

Pharmacists caring for transgender persons

Am J Health-Syst Pharm. 2016; 73:e557-61

Jennifer Cocohoba, Pharm.D., BCPS, AAHVP, Department of Clinical Pharmacy, School of Pharmacy, University of California San Francisco, San Francisco, CA.

Address correspondence to Dr. Cocohoba (jennifer.cocohoba@ucsf.edu).

This article will appear in the January 15, 2017, issue of *AJHP*.

Copyright © 2016, American Society of Health-System Pharmacists, Inc. All rights reserved. 1079-2082/16/0000-e557.

DOI 10.2146/ajhp151053

Recent media coverage regarding Caitlyn Jenner's gender transition and emerging popular television series and movies have made transgenderism a household discussion topic. The American Psychological Association uses the term *transgender* to describe anyone whose "gender identity, gender expression, or behavior does not conform to that typically associated with the sex to which they were assigned at birth."¹ Related constructs include *gender identity* (one's sense of being male or female or something between) and *gender expression* (outward characteristics such as clothing, hair, voice, body attributes, and behavior). Gender identity and expression can be fluid, and the use of the terms *transgender*, *gender identity*, and *gender expression* continues to evolve with the experiences of the community. Estimates of the number of transgender people tend to be imprecise due to the disparate ways survey data regarding gender are collected and variations in how individuals self-report gender. Results of a survey conducted by the Williams Institute suggest that transgender individuals make up 0.3% of the U.S. population, with approximately 700,000 transgender persons living in the United States.²

Although transgender persons are appearing more often in the popular media, the overall health and health-related needs of this community are not well understood. Research on transgender individuals is sparse due to many factors, including the challenge of identifying individuals who are willing to come forward for research and the population being low on funding priority lists. Of all the research studies funded by the National Institutes of Health (NIH) during the period 1989–2011, only 0.5% examined lesbian, gay, bisexual, or transgender health concerns; studies that addressed transgender health made up a very small proportion of that subgroup.³ As funding initiatives evolve, an increasing number of studies have uncovered health disparities between transgender persons and their cisgender counterparts (i.e., persons whose sense of personal identity and gender agrees with their birth sex). In a survey of 6,450 individuals, transgender persons were four times more likely than the general population to have an income less than \$10,000 per year, were less likely to have health insurance, and often experienced discrimination in the form of refusal of care or verbal harassment by healthcare providers.⁴ Lived experiences of transgender persons can take an important toll on mental health: 41% of respondents had attempted suicide, as compared with 1.6% of the general population, and many reported suffering from depression. Data from cohort studies suggest that transgender women are at four times higher risk for acquiring human immunodeficiency virus (HIV) infection relative to the general population.⁵ Transgender people may also be more likely than other people to use tobacco products.⁶ These health

outcomes for transgender persons are strongly influenced by experiences of sexual stigma—the negative regard, inferior status, and relative powerlessness that society collectively accords to any nonheterosexual behavior—and discrimination, both inside and outside the health-care system, and by healthcare team members' lack of understanding of transgender health issues.⁷⁻⁹ These factors remain important barriers, and transgender patients may ultimately avoid seeking care because of them. Recent trends in the literature suggest that there may be a rising consciousness of transgender issues among healthcare providers. Studies suggest a burgeoning awareness of the lack of training in transgender health and recognition of the shortcomings of hospitals and clinics in making transgender persons feel welcome, respected, and comfortable enough to seek care.¹⁰⁻¹² Influential groups are recognizing the need to set priorities that address transgender health issues. For example, the Institute of Medicine published a report outlining research priorities for lesbian, gay, bisexual, and transgender (LGBT) persons in 2011.¹³ The Department of Health and Human Services' Healthy People 2020 initiative includes a goal to "improve the health, safety, and well-being of [LGBT] individuals."¹⁴ Despite this cognizance of the importance of recognizing and addressing transgender health issues, there is still much work to be done to translate these principles into day-to-day healthcare practice.

The health inequities, gaps in care, and paucity of research discussed above present unique opportunities for the profession of pharmacy to substantively contribute to precision medicine for transgender persons. NIH defines precision medicine as

“an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.”¹⁵ Medications are one means people use to target their gender expression; societally defined male and female characteristics encompass a broad spectrum, and an individual may wish to enhance any number of characteristics using medication therapy. Precision medicine can allow transgender persons to individualize their therapy to achieve their desired gender expression. There may be a handful of U.S. pharmacists who have experience caring for transgender individuals and knowledge of their unique health and medication issues, and the pharmacy literature remains deficient in this regard: My brief search of five nationally circulated pharmacy journals unearthed only three articles that specifically addressed transgender medication therapies and eight other articles that mentioned the transgender community in the context of HIV prevention methods, mental health, men’s and women’s health, or cultural competence.

Stepping stones and tools. In order for more pharmacists to begin playing an active part in the care of transgender individuals, certain foundational elements need to be put into place. First, pharmacists require education on transgender medicine and drug therapies commonly used by members of the transgender community. These medications may include sex steroids and other adjunctive therapies used to produce secondary sex characteristics that are in line with the individual’s desired gender expression. In 2011 the World Professional Association for Transgender Health published the seventh version of its “Standards of Care for the Health of Transsexual, Transgender, and Gender-Nonconforming People.”¹⁶ Local clinics with experienced health-care providers may have developed their own protocols and guidelines. Familiarity with these guidelines and the medications contained within can

help pharmacists appreciate the continuum of gender that transgender persons use in their individual expressions. For example, some choose not to use medicines to enhance sex characteristics. Yet, familiarity with the medications used for such purposes can help pharmacists recognize when patients are beginning the process of medical transition or identify those who have already begun medical transition. This foundational understanding can assist pharmacists in individualizing treatment and monitoring medication safety. In one example, intramuscular doses of estradiol valerate for feminization total an average 80 mg monthly, whereas the typical doses used for hypogonadism total approximately 20 mg monthly. Pharmacists familiar with the added risks of deep vein thrombosis (DVT) with higher-dose estrogen therapy can assist by monitoring patients’ blood pressure, weight, and pulse; asking about swelling and warmth in the extremities; and counseling patients on signs and symptoms of DVT. Optimal calculation of creatinine clearance in transgender persons requires taking into account muscle mass and hormone therapy: Pharmacists can provide valuable clinical judgment when medications must be renally dosed.^{17,18}

Along with increasing their baseline level of knowledge regarding transgender medicine, pharmacy practitioners would benefit from increased training in cultural competency to improve their interactions with transgender patients. As with any subgroup, the transgender community is made up of diverse individuals who have had unique life experiences. At the same time, pharmacists can be sensitive to the experiences that appear to be common to many within the group. Qualitative studies and surveys have documented marginalization of LGBT persons within the medical system and instances of discrimination experienced by transgender individuals seeking healthcare. Although there are no published studies specifically examining transgender individuals’

perceptions of pharmacy care, pharmacists should strive to foster pharmacy environments that are welcoming to all patients. Pharmacists must be mindful of how they address their transgender patients and the gender pronouns they use.¹⁹ It is simply a matter of asking the patient what name he or she would like to be addressed by and what gender pronoun is preferred. Electronic health and pharmacy records are often difficult to modify, and the name and gender documented in health records or on government-issued identification cards may be discordant with the chosen forms of address. Another general pharmacy consideration includes offering private spaces for consultation. Raising awareness of some of these issues faced by transgender individuals can occur during pharmacy school; a transgender panel discussion conducted at one pharmacy school as part of a required diversity course was well received by students and thought to be useful for future practice.²⁰

As transgender persons are less likely to have health insurance and less likely to be engaged in care, they are also likely to have poor access to medications; this includes both hormone therapy and medicines required for treatment of chronic diseases. Pharmacists can have a strong impact in facilitating access to medications for these patients. Many payers do not cover hormone therapies used by transgender persons, and use of these medications can be cost prohibitive if patients have to pay out of pocket. Pharmacists can increase access by providing additional support for medication therapy for transgender (and other) patients who are underinsured or uninsured. This support can include helping patients navigate through complex prior-authorization processes, learning the diagnosis codes through which coverage of these medicines might be obtained, and referring patients to compounding pharmacies that may be able to offer hormone therapy at lower prices. By becoming more aware of the challenges transgender patients face within the healthcare sys-

tem, improving access to medications, linking patients to culturally sensitive healthcare providers, and serving as an educational resource, pharmacists might be able to discourage the common practice in the transgender community of purchasing sex-steroid hormones and other medications on the street. This practice is dangerous for obvious reasons, such as the potential for purchasing adulterated products, improper or nonsterile administration of injectable hormones, and excessive dosing leading to increased toxicity. Pharmacists can also advocate for LGBT patients by communicating with suppliers and pharmaceutical companies: Drug shortages or difficulty obtaining drugs such as injectable estrogen may drive patients to seek hormones from unsafe sources.

Boundless research opportunities. Many medical practices associated with helping transgender individuals achieve their desired gender expression are based on clinical experience. There have been no randomized controlled trials examining different feminizing or masculinizing regimens, likely due to the ethics of conducting such trials. Not all transgender individuals want to (or are able to) undergo sex reassignment surgery, and chronic medication therapy may be required. Research studies have begun to address potential sex-related differences in absorption, distribution, metabolism, and elimination of medications. It will also be important to conduct research on how pharmacokinetic parameters might be altered in transgender persons taking hormone therapy and how this might affect drug response and optimal dosing. These areas are ripe with opportunity for pharmacists to contribute to the body of knowledge regarding the safety and efficacy of medication use in transgender patients. The profession of pharmacy needs to continue supporting the development of clinician-scientists who can lead research to address gaps in knowledge of the medication therapies used by transgender patients. This support can include formal training in

research methods during pharmacy school, postgraduate residencies, and fellowships and supportive mentoring for early-career pharmacists interested in creating research platforms around transgender precision medicine.

Regimens used for feminization and masculinization include various combinations of sex steroids (estrogen- or testosterone-based regimens) and supportive therapies (e.g., spironolactone, progesterones, finasteride).¹⁶ Little is understood about patients' unique responses to those therapies. Research is needed to better understand pharmacokinetic factors, dose-response relationships, and epigenetic factors that play a role in the speed and extent to which feminization or masculinization occurs in a particular patient. There are opportunities to conduct clinical research on a host of other types of medications, such as dietary supplements and herbal therapies, to determine whether they are actually beneficial (or are potentially harmful) when used by transgender patients seeking to achieve a certain gender expression. For example, no published research studies have examined the effects of phytoestrogens or dehydroepiandrosterone (DHEA), but these more "natural" agents for transitioning are commonly mentioned on transgender blogs and Internet sites. Data from a large European cohort study suggested that long-term hormone therapy in transgender patients is safe.²¹ Electronic pharmacy records that hold prescription information may be an untapped pharmacovigilance tool that can contribute to confirming this finding. There may be ways to use these records to identify trends in sex-steroid prescribing patterns and (by combining medication-use and health outcomes data) identify signals for adverse effects.

There is a great need for further research on sex-steroid interactions with other medications. For example, transgender patients are at higher risk for acquiring HIV disease than the general population, and there are

many potential interactions among hormones they might be using and antiretroviral medications. There is very limited research on this topic; typically, the hormones used in drug-interaction studies are derived from oral contraceptives (e.g., ethinyl estradiol)—not the types of estrogens used in medical transition regimens—and the doses studied are not nearly equivalent to those usually used by transgender individuals.²²⁻²⁴ There are also potential pharmacodynamic interactions that could be studied (e.g., concurrent use of testosterone and nevirapine, which may raise the risk of hepatotoxicity). To complicate matters further, hormone therapy may have an impact on HIV disease progression and transmission, and this requires further study.²⁵

The potential for increased cardiovascular risk and other metabolic effects of sex steroids provides other areas for research for pharmacists.²⁶⁻²⁹ Although reported experience in cohort studies suggests that hormone therapy is safe and effective, there have been documented increases in triglycerides and potential alterations in blood pressure in hormone users. The magnitude of potential risk associated with sex-steroid use is yet to be determined; research needs to be conducted on medications for cardiovascular risk reduction, therapeutic lifestyle changes, and other issues involved in keeping transgender patients safe and healthy.

There is also the opportunity for pharmacists to conduct health services research, including the development and testing of pharmacy-based interventions to improve health in the transgender community. As transgender individuals are at increased risk for HIV infection, pharmacy-based HIV testing programs and HIV prevention efforts, such as syringe access for i.v. drug users and provision of pre-exposure prophylaxis medications, are all potential models that may increase access to care for transgender clients. Pharmacy-based programs to encourage smoking cessation may be

very effective in this population and might mitigate cardiovascular risk. Existing pharmacy programs that offer preventive health interventions, such as immunizations and blood pressure and other screening services, may be particularly important for transgender patients who do not have primary care providers and for those who remain wary of seeking care within traditional health systems due to negative experiences.

Conclusion. With the various changes occurring in healthcare, the profession of pharmacy is faced with great opportunities. Alternative care models involving pharmacists may be a venue for encouraging transgender patients to engage in primary care. Pharmacists can assist in tailoring therapy at the level of the individual patient and conducting research to help guide clinical decisions. Through the processes of providing culturally sensitive care, getting involved in precision medicine, and conducting clinical research, pharmacists will be poised to have a substantial positive impact on health in the transgender community.

Acknowledgments

Madeline Deutsch, M.D., Efen Bose, Pharm.D., and Timothy Mok, Pharm.D., are acknowledged for assistance in manuscript preparation.

Disclosures

The author has declared no potential conflicts of interest.

References

- American Psychological Association. Answers to your questions about transgender people, gender identity, and gender expression. www.apa.org/topics/lgbt/transgender.pdf (accessed 2016 Jun 29).
- Gates GJ. How many people are lesbian, gay, bisexual, and transgender? (April 2011). <http://williamsinstitute.law.ucla.edu/research/census-lgbt-demographics-studies/how-many-people-are-lesbian-gay-bisexual-and-transgender/> (accessed 2015 Dec 12).
- Coulter RW, Kenst KS, Bowen DJ, Scout. Research funded by the National Institutes of Health on the health of lesbian, gay, bisexual, and transgender populations. *Am J Public Health*. 2014; 104:e105-12.
- Grant JM, Mottet LA, Tanis J et al. Injustice at every turn: a report of the National Transgender Discrimination Survey (2011). www.endtransdiscrimination.org/report.html (accessed 2015 Dec 1).
- Herbst JH, Jacobs ED, Finlayson TJ et al. Estimating HIV prevalence and risk behaviors of transgender persons in the United States: a systematic review. *AIDS Behav*. 2008; 12:1-17.
- Sell RL, Dunn PM. Inclusion of lesbian, gay, bisexual and transgender people in tobacco use-related surveillance and epidemiological research. *J LGBT Health Res*. 2008; 4:27-42.
- Herek GM. Confronting sexual stigma and prejudice: theory and practice. *J Soc Issues*. 2007; 63:905-25.
- Kosenko K, Rintamaki L, Raney S, Maness K. Transgender patient perceptions of stigma in health care contexts. *Med Care*. 2013; 51:819-22.
- Cruz TM. Assessing access to care for transgender and gender nonconforming people: a consideration of diversity in combating discrimination. *Soc Sci Med*. 2014; 110:65-73.
- Buchholz L. Transgender care moves into the mainstream. *JAMA*. 2015; 314:1785-7.
- Lim FA, Brown DV Jr, Justin Kim SM. Addressing health care disparities in the lesbian, gay, bisexual, and transgender population: a review of best practices. *Am J Nurs*. 2014; 114:24-34.
- McClain Z, Hawkins LA, Yehia BR. Creating welcoming spaces for lesbian, gay, bisexual, and transgender (LGBT) patients: an evaluation of the healthcare environment. *J Homosex*. 2016; 63:387-93.
- Institute of Medicine. The health of lesbian, gay, bisexual, and transgender people: building a foundation for better understanding. Washington, DC: National Academies Press; 2011:1-306.
- HealthyPeople.gov. 2020 topics and objectives: lesbian, gay, bisexual, and transgender health (2013). www.healthypeople.gov/2020/topicsobjectives2020/overview.aspx?topicid=25 (accessed 2016 Jul 5).
- National Library of Medicine. Genetics home reference: your guide to understanding genetic conditions. <http://ghr.nlm.nih.gov/primer/precisionmedicine/definition> (accessed 2016 Jul 5).
- Coleman E, Bockting W, Botzer M et al. Standards of care for the health of transsexual, transgender, and gender-nonconforming people. *Int J Transgend*. 2011; 13:165-232.
- Leach C, Bishop B. Pharmacotherapy considerations in the management of transgender patients: an alternative viewpoint. *Pharmacotherapy*. 2016; 36:e28-9.
- Fernandez JD, Tannock LR. Metabolic effects of hormone therapy in transgender patients. *Endocr Pract*. 2016; 22:383-8.
- Deutsch MB, Buchholz D. Electronic health records and transgender patients—practical recommendations for the collection of gender identity data. *J Gen Intern Med*. 2015; 30:843-7.
- Parkhill AL, Mathews JL, Fearing S, Gainsburg J. A transgender health care panel discussion in a required diversity course. *Am J Pharm Educ*. 2014; 78:article 81.
- Asscheman H, Giltay EJ, Megens JA et al. A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones. *Eur J Endocrinol*. 2011; 164:635-42.
- Song IH, Borland J, Chen S et al. Dolutegravir has no effect on the pharmacokinetics of oral contraceptives with norgestimate and ethinyl estradiol. *Ann Pharmacother*. 2015; 49:784-9.
- Mildvan D, Yarrish R, Marshak A et al. Pharmacokinetic interaction between nevirapine and ethinyl estradiol/norethindrone when administered concurrently to HIV-infected women. *J Acquir Immune Defic Syndr*. 2002; 29:471-7.
- Ouellet D, Hsu A, Qian J et al. Effect of ritonavir on the pharmacokinetics of ethinyl oestradiol in healthy female volunteers. *Br J Clin Pharmacol*. 1998; 46:111-6.
- Cabrera-Munoz E, Hernandez-Hernandez OT, Camacho-Arroyo I. Role of estradiol and progesterone in HIV susceptibility and disease progression. *Mini Rev Med Chem*. 2012; 12:1049-54.
- Asscheman H, T'Sjoen G, Lemaire A et al. Venous thrombo-embolism as a complication of cross-sex hormone treatment of male-to-female transsexual subjects: a review. *Andrologia*. 2014; 46:791-5.
- Xiang J, Wang Y, Su K et al. Ritonavir binds to and downregulates estrogen receptors: molecular mechanism of promoting early atherosclerosis. *Exp Cell Res*. 2014; 327:318-30.

28. Elamin MB, Garcia MZ, Murad MH et al. Effect of sex steroid use on cardiovascular risk in transsexual individuals: a systematic review and meta-analysis. *Clin Endocrinol (Oxf)*. 2010; 72:1-10.
29. Fernandez JD, Tannock LR. Metabolic effects of hormone therapy in transgender patients. *Endocr Pract*. 2016; 22:383-8.