ADVANCING EXCELLENCE IN TRANSGENDER HEALTH

Primary Care and Preventive Health Needs of Transgender Patients

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Massachusetts League of Community Health Centers

Continuing Medical Education Disclosure

- Program Faculty: Julie Thompson, PA-C
- Current Position: Physician Assistant, Fenway Health
- Disclosure: No relevant financial relationships. All hormone therapy for transgender people is off-label.

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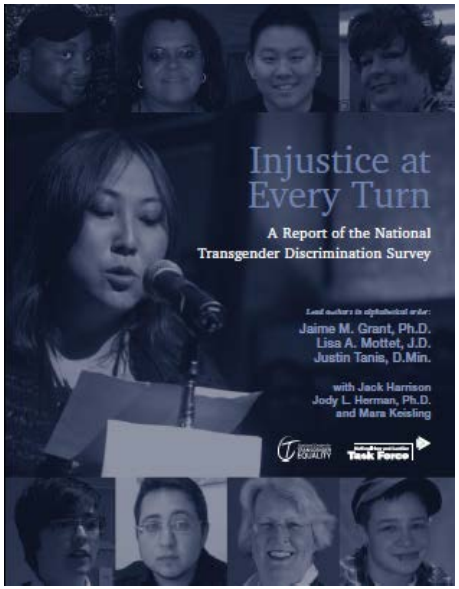
Objectives

1. Morbidity and Mortality
   - Transphobia/gender abuse
   - Marginalization
2. Primary Care — Integrated approach to trans health
   - Access to care
3. Primary Preventive Screening Recommendations

Barriers to Medical Care for Transgender Patients

- Economically disadvantaged
- Geographic and social isolation
- Lack of insurance coverage
- Lack of provider training and competence
- Overt or covert harassment by provider or support staff. Lack of support and training by clinic
- Stigma of Gender Clinics



2015 U.S. TRANSGENDER SURVEY

Morbidity and Mortality in the Transgender Community

European Journal of Endocrinology (2011) **164** 635–642 ISSN 0804-4643

CLINICAL STUDY

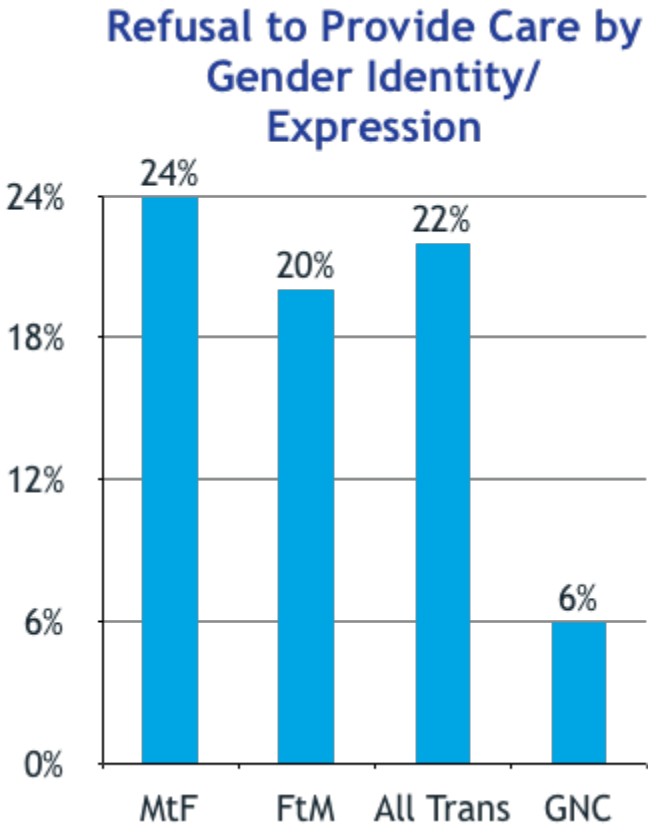
A long-term follow-up study of mortality in transsexuals receiving treatment with cross-sex hormones

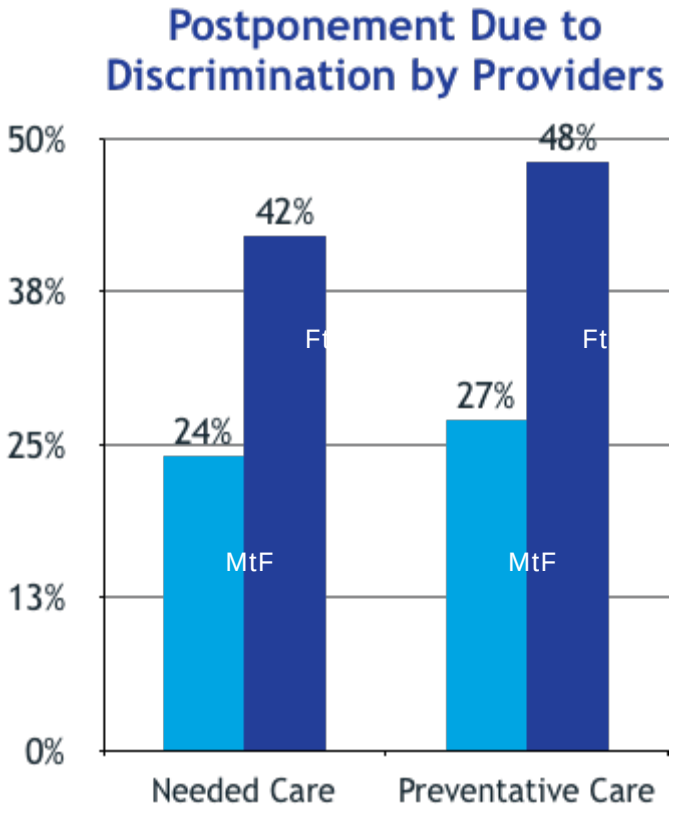
Henk Asscheman[1], Erik J Giltay[3], Jos A J Megens[2], W (Pim) de Ronde[1], Michael A A van Trotsenburg[2] and Louis J G Gooren[1]

- Significant increase in mortality is seen amongst transgender individuals compared to the general population
  - 50% higher mortality rate in **MTF** patients
- Most of the increase in mortality was due to higher rates of **AIDS, suicide, drug-related deaths**

Barriers to Medical Care for Transgender Patients

- Discrimination, abuse, and lack of access to care





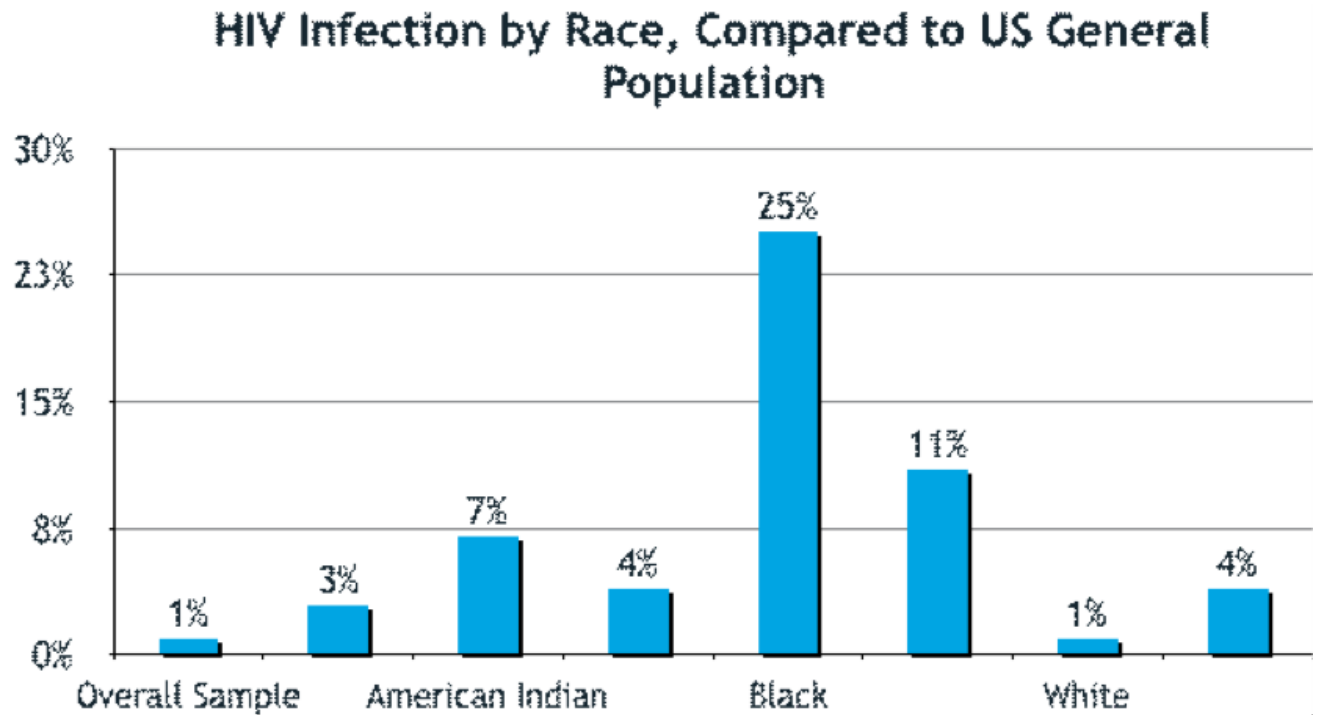
Source: National Transgender Discrimination Survey, 2011

HIV Infection

- NTDS – Over 4 times the national average of HIV infection
- Self reported incidence of HIV infection was 2.64% overall, 4.28% in MTF, and 15.3% in self-identified sex workers
  - Rate of 0.6% in the general population
- HIV infection: Average rate about 27% in studies done on MTF (mostly urban) populations
- Rates in FTM are not well-documented, seem to be low (only 0.51% in the NTDS)
  - BUT, FTM report relatively high rates of high-risk sexual behavior

Death rates due to AIDS is 30 times higher for trans individuals

HIV Infection



- Increased health disparities for trans women of color
  - In NTDS, 24.9% of black trans women and 10.9% of Latina trans women were HIV infected

Depression and Suicide

- 82% of USTS respondents reported seriously contemplating suicide at some point in their life
- 40% of transgender/gender variant individuals report having attempted suicide
  - 7% attempted suicide in the past yr (compared with 0.6% of general pop)
  - 71% of those who have attempted, did so more than once

- Suicidality was associated with:
  - Family support
  - Victim of physical or sexual violence
  - Homelessness
  - Sex work
  - Loss of job secondary to their gender identity

Depression and Suicide

- >1/3 (34%) reported that their first suicide attempt was at the age of 13 or YOUNGER
  - 92% reported that their first attempt was before they were 25yrs old

- Suicide deaths 6 times higher than in general population in Dutch cohort

Trauma and Abuse

- In a study looking at 571 trans women in the NYC Metro area, lifetime prevalence of psychological and physical abuse are 78% and 50%, respectively

- Previous and ongoing trauma stands out as significant risk factor and clinically challenging
  - 38-60% past experiences of physical violence
  - 27-46% victims of sexual assault
  - Most violence attributable to gender identity or expression

Trauma and Abuse

- Persistent abuse was very high during adolescence—most often perpetrated by parents or other family members

Substance Abuse

- Drug-related deaths in MTF were 13 times higher than in the general population in the Dutch cohort

- USTS: 29% of respondents used illicit drugs to cope with mistreatment due to gender identity or expression … this is 3x the general US population (10%)

Homelessness

- Rates of homelessness
  - Nearly 1/3 (30%) of respondents have experienced homelessness at some point in their life
  - 12% experienced homelessness within the past year because they were transgender
    - 26% of respondents who were homeless in the past year avoided staying in homeless shelters because they feared they would be mistreated as a transgender person
    - 70% of those who stayed in a shelter in the past yr reported some form of mistreatment for being transgender

Homelessness is associated with higher rates of sex work, drug use, HIV+ status, and suicide attempts

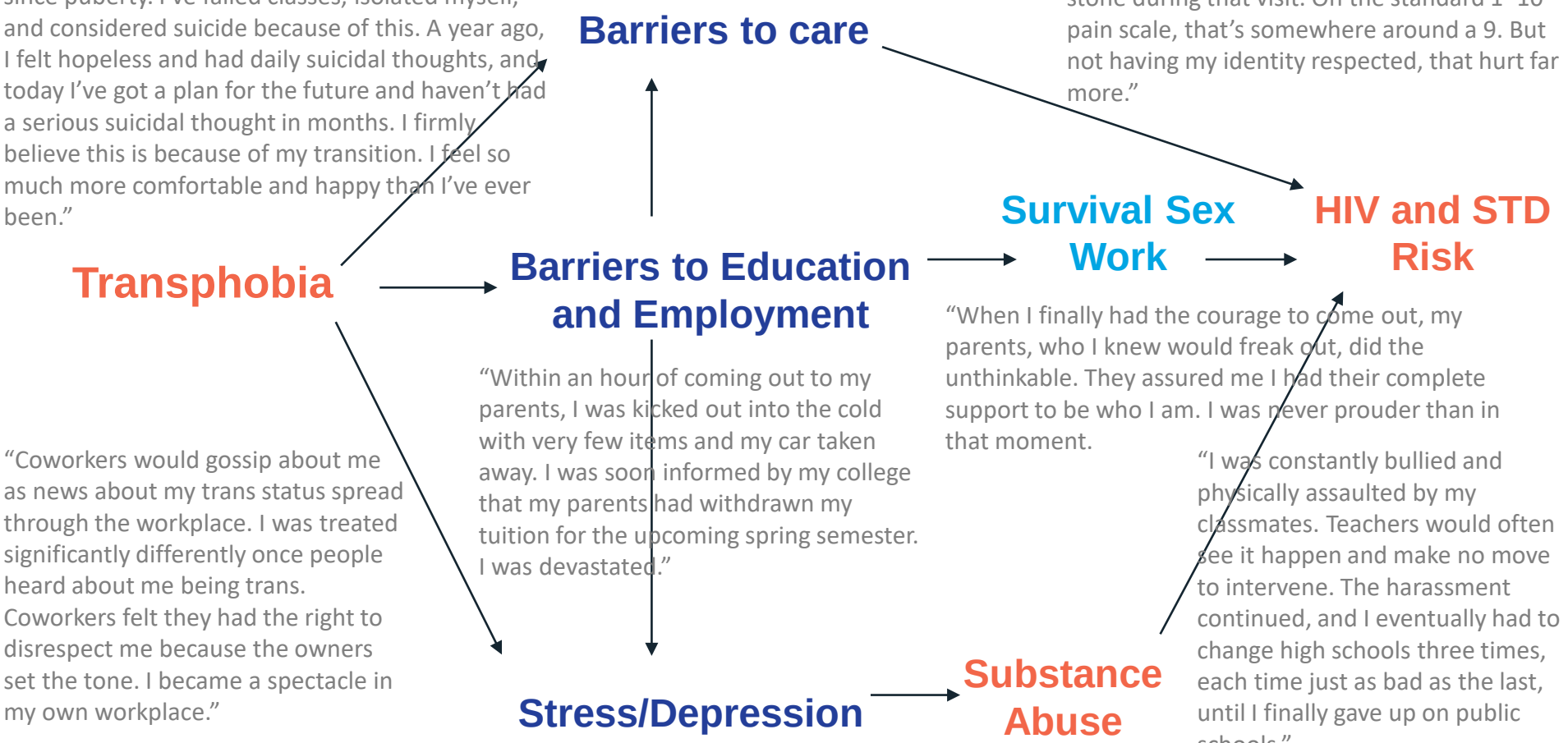
"I've tried shelters. The men's ones aren't safe for trans men: if those men find out who you are, you're opening yourself up to physical and sexual violence. And when I turned to the women's shelters, I was too masculine to make the women comfortable."

"My first time in jail, and possibly the time I became infected with HIV, was the scariest of all. There were so many times I was in jail and participated in unprotected sex out of fear and necessity. This is just one of the harsh realities for young vulnerable trans women like myself. It is truly bewildering that this reality was so commonly accepted among trans women of color."

"I couldn't find work. I watched one guy throw away my application literally 30 seconds after turning it in. I resorted to escorting. It's the only way to keep food in my belly and a roof over my head."

"I have struggled with depression and anxiety ever since puberty. I've failed classes, isolated myself, and considered suicide because of this. A year ago, I felt hopeless and had daily suicidal thoughts, and today I've got a plan for the future and haven't had a serious suicidal thought in months. I firmly believe this is because of my transition. I feel so much more comfortable and happy than I've ever been."

"I was consistently misnamed and misgendered throughout my hospital stay. I passed a kidney stone during that visit. On the standard 1–10 pain scale, that's somewhere around a 9. But not having my identity respected, that hurt far more."



"When I finally had the courage to come out, my parents, who I knew would freak out, did the unthinkable. They assured me I had their complete support to be who I am. I was never prouder than in that moment.

"Within an hour of coming out to my parents, I was kicked out into the cold with very few items and my car taken away. I was soon informed by my college that my parents had withdrawn my tuition for the upcoming spring semester. I was devastated."

"Coworkers would gossip about me as news about my trans status spread through the workplace. I was treated significantly differently once people heard about me being trans. Coworkers felt they had the right to disrespect me because the owners set the tone. I became a spectacle in my own workplace."

"I was constantly bullied and physically assaulted by my classmates. Teachers would often see it happen and make no move to intervene. The harassment continued, and I eventually had to change high schools three times, each time just as bad as the last, until I finally gave up on public schools."

Nuttbrock 2009, Psychiatric Impact of Gender-Related Abuse Across the Life Course of Male-to-Female Transgender Persons. JSexResearch

Impact of Gender Affirming Care

- Impact of gender affirming care as it relates to health outcomes and impact on quality of life
  - E. Willson, et al 2015, S. Reisner et all 2016, E Gomez-Gil et al 2012, White Hughto et al 2016, T. Ainsworth 2010, S. Colton Meirer et al 2011, J. Sevelius 2013, R. Testa et al 2012, etc…

*** The ability to access transition-related medical care has an overall positive impact on physical health, mental health, and quality of life**

- High rates of physical violence due to being "visibly gender non-conforming." Suicide attempts were significantly related to experiencing physical violence
- Suicide and engagement in HIV-related risk behaviors explained has coping responses to extreme discrimination

**Hormonal therapy assoc w/ higher scores in general and mental health

**Hormones, breast augmentation, and genital surgery all assoc w/ lower odds of SI, binge drinking, and drug use

- African Americans and Latinas were estimated to have the lowest utilization of any transition-related medical care

Primary Care

- Increasing access
  - Caregiver need not be an endocrinologist

- Increasing comprehensive care
  - Goal of care is to facilitate affirmation and alleviate gender dysphoria
  - Two categories
    - General health concerns — promote and ensure physical health and emotional and social well-being
    - Issues specific to transgender people — Varying emotional, behavioral, medical, surgical and ethical issues

Advances in Treating Gender Dysphoria

"The latest 2011 revisions to the SOC realize that transgender, transsexual, and gender nonconforming people have **unique health care needs to promote their overall health and well-being, and that those needs *extend beyond hormonal treatment and surgical intervention.*"**

Eli Coleman, PhD, SOC Committee Chair, Professor and Director at Program in Human Sexuality, University of Minnesota.

- Increasingly standards of care are focused on *individualized* approaches to alleviate gender dysphoria.
- Approaches use various combinations of psychotherapy, hormone therapy, and surgery, AND case work, social work, OB, cardiology, etc. to affirm gender and provide quality health care

Providing Care

Cultural Competency and Cultural Humility

- Familiarize yourself with commonly used terms and the diversity of identities
- If you are not sure what terms to use, **ask** your patient what they prefer
- **Listen** to how people describe their own identities, partners, and bodies; use the same terms!
  - Refer to patients by their preferred name and pronouns
  - Refer to body parts by their preferred name
- Avoid asking questions out of curiosity; ask what you NEED to know
- **Listen** to people's experiences
  - Recognize that many have had negative experiences in the past and may perceive "slights," even when not intended
- **Don't forget the basics!**

Taking a History

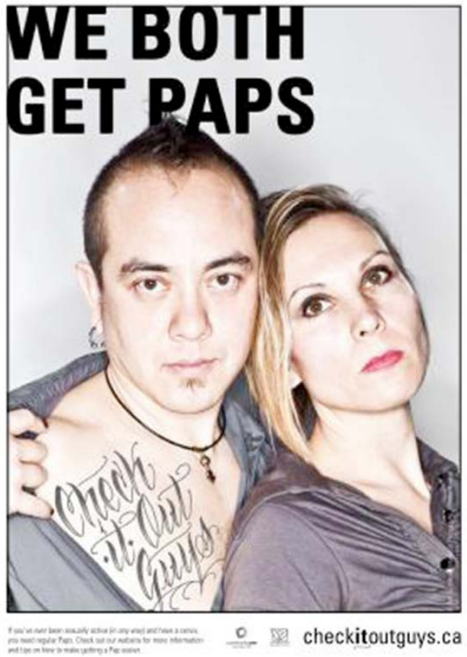
- Same as for all patients, but pay specific attention to health disparities
- Be aware of contexts that increase health risks
  - What are risk factors for smoking, substance use, or engaging in sexual risk behaviors? What is the incidence of trauma/ abuse in this population?
- Ask about social support; be aware of possible rejection by family or community of origin, harassment, and discrimination
- Ask about use of cross-sex hormones, gender affirmation surgeries, and use of silicone

Preventive Health and Primary Care

- Treat the anatomy that is present:

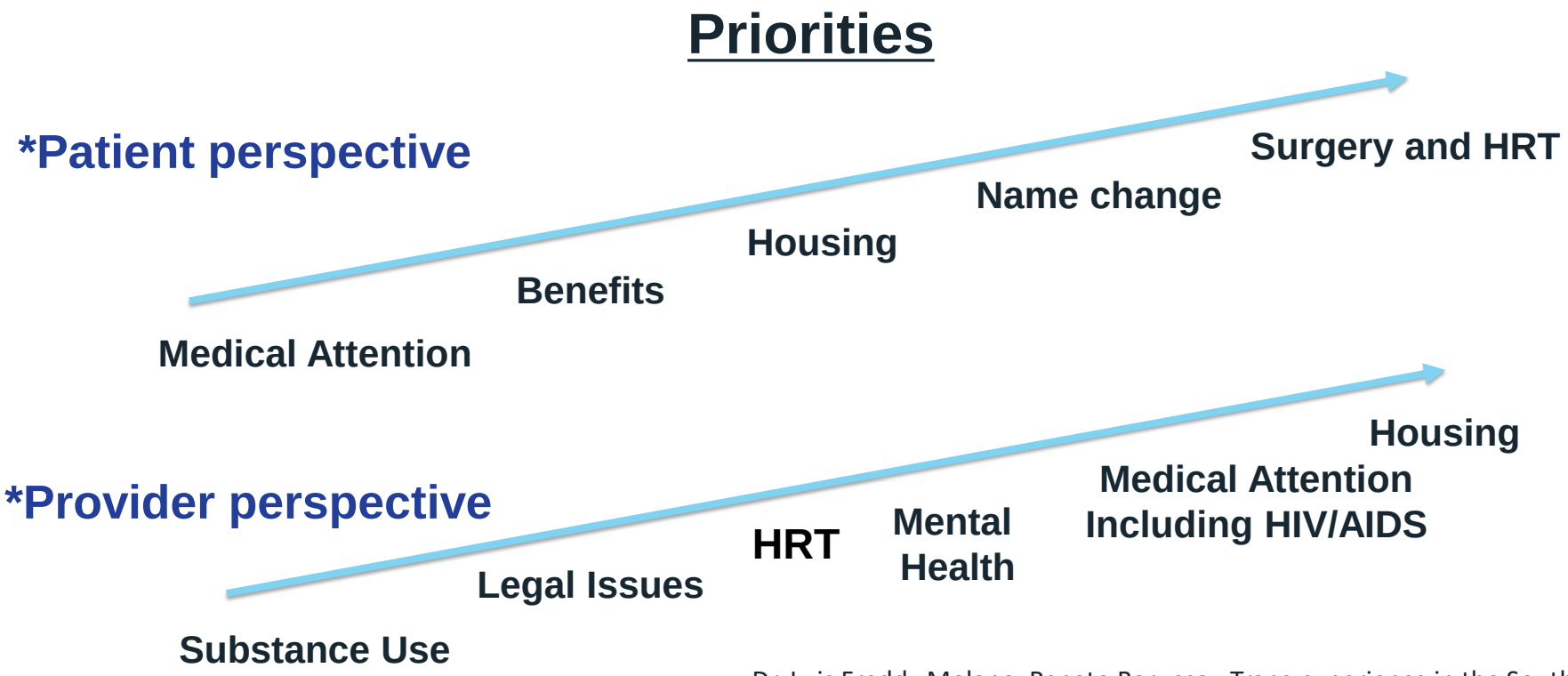
  If you have it, check it!

- Clinical care should be based on an up-to-date anatomical inventory:
  - Breasts
  - Cervix
  - Ovaries
  - Penis
  - Prostate
  - Testes
  - Uterus
  - Vagina



Guidelines for Clinicians

- Recognize that the need to affirm one's gender identity can supersede other critical health concerns — Meet the patient where they are at.



Dr. Luis Freddy Molano, Renato Barucco. Trans-experience in the South Brox
http://www.nyhiv.org/pdfs/FreddyMolanoTransgenderPresentationUSCA.pdf

Preventive Health for Transmasculine Individuals

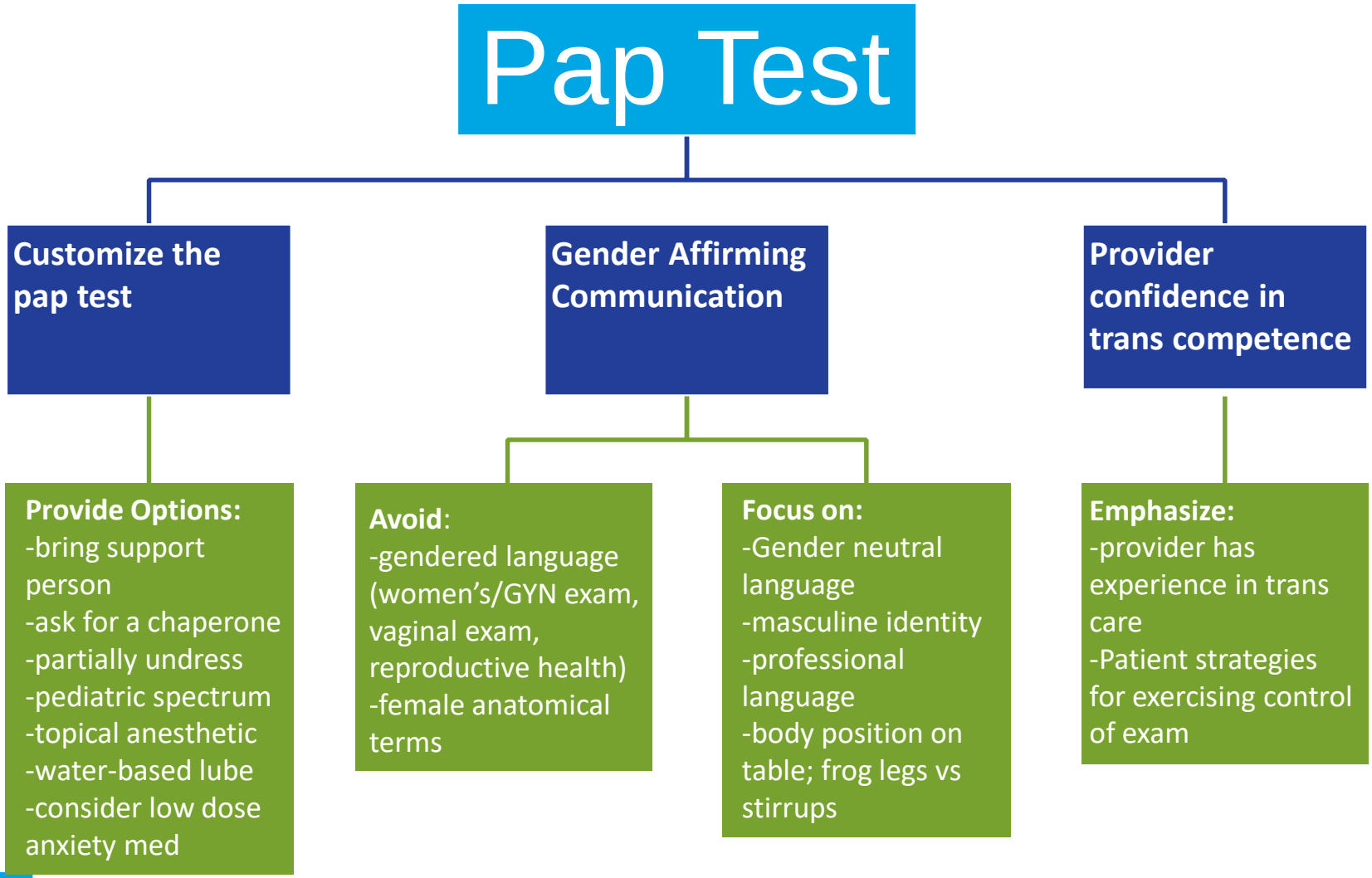
Health Maintenance in Transmasculine Individuals

Pap smears

- As per natal females
  - Cervical cancer screening should never be a requirement for testosterone therapy
- Testosterone can cause atrophy of the cervical epithelium mimicking dysplasia
- Increase in “unsatisfactory” samples seen: 10.8% (10 times higher than in non-trans women) [1]
  - Transmasculine indiv found to have reduced screening rates and longer latency to follow-up testing [1,2]

1. Peitzmeier, et al. J Gen Intern Med. 2014; 29(5):778-784. FtM Patients Have a High Prevalence of Unsatisfactory Paps Compared to Non-Transgender Females: Implications of Cervical Cancer Screening
2. Peitzmeier, et al. Am J Prev Med. 2014; 47(6):808-812. Pap Test Use is Lower Among FtM Patients than Non-Transgender Women

Health Maintenance in Transmasculine Individuals



Health Maintenance in Transmasculine Individuals

Endometrial hyperplasia

- Futterweit, et al (1986): 9/19 FtM patients had proliferative endometrium at the time of hysterectomy; 3/19 had endometrial hyperplasia.

- Perrone, et al (2009): 27 FtM undergoing endometrial bx; all had atrophic endometrium similar to post-menopausal controls.
- Grynberg, et al (2010):112 FtM given androgen for at least 6mo prior to THSO - endometrial atrophy in 45%

* Urban, Teng & Kapp (2011): First case report of endometrial carcinoma in an FtM patient after 7 years on testosterone tx

Health Maintenance in Transmasculine Individuals

Endometrial hyperplasia

- Hysterectomy for 1° prevention of endometrial cancer is NOT currently recommended
- Routine screening for endometrial cancer in transmen with ultrasound is not evidenced based and unrealistic
  - Expense
  - Tolerability
- Unexplained bleeding needs to be explored and patients need to inform their providers when this occurs

Health Maintenance in Transmasculine Individuals

Pelvic Pain and Abnormal Uterine Bleeding

*Acute:

- Estrogen-deficient atrophic changes vs infectious
- Testosterone Dose, administration, frequency
- Depression, trauma history, PTSD

*Chronic/Persistent:

- Cessation of menses expected within 6mo - combo of T inducing suppression of ovulation and endometrial atrophy
  - Musculoskeletal disorders - genotypic female skeleton and increased muscle mass
  - Body habits
  - Structural - Endometrial polyps, adenomyosis, leiomyomata, endometrial hyperplasia, malignancy
  - Adhesions from prior surgeries/post-surgical sequelae
  - Non-structural - pregnancy, coagulopathy, ovulatory dysfunction

Health Maintenance in Transmasculine Individuals

Mammograms and CBE

- As per natal females if no chest reconstruction
- If post-op — no reliable evidence exists to guide screening recommendations
  - yearly chest exams?

- 2013, 2015 Gooren (Dutch cohort): Total of 4 reported cases of breast cancer in FtM cohort — 20.4/100,000 incidence
- 2015 Brown (US VA system): 7 cases in transmasculine individuals, but with incidence still less than the non-trans general population data (20.0/100,000 VHA yrs)

- 2009 Grynberg, et al: 100 mastectomies in transmen after avg of 3.7 years on T.
  - 93% with decreased glandular tissue and increased fibrous connective tissue

Health Maintenance in Transmasculine Individuals

Bone density screening

- T appears to be overall protective: Larger trabecular bone size after just 1yr, and most studies show preservation of cortical bone(G T'Sjoen 2015)
  - Increased muscle mass / mechanical loading
  - Role of aromatization of T to estrogen

- Insufficient evidence to guide recommendations. *Consider >65 yrs old, or post-gonadectomy and off hormone therapy >5yrs*

- Measuring LH levels: LH is inversely proportional to bone density measures — may be a marker for adequate levels of testosterone to preserve bone mass (Ruetsche, 2005)

Health Maintenance in Transmasculine Individuals

Contraception

- Testosterone does not reliably prevent ovulation
- Consider LARCs without estrogen
  - Mirena IUD
  - Nexplanon
  - Depo-Provera

Original Research

Transgender Men Who Experienced Pregnancy After Female-to-Male Gender Transitioning

Alexis D. Light, MD, MPH, Juno Obedin-Maliver, MD, MPH, Jae M. Sevelius, PhD, and Jennifer L. Kerns, MD, MPH

Pregnancy

- Important to discuss an individual's desires and opening door to conversation about what is possible and options available
  - Wierckx, 2011 Reproductive Wish in Transsexual Men: 50 trans men surveyed
    - **More than half** (54%) expressed a desire to have children
    - 37.5 % would have preserved oocytes if it had been possible

Health Maintenance in Transmasculine Individuals

Cardiovascular Disease

- No increased risk of cardiovascular or cerebrovascular events in several short and medium-term follow up studies
  - Increase systolic blood pressure
  - Decreased in HDL
  - Increased BMI

- In Asscheman's 2011 series, only 1 MI in FTM at age 72 after 42 years of testosterone tx.

Health Maintenance in Transmasculine Individuals

- Trans men seem to have an increase in obesity compared to their natal male counterparts (though not natal female), poorer lipid profile, elevated blood pressure, and potential increase in hematocrit
- Trans men have increased smoking rates compared to the general public

ALL of these factors together lead to concern for possible future cardiovascular events

Health Maintenance in Transmasculine Individuals

Diabetes

- Slightly higher prevalence of Diabetes type 2 than control population
  - Comparison to PCOS/androgen excess in non-trans women
    - No correlation between T levels and IR parameters either in women with PCOS nor in FtMs before or after T treatment
    - IR parameters were more strongly associated with obesity than attributable to T levels, as was also apparent from the sensitivity analysis of women with PCOS comparing FtMs with PCOS women of similar BMI and age
    - Administration of oral contraceptives to PCOS women decreases T levels, with no change of fasting insulin and IR indices

Cupist S, et al. The Impact of Testosterone Administration to Female-to-male Transsexuals on Insulin Resistance and Lipid Parameters Compared with Women with Polycyctic Ovary Syndrome. Fertil Steril, 2010; Dec 94 (7): 2647-53

- Increased endocrine screening prior to initiation of hormone therapy

Preventive Health for Transfeminine Individuals

Health Maintenance in Transfeminine Individuals

Pelvic exam/PAP smear

- Pelvic exam to assess surgical site, and then follow ups for general genital issues or concerns

Health Maintenance in Transfeminine Individuals

The pH and microflora of the neo-vagina

- Differs significantly from a natal female vagina
  1. Lack of lactobacilli
     - Natal females primarily colonized with lactobacilli, which gives antimicrobial protection
  2. Alkaline environment — lower estrogen in vaginal tissue —> no up-regulation of proton pumps and lack of protective mucus production
  3. Mixed microflora of aerobe and anaerobe species — typically found on the skin, intestine, and in bacterial vaginosis

  ** More complex BV — specifically presence of anaerobes — are difficult to treat
     - Consider treatment with clindamycin or amoxicillin

- NO candida seen

- No proper recommendations on optimal vaginal hygiene, but some speculate best to douche with warm water alone, if anything at all

Weyers S, et al. Microflora of the Penile Skin-lined Neovagina of Transsexual Women. BMC Microbiology, 2009, 9:102

Health Maintenance in Transfeminine Individuals

Hyperprolactinemia:

- Initial, transient elevation of prolactin not uncommon
- Prolactinomas - uncommon.
  - 5 cases of prolactinomas have been found in MTF patients — 10mo, 14, 18, 20, and 30 years after initiation of hormone tx
  - So, unclear if or how long to monitor, since this is quite rare

- Some suggestion that an excessive first year increase in serum prolactin concentration may identify patients at risk for autonomous prolactin secretion later in life (n=2) (Bunck 2009, Cunha 2015)
- Role of estrogen vs cyproterone acetate as cause for hyperprolactinemia (Fung 2016, Nota 2017)

Health Maintenance in Transfeminine Individuals

Mammography and CBE

- Degree and duration of estrogen exposure
  - WHI: Progestin, with estrogen, increases risk of breast cancer
- 13 Cases total in literature (3 not related to E use)
- NO increase in incidence of malignancy over the general population (incidence 20/100,000 - compared to 1.2 and 170/100,000 pt-yrs of followup for natal men and women)
- The VHA study showed the detection was late and outcomes poorer for MtF

  (Gooren 2013, Brown 2015)

- Risk factors for male breast cancer: BRCA mutations, obesity, androgen insufficiency (Klinefelter), estrogen exposure
- Ductal carcinoma is most common histological subtype of CA in natal men - most cases of CA in MtF were ductal
- ***Recommendations: Patients over age 50 who have been on feminizing endocrine agents over 5 years**

Health Maintenance in Transfeminine Individuals

Prostate exam

- as per natal men
  - Androgen antagonists may falsely decrease serum PSA levels
  - Feminizing hormonal therapy appears to decrease prostate volume and the risk of prostate cancer but to an unknown degree — effectively receiving androgen deprivation therapy!
  - In natal men, orchiectomy before age 40 appears to prevent prostate CA
  - 3 reported cases of prostate cancer in the Dutch cohort (2011) All three had orchiectomies and started hormone therapy AFTER age 40.

Health Maintenance in Transfeminine Individuals

Bone Density Screening

- Somewhat mixed results — Increase in osteopenia and osteoporosis compared to natal men, but generally preserved compared to natal women
  - Observed lower BMD in MTFs **PRIOR** to start of estrogen therapy
    (Van Caenegem, 2013)
  - Start of androgen-blockers for ~1yr, before prescribing estrogen therapy

- Decreased levels of bone turnover markers in setting of hormone therapy

- **Recommendations: Consider if over age 60 and off estrogen therapy for longer than 5 years**
  - not routinely indicated prior to orchiectomy

Health Maintenance in Transfeminine Individuals

Cardiovascular Disease

- Higher cardiovascular mortality rate in trans women than the general population
  - 64% increased risk (95% CI 43 to 87) in cardiovascular mortality was seen, however no significant difference was seen for cerebrovascular mortality
    (Asscheman, 2011)

- Maj Factors – Estrogen types (ethinyl estradiol), cyproterone acetate, supratherapeutic hormones, smoking status, obesity, baseline CV health, diabetes

- Exogenous estrogen can increase blood pressure
  - Spironolactone can lower BP
- Increased HDL and decreased LDL cholesterol, but increased triglycerides

Health Maintenance in Transfeminine Individuals

- **Weirckx, 2013**

Table 5 Description of cardiovascular events in trans women.

	Age at event (years)	Duration of HRT (years)	Cardiovascular risk factors
Venous thrombosis and/or pulmonary embolism			
Case 1	33	1	Smoker
Case 2	28	1	HC
Case 3	54	1	Smoker
Case 4	53	22	Smoker, HC, and HT
Case 5	54	1	Smoker, HC, and clotting disorder
Case 6	38	2	Smoker, HC, and surgery
Case 7	32	1	Smoker
Case 8	50	3	Smoker and HT
Case 9	32	2	HC and surgery
Case 10	44	2	Surgery
Case 11	58	11	HC
Myocardial infarction			
Case 1	52	1	Smoker and HC
Case 2	50	1	Former smoker
Case 3	42	2	Smoker, HC, and HT
TIA/CVD			
Case 1	33	2	Smoker, HC, and surgery
Case 2	53	2	Smoker, HC, HT, and type 2 diabetes mellitus
Case 3	56	10	HT and mechanic heart valve
Case 4	58	20	Smoker and HC
Case 5	56	2	Smoker

HC, hypercholesterolemia; HT, hypertension.

  - Ethinyl estradiol assoc w/3-fold increased risk of CV death (Gooren, 2011)

- Recommendations:
  - Avoid prescribing ethinyl estradiol at any point
  - Consider transdermal or low-dose oral estradiol in patients >40yrs old
  - Lifestyle behaviors — healthy diet, smoking cessation, exercise — can reduce cardiovascular risk!

Health Maintenance in Transfeminine Individuals

Venous thromboembolism

- In the Dutch cohorts, rates of 2.6% annually in first year, falling to 0.4 % thereafter, with 1 – 2% risk of death from PE,
  - BUT all but 1 of these patients was using oral ethinyl estradiol
  - Similar to CVD rates seen on controlled natal females using OCPs with high dose (50mcg) ethinyl estradiol

- Belgian cohorts also showed increased incidence of VT (6-8%), but ONLY in patients treated with ethinyl estradiol

Health Maintenance in Transfeminine Individuals

Venous thromboembolism

	Matched OR			
	Cases	Controls	Crude	Adjusted*
Nonuse	145	384	1	1
Oral Estrogen	45	39	3.6 (1.5-8.8)	4.2 (1.5-11.6)
Transdermal Estrogen	67	180	0.8 (0.4-1.6)	0.9 (0.4-2.1)

Adjustment for obesity status, familial history of VTE, history of varicose veins, education, onset of menopause, hysterectomy, and cigarette smoking

Circulation 2007

Health Maintenance in Transfeminine Individuals

Diabetes:

- Higher prevalence of DM, but almost all diagnoses made BEFORE starting estrogen therapy in trans female (Weirckx, 2013)

- Studies suggesting increased insulin resistance in the setting of estrogen, but no observed direct link between estrogen treatment and development of DM

Health Maintenance: Health Care Measures

- Sex-based health calculators — Which way do I go?! Natal sex vs affirmed gender
  - Exposure to endogenous vs exogenous hormones
  - Age of initiating gender-affirming hormones

Guidance may change as individuals begin to access puberty blocking medications and cross-sex hormones therapy

Questions?

Resources

- **UCSF Center of Excellence for Transgender Health Guidelines**
  - http://transhealth.ucsf.edu/trans?page=lib-00-00
- **Tom Waddell Health Center**
  - https://www.sfdph.org/dph/comupg/oservices/medSvs/hlthCtrs/TransGendprotocols122006.pdf
  - Vancouver Coastal Health Guidelines
  - http://transhealth.vch.ca/resources/careguidelines.html
- **The Endocrine Society Guidelines (First published September, 2009)**
  - http://www.endo-society.org/guidelines/final/upload/Endocrine-Treatment-of-Transsexual-Persons.pdf
- **Transline**
  - http://project-health.org/transline/
- **Surgical options:**
  - http://www.surgery.ubc.ca/presentarch/SRS.pdf
  - http://ai.eecs.umich.edu/people/conway/TS/SRS.html#anchor66325
  - http://ai.eecs.umich.edu/~mirror/FFS/LynnsFFS.html
  - http://ai.eecs.umich.edu/people/conway/TSsuccesses/TSsuccesses.html
  - http://www.thetransitionalmale.com/