

Beyond Paps, Periods, and Pills

**Considering the Clinical Care of Women: A Case Based
Discussion**

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**NECHA/NYSCHA Annual Meeting
November 2017**

....about 15 mi outside Boston



...The other school that starts with
“W”




....Still all women



....and, yes, one of our alums has just written a book: “What Happened”



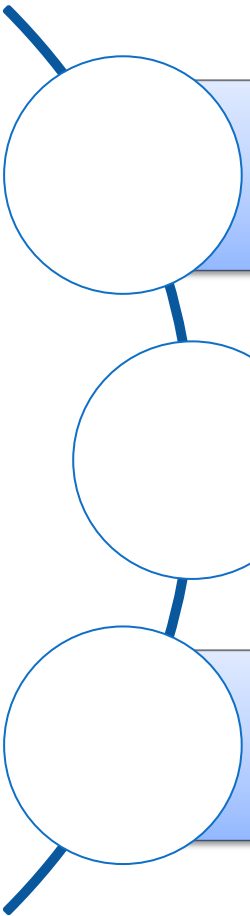
Questions for you.....

- 
- Is caring for women and women's health the same?
 - Are the terms interchangeable?
 - Why does it matter?

Caring for Women > Women's Health



Today's Objectives

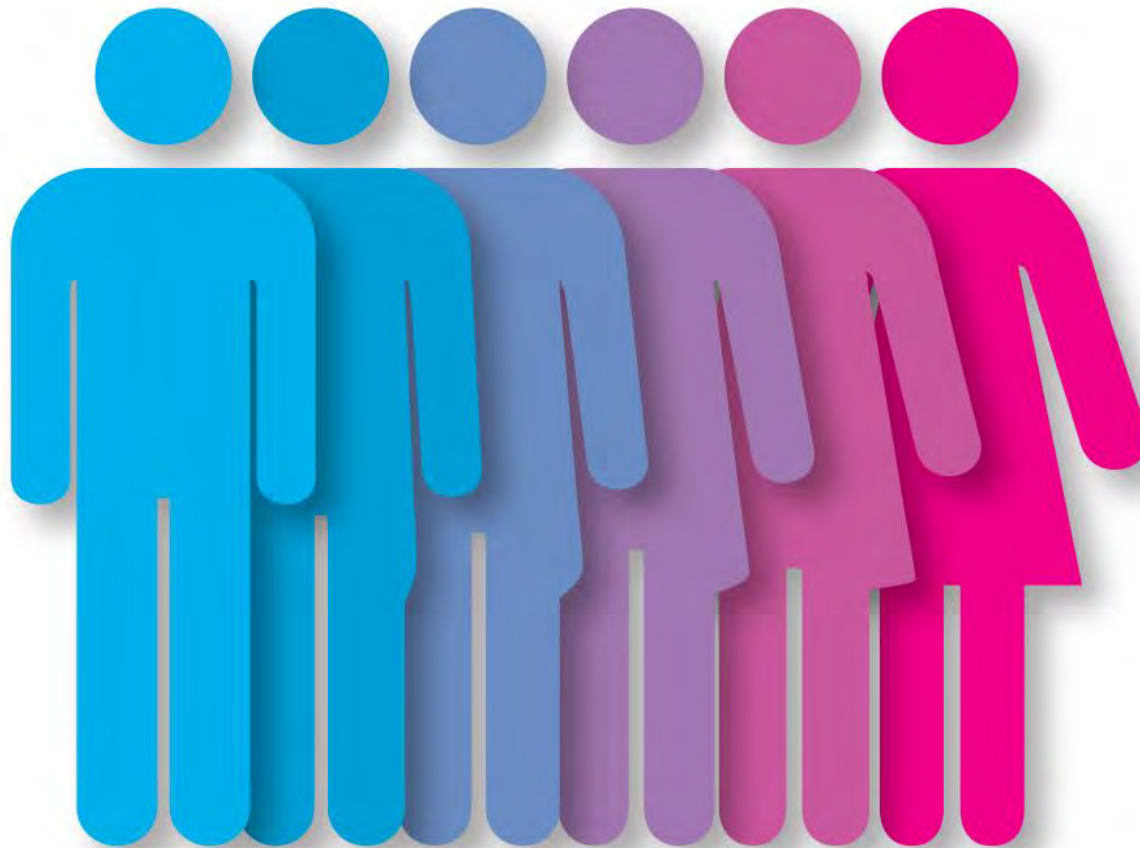


Contextualize the role and some of the implications that sex-based research can have on patient care


Identify examples of common diagnoses that present differently in women compared to men

Consider how clinical care might be approached differently in these common diagnoses

Sex and Gender



Questions for you.....

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Sex - Based Clinical Research 1950's - 1980's



medscape® www.medscape.com



"Really?"

Yes...
des PLEX®
 to prevent ABORTION, MISCARRIAGE and
 PREMATURE LABOR

*recommended for routine prophylaxis
 in ALL pregnancies...*

96 per cent live delivery with **des PLEX**
 in one series of 1200 patients*—
 — bigger and stronger babies, too.†

No gastric or other side effects with **des PLEX**
 — in either high or low dosage‡,§

Source: J Midwifery Womens Health © 2003 Elsevier Science, Inc



Sex - Based Clinical Research 1990's – 2000's



- 1990 - Office of Research on Women's Health
- 1993 – NIH Revitalization Act and FDA Reversal
- 2001 – Phase III Inclusion Guidelines

Sex - Based Clinical Research 20 years later

2011 NIH Report – 56% in
12,000 NIH studies are women
Women are involved earlier in
Phase III trials

Sex - Based Clinical Research 20 years later

- NIH can now look across the Institute for trial enrollment gaps
- Faster translation with more analysis and better reporting
- More attention to enrollment and retention of underrepresented minorities of both sexes
- More is being demanded of science

Sex - Based Clinical Research 20 years later



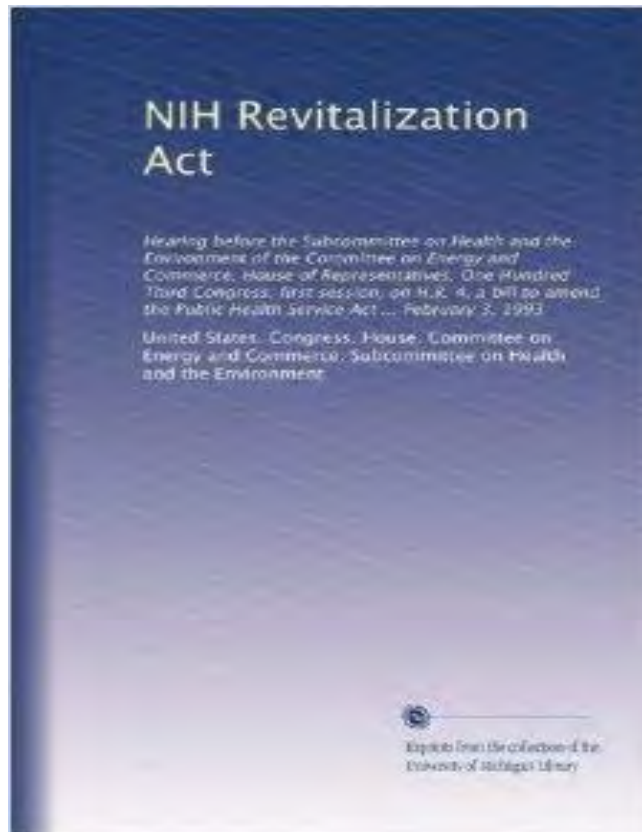
Bias in animal models

Politics -- can influence data sharing, study design, interpretation.....

Researchers can “explain away” the limitations

Sex - Based Clinical Research 20 years later

1993



2014



Cases

Minnie Header

Lotty Gasser

Maya Grainer

Nia Torre

Melanie Collier-
Shotz

“Minnie” Header



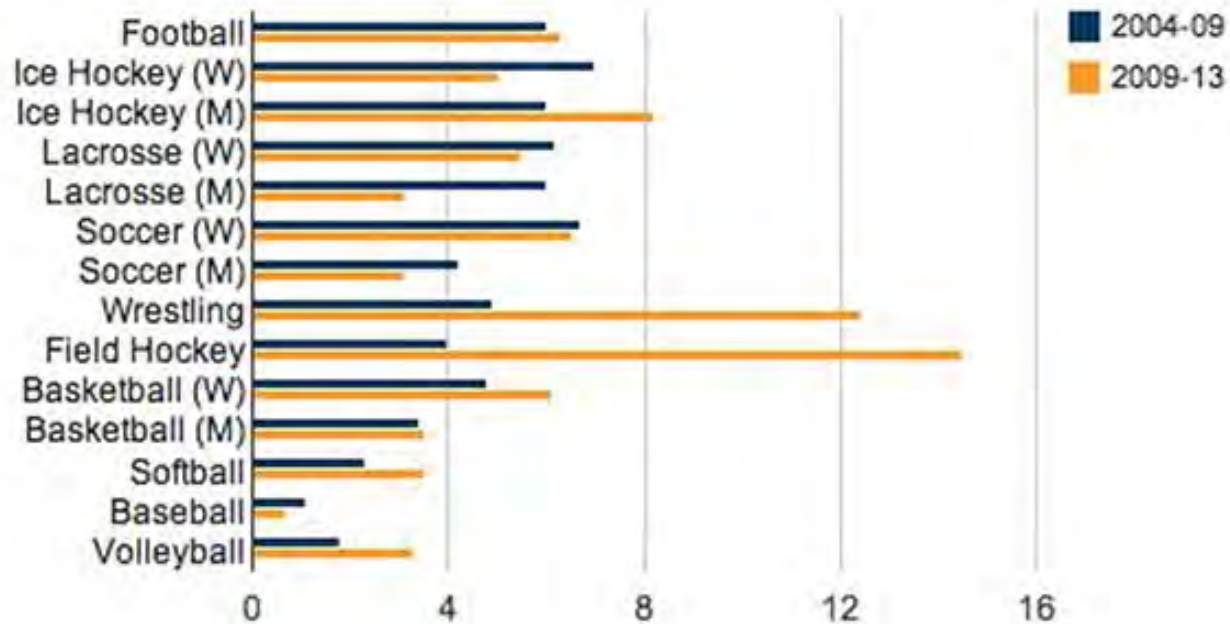
Concussion in Female Athletes

Presentation

- Annual estimates –up to 3.8 million
 - Male: Female – 2-2.8:1
- Female vs Male
 - Higher risk: neck strength and girth, ball:head ratio
 - More rapid symptom onset
 - More cognitive impairment (1.7-2x)
 - Higher reporting rates

Concussion in Female Athletes

Sports-Related Concussions in College Athletes,
per 10,000 athletic exposures



Source: The National Academies

Physiology of Concussion in Female Athletes



- Longer recovery
- Is estrogen neuroprotective? (animal models)
- Neurometabolic cascade – higher rate of glucose metabolism and cerebral blood flow mismatch

Concussion in Female Athletes

- Evaluation
 - Clinical history w/sx assessment
 - ↑ Neurobehavior and somatic sx
 - Neurocognitive assessment
 - Sex-corrected normative data
 - Balance test
- Management
 - Re-examine
 - Repeat neurocognitive testing <-> baseline comparison
 - Graduated RTP after asymptomatic at rest and integrate with cognitive exertion

Lottie Gasser

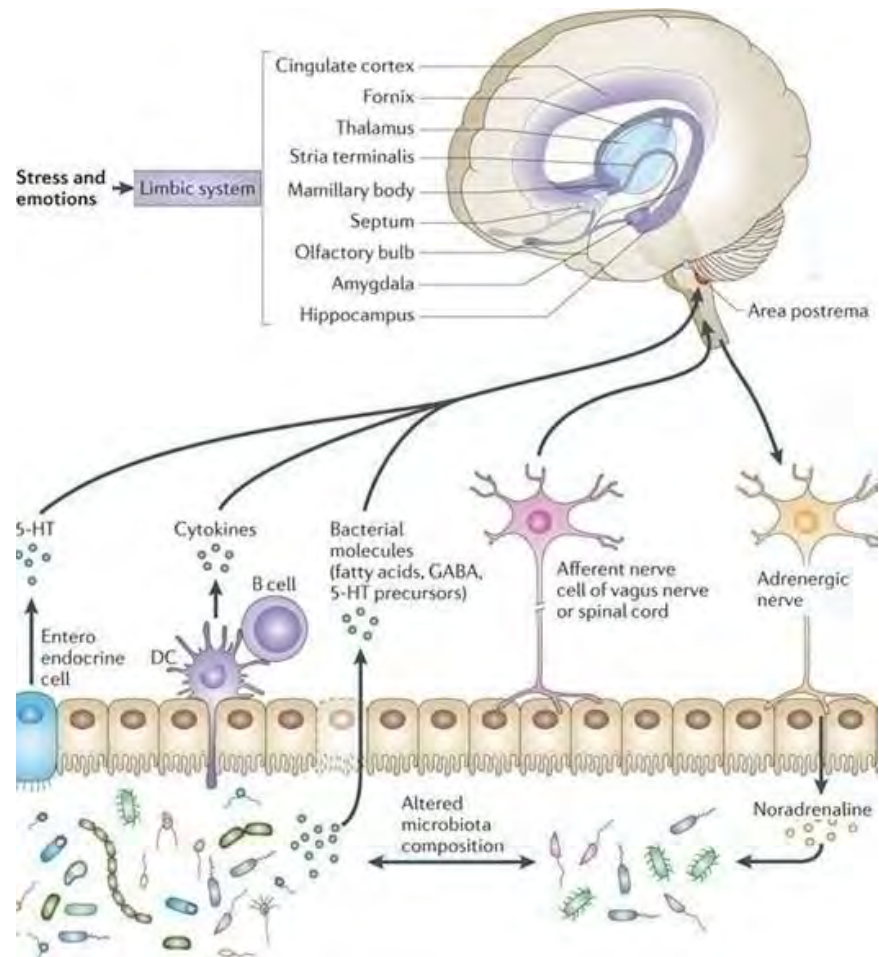


Irritable Bowel

Presentation

- Prevalence in U.S.: up to 20%, Female: male ratio = 1.5-3:1
- 50% < 35 y/o
- Underlying mechanism poorly understood
 - Cytokine interleukin 10
 - 5 HT (serotonin) in the gut and brain
 - Visceral hypersensitivity (balloon study blinded vs predicted stimulation)
 - Central pain processing (gut->cortex)
 - SERTs

IBS: Gut-Brain Connection



Rome III diagnostic criteria* for irritable bowel syndrome

Recurrent abdominal pain or discomfort ¶ at least three days per month in the last three months associated with two or more of the following:

(1) Improvement with defecation

(2) Onset associated with a change in frequency of stool

(3) Onset associated with a change in form (appearance) of stool

* Criteria fulfilled for the last three months with symptom onset at least six months prior to diagnosis.

¶ Discomfort means an uncomfortable sensation not described as pain. In pathophysiology research and clinical trials, a pain/discomfort frequency of at least two days a week during screening evaluation for subject eligibility.

Reproduced with permission from: Longstreth GF, Thompson WG, Chey WD, et al. Functional bowel disorders. Gastroenterology 2006; 130:1480.

Irritable Bowel



More females with IBS-C

- Prevalence proportional to intensity of sx



Can cluster in families
(parent studies)



More females with Post-
Infectious- IBS

Irritable Bowel

Differences to keep in mind

- Intestinal anatomy
- Pain activation(PET and fMRI)
- Other chronic pain syndromes
- Post Infectious- IBS
- Symptom profiles and impact on daily life

Irritable Bowel

Management

- Diet, ↑ fibre and OTC antispasmodics/diarrheals, CBT – no sex-specific efficacy
- Link between IBS-IBD
- Some Rx's with differential efficacy in women:
 - SSRI's (afferent gut -> brain axis)
 - TCA (pain perception)
 - Alosetron
 - Renzapride
 - Tegaserod
 - Lubiprostone

IBS: Complementary Tx

Alternative and Complementary Therapies Used by Patients with Irritable Bowel Syndrome

<i>Therapy</i>	<i>Proposed Action</i>	<i>Notes</i>
Acupuncture	Relief of chronic pain	No definitive studies available; results of existing studies are mixed
Hypnosis	Relief of chronic pain	No definitive studies available
Peppermint oil	Natural antispasmodic believed to relax intestinal smooth muscle	Ineffective in 2 crossover trials; some effect noted in one parallel trial
Ginger	Natural antispasmodic believed to relax intestinal smooth muscle	No evidence from high-quality trials
Aloe	Natural antispasmodic believed to relax intestinal smooth muscle	No evidence from high-quality trials
Chinese herbal therapy	Natural antispasmodic believed to relax intestinal smooth muscle	Global improvement noted in 1 study
Probiotics	Aim to replenish the beneficial intestinal bacteria that may be lacking in patients with IBS	<i>Bifidobacteria infantis</i> showed symptom improvement in early clinical studies

Maya Grainer



Migraine

Presentation

- U.S. Prevalence: 28 million (>12 y/o)
 - Cost to society \$US 20 billion annually
 - Female:Male 3:1
- Hormonal influences change the slope of the prevalence curves
 - Puberty, pregnancy, breast feeding, menopause
- Generally, in females: more frequent, last longer, more severe, more likely to relapse

Migraine

Evaluation

- History
 - Diaries
- Rule out alternative causes
 - Appropriate studies
- Make the diagnosis
- Understand the impact

Migraine

Management

- Lifestyle: sleep, exercise, meals, stress, etc
- Abortive/Acute
 - Triptan/DHE + NSAIA/Acetaminophen
- Prophylaxis - >8/mo or significant disability
 - B-blockers,
 - Antiepileptics
 - Calcium channel blockers (off-label)
 - ACE Inhibitors and Angiotensin II receptor blockers (ARB's)
- Interventional - >15/mo x >3 mo (w/8+migraine)
 - Botox
- Complementary – Feverfew, Magnesium, Coenzyme Q10
 - Meditation, biofeedback, sleep esp in pregnancy

Migraine

- Additional considerations
 - Antiepileptics
 - Use with OCP's: valproic acid, topiramate (<200mg), gabapentin, levetiracetam
 - Topamax: wt loss – 2-4% body wt – dose dependent; pregnancy category D – oral clefts in progeny (2011)
 - Lamotrigine – esp migraine with aura
 - Menstrual
 - Short-term premenstrual:
 - Naproxen
 - Frovatriptan (5mg bid x 1d – D#-2 HA, then 2.5mg bid x 4d)
 - Naratriptan (1mg bid x 6d – D#-3)
 - Magnesium (360mg - D#15)
 - Continuous hormonal contraception (w/out aura)
 - Progestin-only, progestin-only IUD (w/ aura) Angiotensin receptor blocker (ARB), Gabapentin prophylaxis?
 - Cautionary tale: Valproic acid – Pregnancy category X risks in childbearing women (teratogenicity, low IQ progeny);
 - Tremor, alopecia with long term use; Bleeding diathesis, thrombocytopenia, pancreatitis, hyperandrogenism, obesity, PCOs

Melanie Collier-Shotz



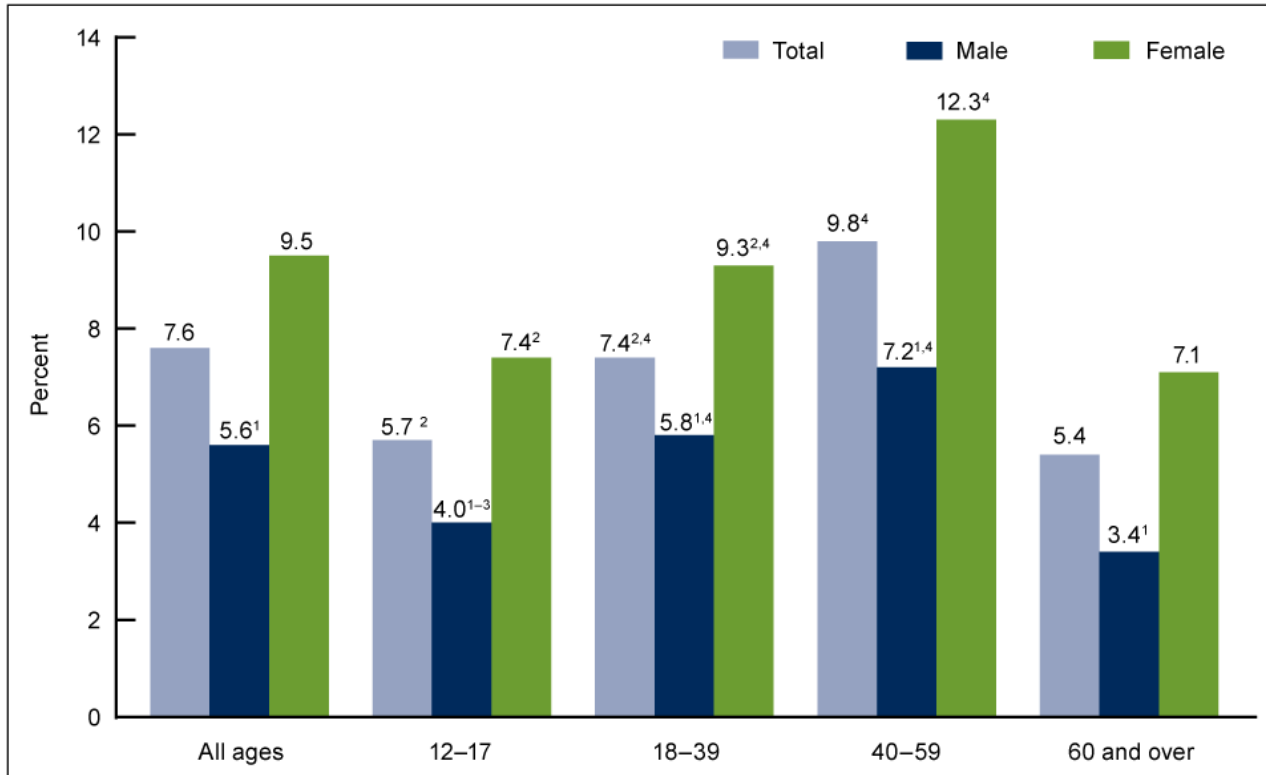
Depression

Prevalence

- In the U.S.: Overall – 8%; Female to male ratio: 1.6:1
 - Women are twice as likely to experience mood and anxiety disorders as men
 - Women have an earlier age of onset of 1st major depressive episode than do men
 - More likely to have concomitant somatic sx
 - Women often have larger social networks but there's a cost
 - Women more often cope by internalizing their stress (ie sleeping, under/overeating, etc) while males engage in more physical behavior and substance/alcohol use

Depression in U.S. Age & Sex, 2009-12

Figure 1. Percentage of persons aged 12 and over with depression, by age and sex: United States, 2009–2012



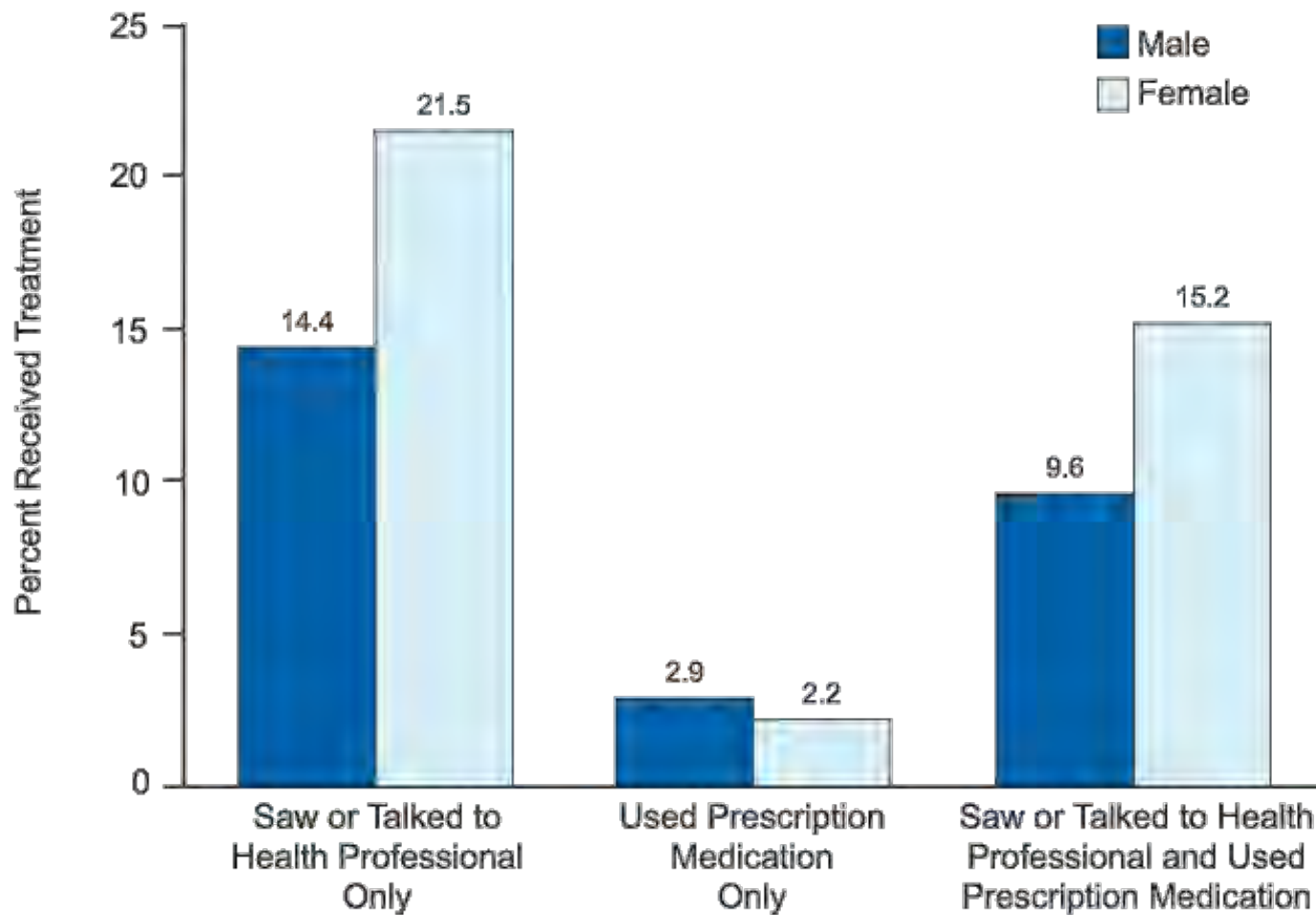
¹Males have significantly lower rates than females overall and in every age group.

²Significantly different from 40–59. ³Significantly different from 18–39. ⁴Significantly different from 60 and over.

NOTES: Depression is defined as having moderate to severe depressive symptoms. Access data table for Figure 1 at:

http://www.cdc.gov/nchs/data/databriefs/db172_table.pdf#1.

SOURCE: CDC/NCHS, National Health and Nutrition Examination Survey, 2009–2012.



Alcohol Use in Women

- Ethanol pharmacokinetics
 - Equal amounts -> higher BAC's
 - Women more susceptible to toxic effects
 - Lower threshold for women to develop cirrhosis
- Women may have more cognitive and motor impairment

Combined Depression and Substance Use in Women

- Women more likely to use substances to self medicate stress or attenuate depression -> transition to addiction more quickly
 - Males more likely to initiate based on risk-taking, experimentation
- Study: 713 HS males and females
 - Females using both alcohol and marijuana reported highest overall depressed mood sx
- Social stigma may make it more challenging for women to admit to an issue

Depression/ Substance Use

Evaluation

- History: family history, psychosocial history, stressful life event(s), trauma
- Medical history and concurrent medications
- Physical Exam, labs

Depression

Management

- Lifestyle modification: exercise, nutrition consultation, sleep hygiene, meditation
- First line SSRI (fluoxetine)
- Second line SSRI (Sertraline, Citalopram)
- Referral
 - Psychotherapy +/- psychopharm
 - Addiction specialist
 - Detox

Yes,
I work out to sweat.
I work out to stay strong.
I work out to pump my heart harder, faster, stronger.

But, more than anything,
I work out to breathe.
I work out to smile.
I work out to be a better, happier, healthier me.



Nia Torre



NECHA/NYSCHA November 2017

ACL Injury

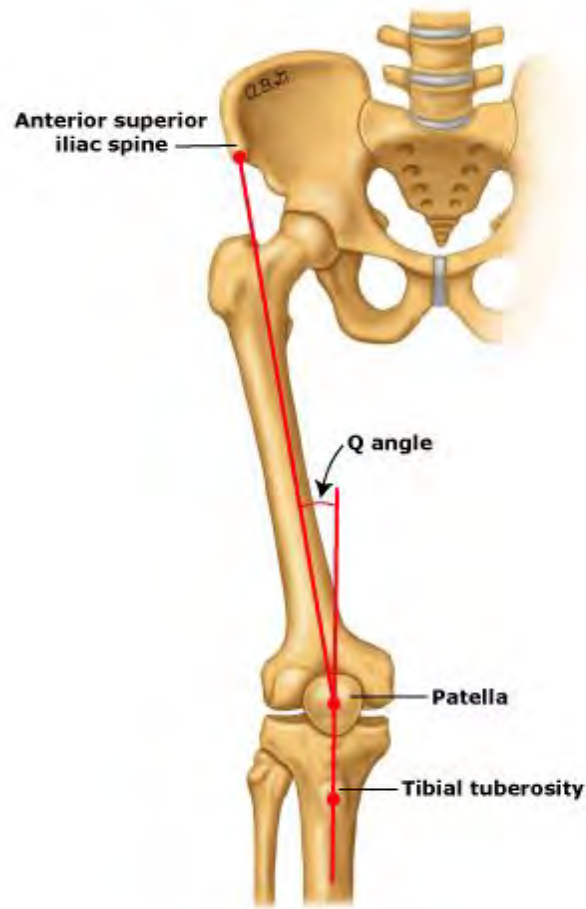
Presentation

- Prevalence - 4:1 Female to Male injury rate
 - Most occur during competition vs training
 - Sharp deceleration/landing sports: soccer, volleyball, basketball, downhill skiing
 - Quadriceps >> hamstring activation on impact
 - Decreased proprioception – compensatory hamstring and balance
 - Post-ACL tear - ↑ DJD

ACL Injury



Q-Angle



ACL Injury

Evaluation


- Screening
 - Assess muscle strength, biomechanics
 - Plyometric Jumping and landing
 - Measuring high knee abduction moments (KAM) to predict predisposition in female athletes
- Post-Injury
 - History
 - “Heard a pop”, swelling, feeling of instability
 - Exam: Lachman’s, Drawer
 - Imaging

ACL Injury

Management

- Rest
- Ice
- Compression (brace)
- Elevation
- Rx: NSAID's – role in long term healing is unclear
- Ortho Referral
 - Surgical vs Nonsurgical

Questions for you.....

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- Is caring for women and women's health the same?
 - Are the terms interchangeable?
 - *Why does it matter?*

It matters because....

- More women than men take anti-depressants; respond more slowly and are less likely to achieve an optimal response to treatment and more likely to stop treatment because of adverse events.
 - *Do we understand why?*
- Female athletes sustain a higher percentage of concussions during play than male athletes do but much of the literature, study, and lay press attention is on male football.
 - *What is the long term impact of girls concussing in this different way?*
- Boys are more likely than girls to receive a diagnosis of peanut allergy early on but by age 24 the prevalence flips.
 - *Why?*
 - Martha Nolan, VP for Public Policy of the Society for Women's Health Research, 2014

Take Aways

1. Examine clinical evidence and medical literature critically.
2. Caring for women (ie “Women’s Health”) includes and goes beyond the reproductive tract...beyond Pap smears, periods, and the use of contraceptive pills.
3. We can and should advocate for higher levels of enrollment of women in clinical trials
4. Call for clearer understanding of how women’s care is impacted by clinical trial and research data.
5. Sex-specific medicine and research better informs the care of women. It better informs the care of everyone!

Want to know more?

- Visit the Office of Research on Women's Health website:
 - <http://orwh.od.nih.gov/>
- Online course - The Science of Sex and Gender on Human Health:
 - <https://sexandgendercourse.od.nih.gov/>
- Principles of Gender-Specific Medicine – Legato et al

Dr. Paula Johnson

New 14th President of Wellesley College!





Thank you!

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