probably among the safer SERMs.

SERMs are effective for maintaining bone density. However, they are, unfortunately, only partially effective for this purpose; significantly more so than no treatment at all, but less so than estrogens. Indeed, SERMs have actually been found to significantly antagonize the effects of estradiol on bone (source). In addition to SERMs, other measures to maintain bone mineral density, such as bisphosphonates like alendronic acid, calcium supplementation, and/or vitamin D supplementation, could be included for further benefit to bone health (source, source). Bisphosphonates have adverse effects and risks however. Weight-bearing exercise is also beneficial for bone density (source). Interestingly, probably due to its off-target antimineralocorticoid activity, spironolactone may be an option to prevent bone density loss; it was found at 100 mg/day in one randomized controlled trial

to fully prevent GnRH agonist-induced bone density loss in women (source). However, this was a single small study that has yet to be replicated, and hence supporting evidence is weak.

Low-dose estrogen supplementation

An alternative to partial estrogens is low-dose estrogen therapy. The problem with this route however is that, in the absence of testosterone, estrogens are highly effective at inducing feminization even at low levels. For example, late pubertal girls and cisgender women with complete androgen insensitivity syndrome (CAIS) have estradiol levels of only 30 to 50 pg/mL (high male range or just above it) yet have complete feminization, including full breast development. See here and here for information and photographs of CAIS women to get an idea. A dosage of oral estradiol of roughly 2 mg/day or estradiol levels of about 30 to 50 pg/mL are what are needed for complete prevention of bone density loss, yet such levels of estradiol are able to induce full feminization (source, source). With that caveat however, estradiol has a much better tolerability and safety profile than SERMs. But taking estradiol in conjunction with marked androgen deprivation, even at only low doses, would essentially be a full transition. It may be feasible to take it at very low doses, achieving estradiol levels of only maybe 20 pg/mL, however. But this would not adequately protect against bone density loss and other menopause-like symptoms, and would likely still produce at least partial feminization. (Even GnRH agonists/antagonists and orchiectomy alone have a rate of mild gynecomastia of as high as 15%; source.)

Onset and reversibility of bone density loss

Somewhat reassuringly, bone density has been found to substantially or fully recover within a few years following discontinuation of progestogen-only birth control (and consequent marked but partial suppression of estradiol levels) in young premenopausal women (source). Hence, a limited-duration treatment period, for instance to try out non-binary/femboy hormone therapy, might be reasonably safe in terms of bone health. However, long-term therapy should definitely ensure adequate measures against bone density loss.

Prevention or minimization of breast development

Suppression or blockade of estrogens

If the goal is to produce full demasculinization and some or full feminization with the sole exception of breast development, there are a number of ways to possibly achieve this. Androgen deprivation without estrogen supplementation will achieve demasculinization without any feminization or breast development (except for bicalutamide monotherapy of course). However, it's not recommended for reasons described above and wouldn't provide feminization. SERMs are an option; in addition to their capacity to treat osteoporosis, they are used to treat gynecomastia in men, and are capable of fully blocking gynecomastia induced by estrogens when used at sufficient doses (source). However, SERMs may allow for only partial feminization rather than full. Aromatase inhibitors, in contrast to SERMs, have no apparent place in this form of hormone therapy, as they are, surprisingly, poorly effective for prevention of gynecomastia (source, source).

A problem with SERMs: increased testosterone levels

A problem with the use of SERMs to prevent breast development is that when they are used in a person assigned male at birth in whom the gonads are intact and testosterone levels are not suppressed, they will induce a substantial increase in gonadal testosterone production and hence

circulating testosterone levels. In men with hypogonadism (low testosterone levels), the SERMs clomifene (20–50 mg/day) and enclomifene (12.5–25 mg/day) increase testosterone levels from about 200–300 ng/dL to about 450–600 ng/dL (a change of about 2.0- to 2.5-fold, with an absolute increase of 250–400 ng/dL in this patient population) (source, source). Because they are so effective at increasing testosterone levels, SERMs are used to treat male hypogonadism as an alternative to exogenous testosterone administration. Worse still, SERMs appear to cause even greater increases in testosterone levels in non-hypogonadal men. One study found that 50 mg/day clomifene increased testosterone levels by about 850 ng/dL in healthy younger men and by about 500 ng/dL in elderly men (source).

If testosterone levels are suppressed, increases in testosterone levels with SERMs will, depending on the degree of testosterone suppression, be less applicable (e.g., with high-dose progestogen therapy) or not applicable at all (e.g., with medical/surgical castration). However, if a SERM is combined with, say, bicalutamide alone, the situation may become even worse. This is because bicalutamide itself produces considerable increases in testosterone levels similarly to SERMs. In elderly men with prostate cancer, bicalutamide monotherapy induces a 1.5- to 2.0-fold rise in testosterone levels, increasing them from about 300–400 ng/dL to about 500–600 ng/dL (an absolute change of about 150–250 ng/dL in this patient group) (source). In healthy younger men, bicalutamide has been reported to increase testosterone levels to the "upper end of the normal male range" (presumably into the range of around 900–1,200 ng/dL) (source).

As bicalutamide is a competitive antagonist of the androgen receptor, its efficacy is fundamentally both dose-dependent and dependent on testosterone levels. Consequently, in combination with a SERM, it is possible that testosterone levels will become too high for bicalutamide to block. Moreover, endogenous androgens and estrogens are together responsible for maintaining normal homeostatic negative feedback on the hypothalamic–pituitary–gonadal axis (HPG axis) in people assigned male at birth. It seems logical that with little to suppress the axis, gonadal production and hence circulating levels of testosterone and estradiol may simply continue to rise until they overwhelm bicalutamide and/or the SERM it's combined with and restore negative feedback on the HPG axis. For these reasons, it's possible that the combination of bicalutamide and a SERM alone might not be a practical option for non-conventional feminizing hormone therapy.

With all of that said however, the combination of bicalutamide and tamoxifen has been assessed in various studies in men with prostate cancer (source), and increases in testosterone levels have, rather surprisingly, not been a problem in these studies. In terms of the findings, bicalutamide and tamoxifen together do, as expected, increase total testosterone levels. However, the rise in total testosterone levels is not much different from that which occurs with bicalutamide alone. Moreover, free testosterone levels are either increased to a certain degree or are not actually raised at all (source, source, source). This is thought to be due to the fact that SERMs have potent estrogenic effects in the liver and result in increased production of sex hormone-binding globulin (SHBG), consequently reducing the fraction of free and hence bioactive testosterone in the circulation. This serves to offset the biological influence of the increase in total testosterone levels. In accordance, and reassuringly, unfavorable changes in markers of androgen receptor signaling, like higher prostate-specific antigen (PSA) levels, have not been observed relative to bicalutamide alone in the studies.

It's not clear why studies of bicalutamide plus tamoxifen have observed increases in total testosterone levels that are not that different from those of bicalutamide alone. Whatever the reason,

these studies suggest that the combination of bicalutamide and tamoxifen (or certain other SERMs) might actually be feasible still for non-conventional feminizing hormone therapy. With that said however, elderly men are a different patient population than non-binary transfeminine people and femboys. Older men have diminished increases in testosterone levels with bicalutamide and SERMs compared to healthy young men. In relation to this, the combination might not be as favorable for younger people assigned male at birth.

Tamoxifen very well may be exchangeable with raloxifene for use in combination with bicalutamide. However, it should be noted that in contrast to tamoxifen, raloxifene has never been studied in combination with bicalutamide. Or, at least, not in gonadally intact men; one study of bicalutamide with raloxifene in castrated men with prostate cancer does exist, but that doesn't provide much in the way of useful information (source). Nor has raloxifene actually been properly studied for prevention of gynecomastia. A single retrospective chart review reported that it was effective for pubertal gynecomastia in boys (source). But that's all the data we have. Conversely, there are many high-quality studies of tamoxifen for prevention of gynecomastia, including in combination with bicalutamide.

In any case, used by themselves in men, raloxifene has been found to result in lower increases in testosterone levels than tamoxifen or toremifene (source). As such, bicalutamide and raloxifene together may indeed be similar in terms of testosterone levels relative to the combination of bicalutamide and tamoxifen. This might just be due to raloxifene having lower efficacy as a SERM than tamoxifen or toremifene at the relevant clinical doses however (source).

Topical androgens

Another possibility for prevention of breast development is topical application of a non-aromatizable androgen (i.e., an androgen that can't be converted into an estrogen), such as dihydrotestosterone (DHT; Andractim), to the breasts. Androgens substantially oppose the actions of estrogens in the breasts, and have been shown to be effective in the treatment of gynecomastia similarly to SERMs (example).

Unfortunately, pharmaceutical topical DHT is only available today in France (link). Some compounding pharmacies in certain countries *might* provide topical DHT preparations. However, DHT is reportedly not available from any compounding pharmacies in the United States (source). In contrast to DHT, testosterone readily converts into estradiol via aromatization and can actually induce some gynecomastia due to excessive estrogenic exposure. As such, unlike non-aromatizable androgens like DHT, use of testosterone for this purpose isn't appropriate. There are few or no other options for topical androgens besides testosterone and DHT, so the practicality of this route is limited.

In contrast to SERMs, topical androgens may not be fully effective for preventing breast development. In addition, topical application of androgens to the breasts is very likely to cause local body hair growth and other local androgenic effects (e.g., masculine skin changes, oily skin, acne), which for many transfeminine individuals is probably unacceptable. Lastly, there is a risk of systemic distribution of the topically applied androgen (example) and hence androgenic or masculinizing effects elsewhere in the body. This risk would be lessened in combination with an androgen receptor antagonist like bicalutamide however, although androgen receptor antagonists also risk blocking the local effects of the topical androgen.

Breast removal surgery and breast irradiation

Two non-medication-based alternatives for prevention of breast development are prophylactic surgical breast removal and prophylactic breast irradiation.

If there is no excess skin, mastectomy, or breast removal surgery, can remove the breasts without leaving obvious scars, as was the case in this young transgender man. Mastectomy is a highly effective means of preventing breast development. Of course, it requires surgery however.

Exposure of the breasts to radiation inhibits subsequent breast development (photos). Irradiation of the breasts is an inexpensive, easy, and effective technique that is commonly used as prophylaxis against gynecomastia in men with prostate cancer treated with estrogens or high-dose bicalutamide monotherapy (source). It is less effective than SERMs however and generally only reduces the severity of gynecomastia rather than fully prevents it (source).

More concerningly, there is a theoretical increased risk of breast cancer with exposure of the breasts to radiation (source). Research has observed a 100-fold higher incidence of breast cancer in young women whose breasts were exposed to radiation during childhood as a consequence of radiotherapy for cancer when compared to other young women (source). On the other hand, limited available evidence so far suggests minimal if any increase in breast cancer incidence in elderly men treated with breast irradiation to prevent gynecomastia (source, source). We have no data on what breast cancer risk might be like in young breast-irradiated transfeminine people. In addition to theoretical cancer risk, low incidences of heart and lung issues have also been associated with breast irradiation in elderly men with prostate cancer (source, source). Due to these health risks, breast irradiation for prevention of breast development may be an inadvisable option.

An obvious drawback of breast development prevention with both surgical breast removal and prophylactic breast irradiation is that they are irreversible. If the person ever changes their mind about not wanting breasts or eventually decides to fully transition (a not uncommon occurrence), there is no going back on the choice to permanently negate breast development.

Degree, onset, and reversibility of breast development

For reasons that are not entirely clear, it's notable that transgender women tend to have suboptimal/poor breast development (source, photo examples). The reason for this is not entirely clear, but there are various theoretical possibilities (link). Likewise, in generally elderly men with prostate cancer, high-dose bicalutamide monotherapy and high-dose estrogen therapy both cause high rates of gynecomastia but produce only mild-to-moderate gynecomastia in 90% of cases (source, source). (Whether their advanced age is a factor here or not is uncertain though.) Hence, any person who was assigned male at birth should, *generally speaking or on average*, not *necessarily* expect a marked degree of breast development. There are always exceptions however, with a subset of transgender women experiencing considerable breast development. Hence, the degree of breast development is a matter of chance, and caution should be advised.

There are a few things to note about breast development. One is that it occurs slowly and is not something that happens overnight. Another is that it's not going to progress further if medications are withdrawn. And finally, it seems to be at least partially reversible if medications are discontinued within a certain amount of time (e.g., one year) (source, source). For these reasons, it should be entirely feasible for a given person to self-monitor their breast development, and, if it becomes too much for their liking, to alter their medication regimen as desired in order to prevent further or reverse existing breast growth. Hence, breast growth is not necessarily something that should be feared excessively.

Summary of main potential treatment options

For full demasculinization and partial to full feminization with the exception of minimal or no breast development, here is a review of the major potential treatment options for feminizing hormone therapy for non-binary people and femboys discussed above:

- High-dose progestogen (e.g., low-dose cyproterone acetate) + androgen receptor antagonist (e.g., bicalutamide or spironolactone) + SERM or low-dose estradiol
- GnRH agonist/antagonist or orchiectomy + SERM or low-dose estradiol
- High-dose bicalutamide + SERM (possibly)

And variations thereof based on the above discussion as well (e.g., 5α-reductase inhibitors, prophylactic mastectomy, additional bone density interventions, etc.).

As some of the commenters have touched on, low- to moderate-dose estradiol monotherapy, resulting in only some or partial suppression of testosterone levels, may also be a useful approach. At least partial breast development is likely to occur with such a route however.

Obtaining care and medications

It may be difficult to find a physician who offers transgender hormone therapy and is familiar with non-conventional hormonal therapy approaches for non-binary transgender people. It can likewise be difficult to find such a physician who is actually *willing* to treat such people. And this is probably *extremely* difficult for cisgender femboys, who may best be served by simply claiming to be non-binary or transgender but just wanting an atypical transition. With these considerations, do-it-yourself (DIY) hormone therapy may oftentimes be the most or only real practical option in this particular situation. For materials on DIY hormone therapy, see the Wiki at r/TransDIY, which includes a list of no-prescription-needed online pharmacies.