A Framework for the Consideration of Chronic Debilitating Conditions in Women

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Framework for the Consideration of Chronic Debilitating Conditions in Women

- Chronic debilitating conditions are a significant burden on the health of women, in part because of longer life expectancies.
- Evidence base for the prevention, diagnosis, and treatment of chronic conditions among women is underdeveloped, in large part because of a lack of intentional research on the health of women and an historical overrepresentation of men in clinical research.
- The National Academies of Sciences, Engineering, and Medicine will convene a committee of experts to review the literature on chronic debilitating conditions in women to produce a consensus study report that explores the existing literature on chronic debilitating conditions in women.
- The review will describe current knowledge, gaps in evidence, and provide a research agenda for the future.

ORWH Mission

- Enhance and expand women's health research
- Include women and minority groups in clinical research
- Promote career advancement for women in biomedical careers

NIH Vision

- Sex and gender integrated into biomedical research
- Every woman receives evidence-based care
- Women in science careers reach their full potential

NIH National Institutes of Health
Office of Research on Women's Health

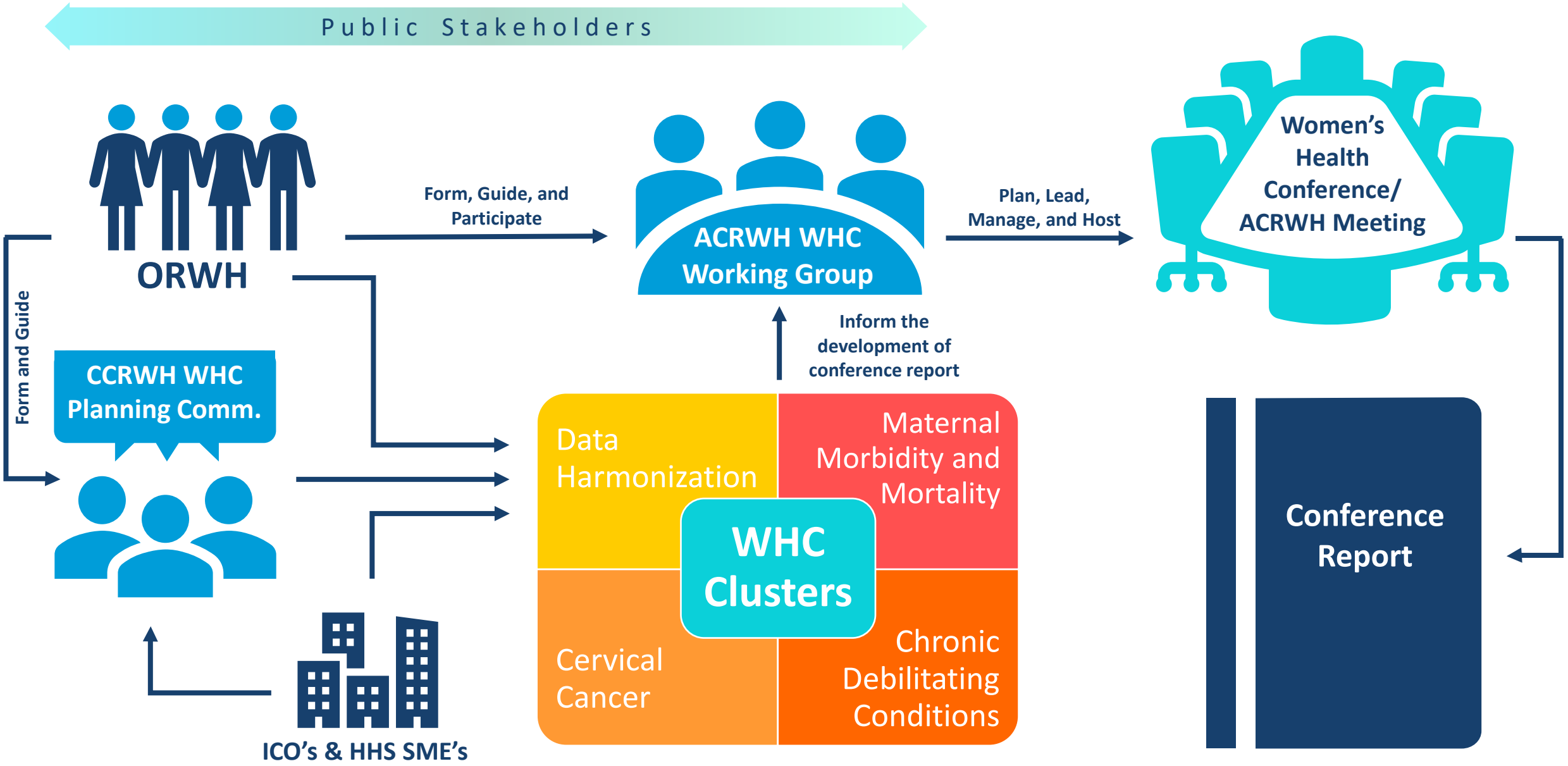
House and Senate "Significant Items" Request a Conference

ORWH to hold the **Advancing NIH Research on the Health of Women: A 2021 Conference** on October 20, as part of the ACRWH Meeting.

- Must include representatives from ORWH, NICHD, NCI, NHLBI, NIDDK, & other relevant ICOs.
- **Evaluate research** and **identify priorities** to advance the study of women's health, particularly:
    1. Rising rates of maternal morbidity and mortality;
    2. Rising rates of chronic debilitating conditions in women; and
    3. Stagnant survival rates among cervical cancer patients.

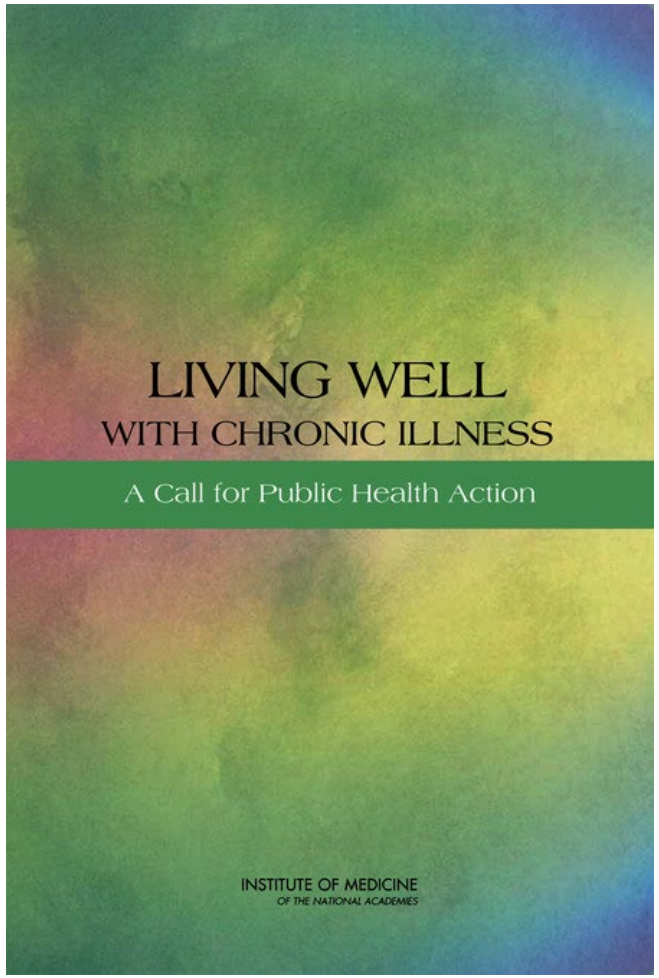
House: https://www.congress.gov/116/crpt/hrpt450/CRPT-116hrpt450.pdf (page 149)
Senate: https://www.appropriations.senate.gov/imo/media/doc/LHHSRept.pdf (page 123)

Broad Input through Paths that Converge along the Way



Defining Chronic Debilitating Conditions

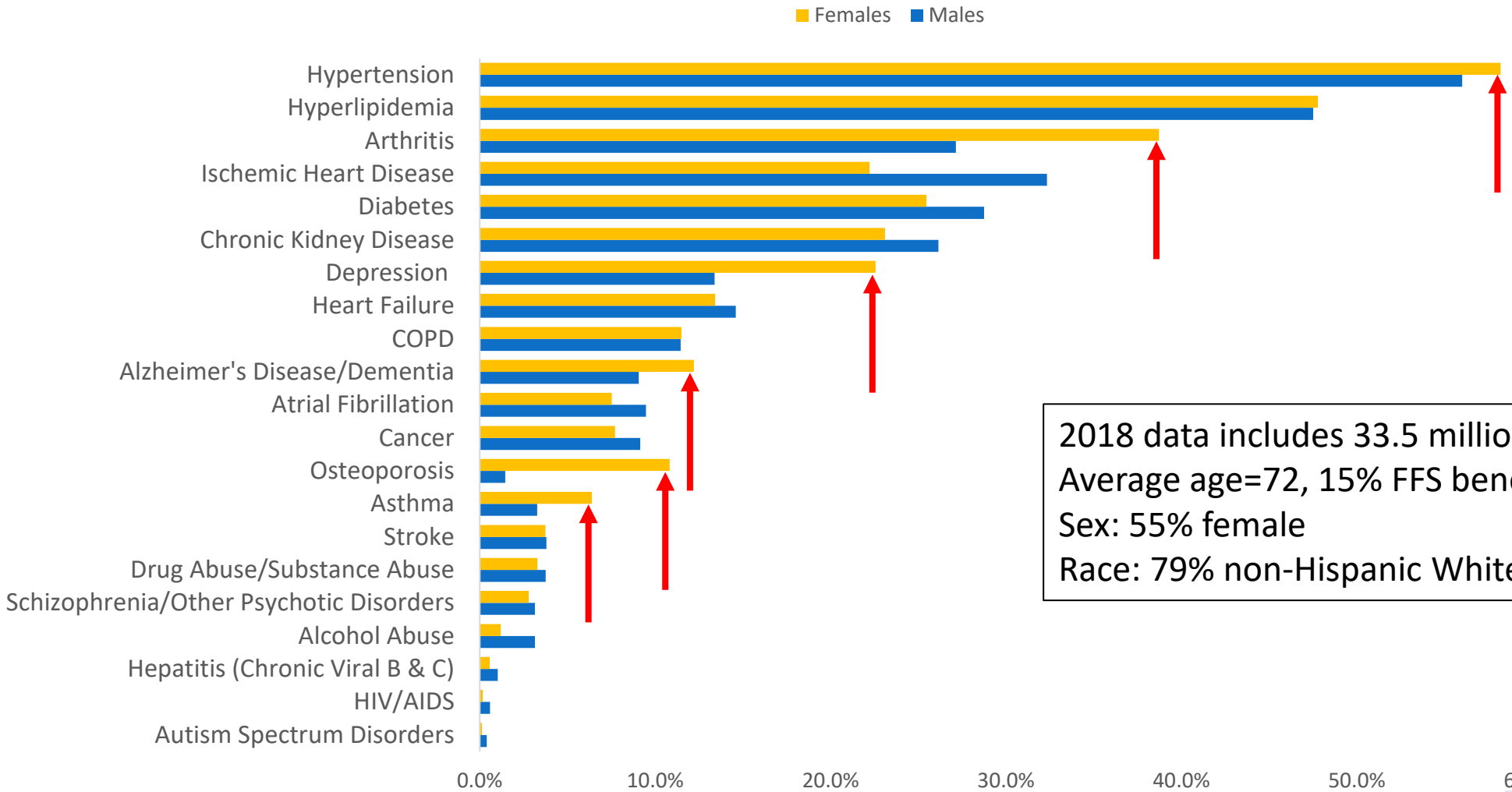
- US Department of Health and Human Services (HHS) 2010: Chronic illnesses are “conditions that last a year or more and require ongoing medical attention and/or limit activities of daily living”
- Centers for Medicare and Medicaid Services (CMS): Provides data on prevalence, utilization, and Medicare spending for specific chronic conditions and multiple chronic conditions
- **Limitations: Not specific to the clinical and/or research frameworks relevant to the health of women**



Institute of Medicine. 2012. *Living Well with Chronic Illness: A Call for Public Health Action*. https://doi.org/10.17226/1327
https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/Chronic-Conditions/Downloads/Methods_Overview.pdf

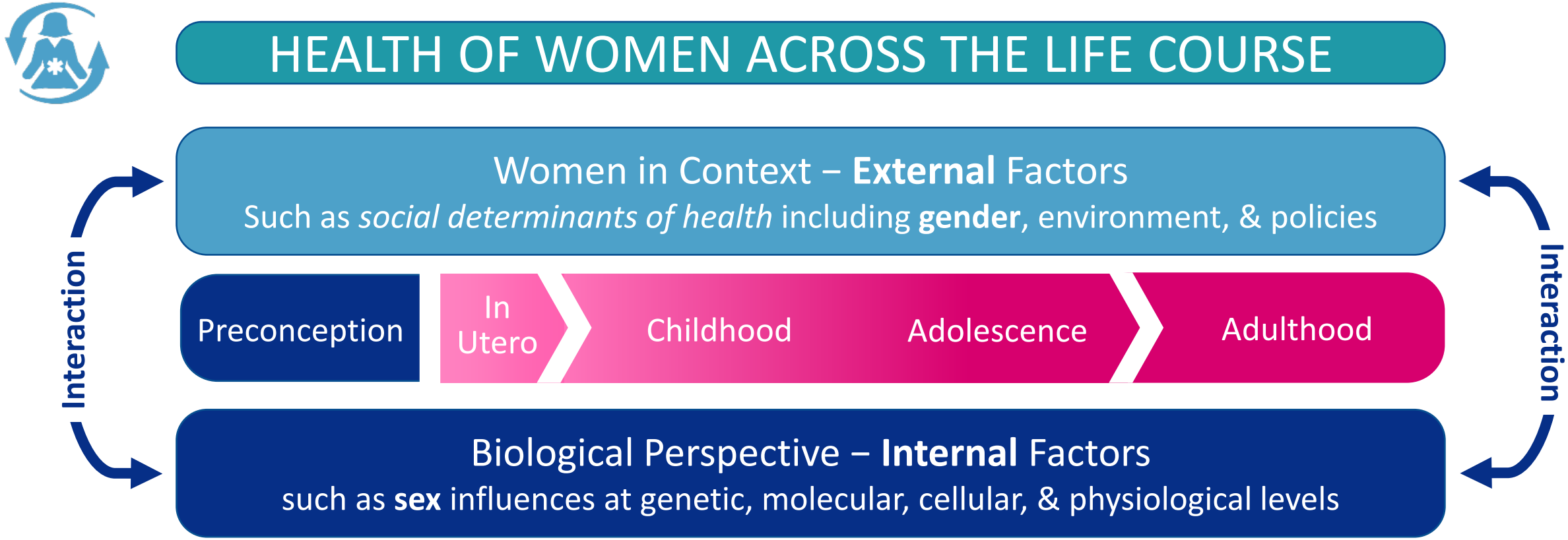
Chronic Conditions that Disproportionately affect Women

Prevalence of Chronic Conditions among Fee-for-Service Beneficiaries by Sex: 2018



2018 data includes 33.5 million FFS beneficiaries
Average age=72, 15% FFS beneficiaries under 65
Sex: 55% female
Race: 79% non-Hispanic White, 9% Black

Multidimensional Framework Represents Intersection of Factors affecting the Health of Women



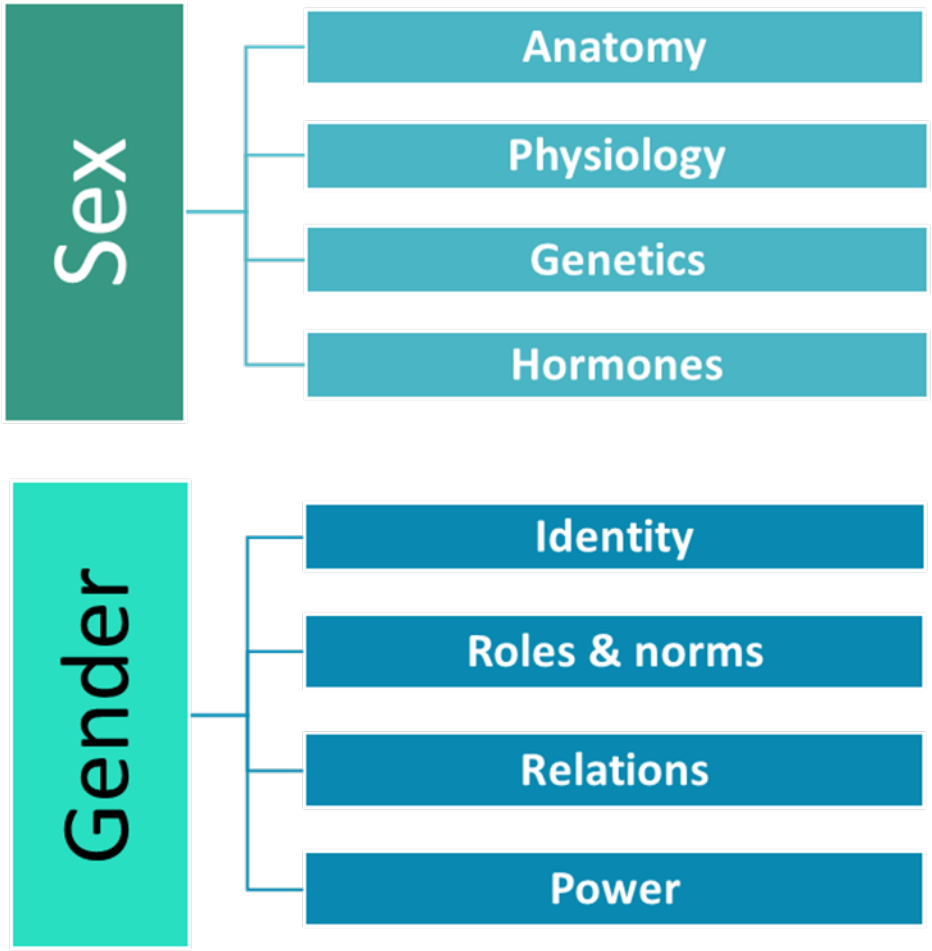
Sex and Gender Contribute to Health

Sex is a multidimensional biological construct based on a set of anatomical and physiological traits (sex traits) that include external genitalia, secondary sex characteristics, gonads, chromosomes, and hormones.

Gender is a multidimensional construct that links gender identity, gender expression, and social and cultural expectations about status, characteristics, and behavior as they are associated with certain sex trait.

Measuring Sex, Gender Identity, and Sexual Orientation. 2022. *NASEM*.

Sex and Gender influence Chronic Disease Incidence and Outcomes

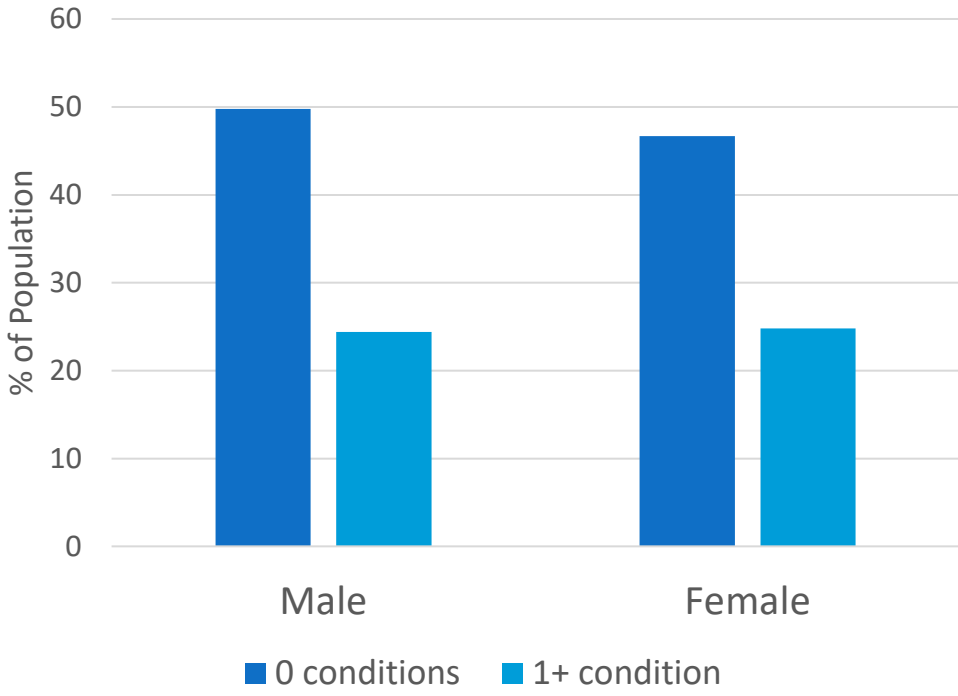


- Sex differences in the immune system influence the risk for certain diseases (e.g., asthma, autoimmunity), as well as response to immune interventions (e.g., vaccines)
- Pregnancy is a “stress test” for health later in life
- Menopause is associated with an acceleration of accumulation of chronic diseases
- Symptoms are often labeled as “atypical,” despite being more common in women
- Diagnostic and referral delays for diseases, such as cancer and arthritis, have been demonstrated for women compared to men

Temkin et al. BMC Women’s Health (2023) 23:162 https://doi.org/10.1186/s12905-023-02319-x

Prevalence of Chronic Conditions in U.S. Adults

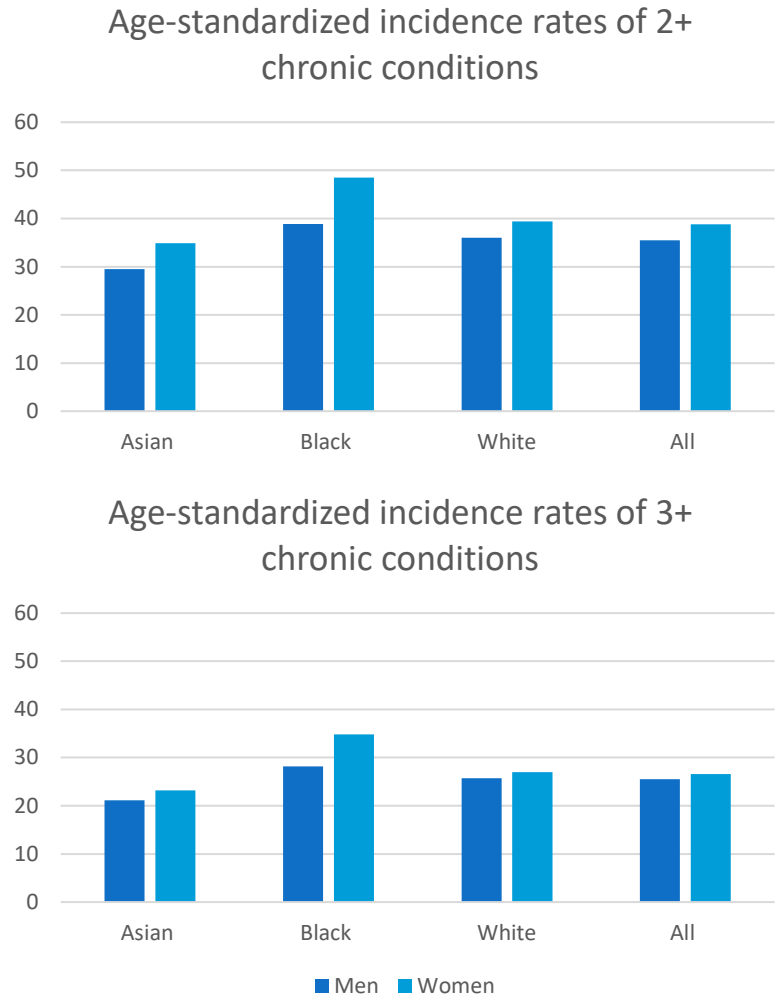
- Overall, women are more likely than men to have a diagnosis of a chronic condition
- Evidence-gaps in women's health persist
- Data disaggregated by sex is infrequently reported
- Few sex-specific guidelines for care



Boersma P, Black LI, Ward BW. 2018. Prev Chronic Dis 2020;17:200130

Multimorbidity is more Common among Women

- Incidence of multimorbidity varies by race and gender
  - Influence of intersection of race and gender is understudied
- Data disaggregated by race, ethnicity and gender is infrequently reported
- Incidence of multimorbity is higher for women than men within racial categories

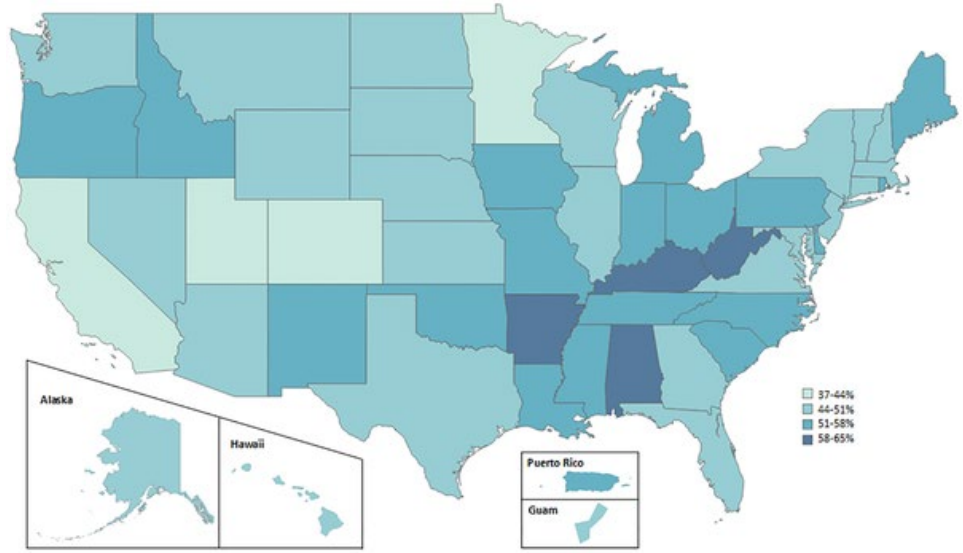


Adapted from St Sauver JL, et al. BMJ Open 2015;5:e006413 http://dx.doi.org/10.1136/bmjopen-2014-006413

Multiple Social Determinants of Health influence the prevalence of Chronic Conditions

- Gender interacts with other social determinants of health
- Influence of intersection of various additional social factors (e.g., income, rurality, education) is understudied

Prevalence of diagnosed multiple chronic conditions among adults aged ≥18 years, by state or territory—Behavioral Risk Factor Surveillance System, United States, 2017.



Newman D, Tong M, Levine E, Kishore S (2020) Prevalence of multiple chronic conditions by U.S. state and territory, 2017. PLOS ONE 15(5): e0232346. https://doi.org/10.1371/journal.pone.0232346

Multimorbidity is more Complex in Women

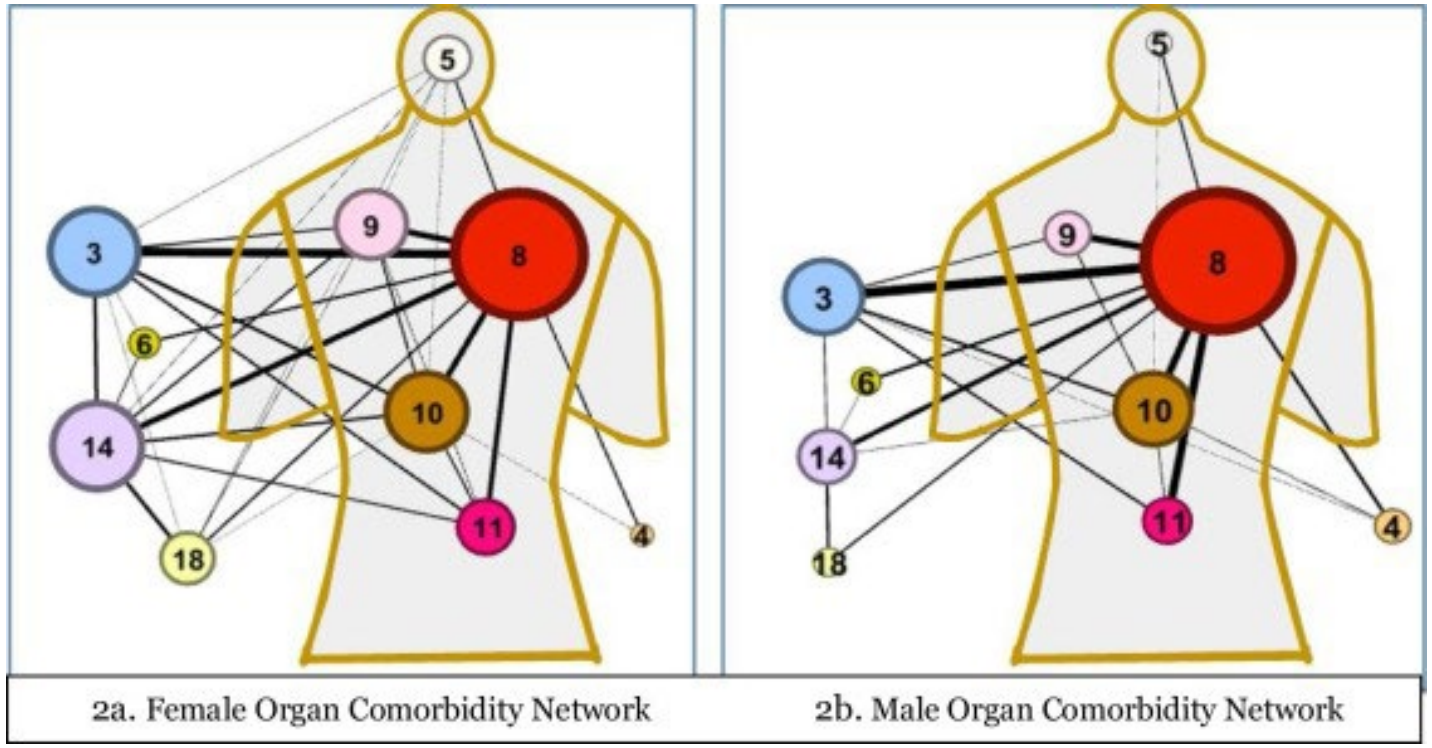
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	18
Infectious and parasitic [1]																	
Neoplasms [2]																	
Endocrine, nutritional, metabolic, and immunity disorders [3]																	
Blood and blood-forming organs [4]			M														
Mental disorders [5]			F														
Nervous system [6]			F														
Sense organs [7]																	
Circulatory system [8]			FM	FM	FM	FM											
Respiratory system [9]			FM		F			FM									
Digestive system [10]			FM	FM	FM			FM	FM								
Genitourinary system [11]			FM					FM	F	FM							
Pregnancy, childbirth, and the puerperium [12]																	
Skin and subcutaneous tissue [13]																	
Musculoskeletal system and connective tissue [14]			FM		F	FM		FM	F	FM	F						
Congenital anomalies [15]																	
Perinatal period [16]																	
Injury and poisoning [18]			F		F			FM	F	F				FM			

*Class 17 is symptoms and thus not included in the analysis

F Association only in Female Network

M Association only in Male Network

FM Association in both Networks

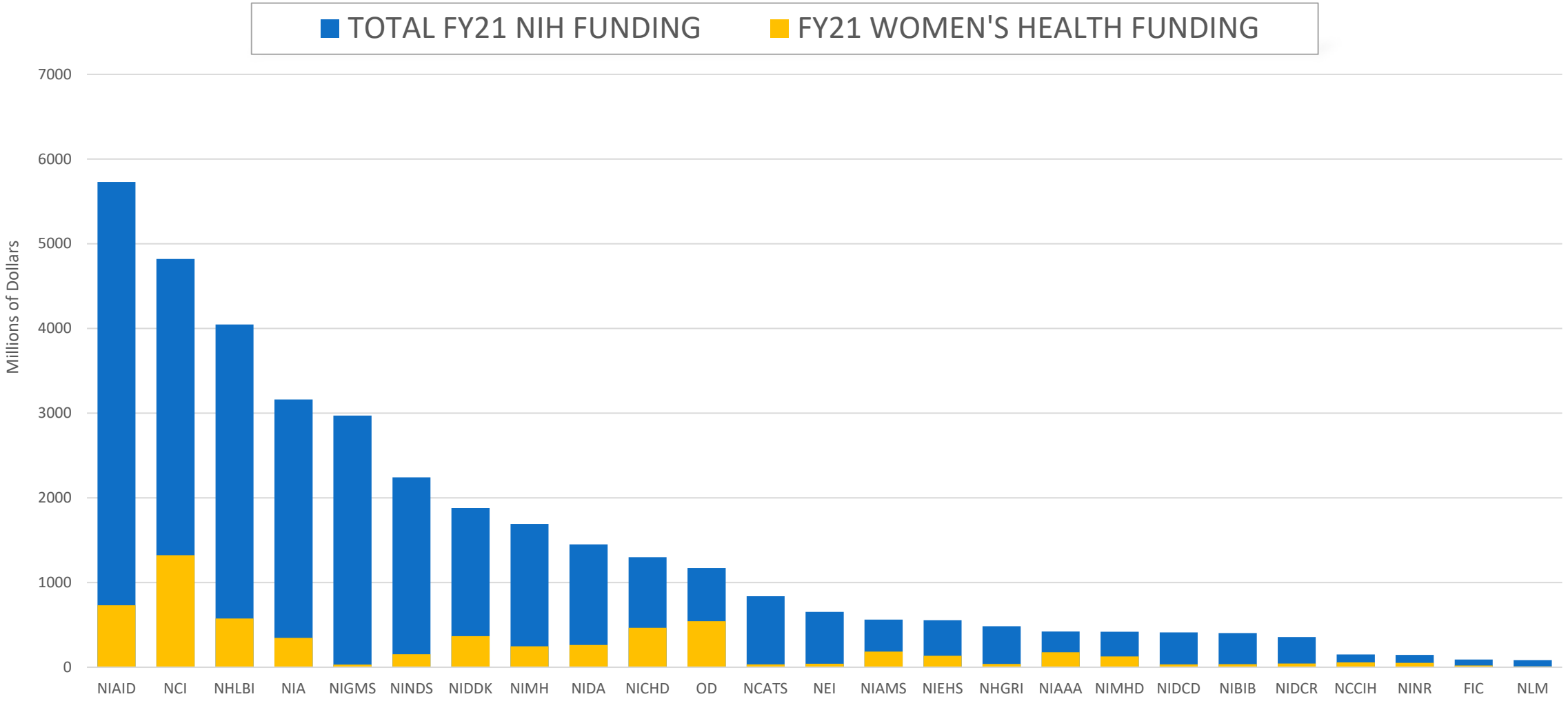


2a. Female Organ Comorbidity Network

2b. Male Organ Comorbidity Network

International journal of medical informatics 108 (2017): 22-28.

NIH Research on Women's Health



https://report.nih.gov/funding/categorical-spending#/

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Leading Causes of Death, by Sex

All races and origins[1], Male, All ages[2]

All races and origins, Male, All ages	Percent
1) Heart disease	24.2%
2) Cancer	21.9%
3) Unintentional injuries	7.6%
4) Chronic lower respiratory diseases	5.2%
5) Stroke	4.3%
6) Diabetes	3.2%
7) Alzheimer's disease	2.6%
8) Suicide	2.6%
9) Influenza and pneumonia	1.8%
10) Chronic liver disease	1.8%

All races and origins[1], Female, All ages[2]

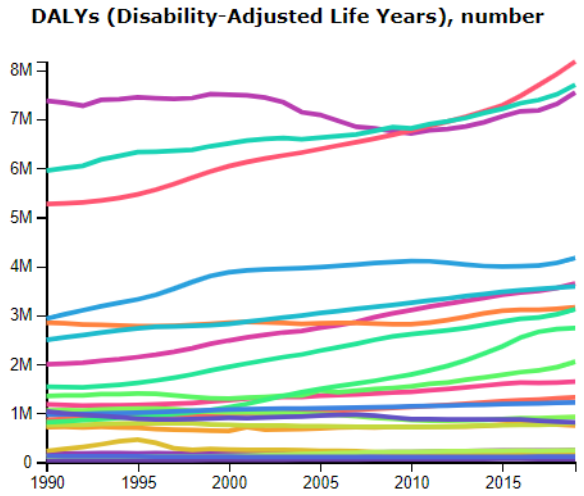
All races and origins, Female, All ages	Percent
1) Heart disease	21.8%
2) Cancer	20.7%
3) Chronic lower respiratory diseases	6.2%
4) Stroke	6.2%
5) Alzheimer's disease	6.1%
6) Unintentional injuries	4.4%
7) Diabetes	2.7%
8) Influenza and pneumonia	2.1%
9) Kidney disease	1.8%
10) Septicemia	1.6%

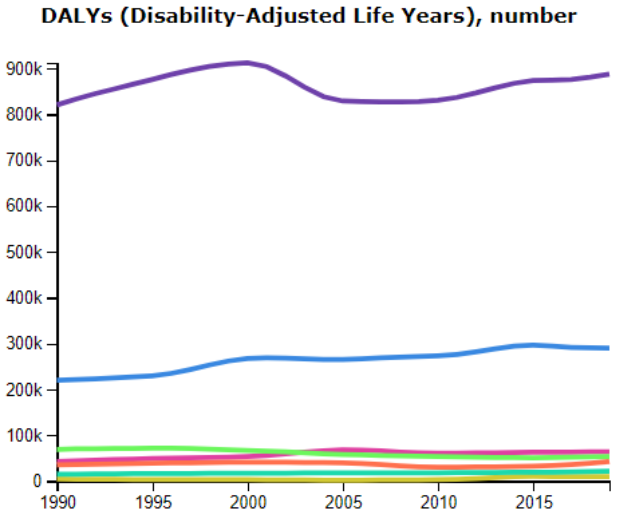
https://www.cdc.gov/women/lcod/index.htm

US causes of Morbidity (Female)

Cause	Number
Musculoskeletal disorders	8,170,164.74
Neoplasms	7,697,814.91
Cardiovascular diseases	7,538,622.23
Mental disorders	4,164,912.62
Chronic respiratory diseases	3,643,271.28
Neurological disorders	3,583,213.30
Other non-communicable diseases	3,162,588.84
Diabetes and kidney diseases	3,118,087.30
Substance use disorders	2,736,126.15
Unintentional injuries	2,050,026.93

Cause	Number
Gynecological diseases	887,253.85
Premenstrual syndrome	289,608.07
Uterine fibroids	64,009.99
Endometriosis	53,777.58
Polycystic ovarian syndrom	42,738.54
Genital prolapse	21,613.33
Female infertility	9,774.21





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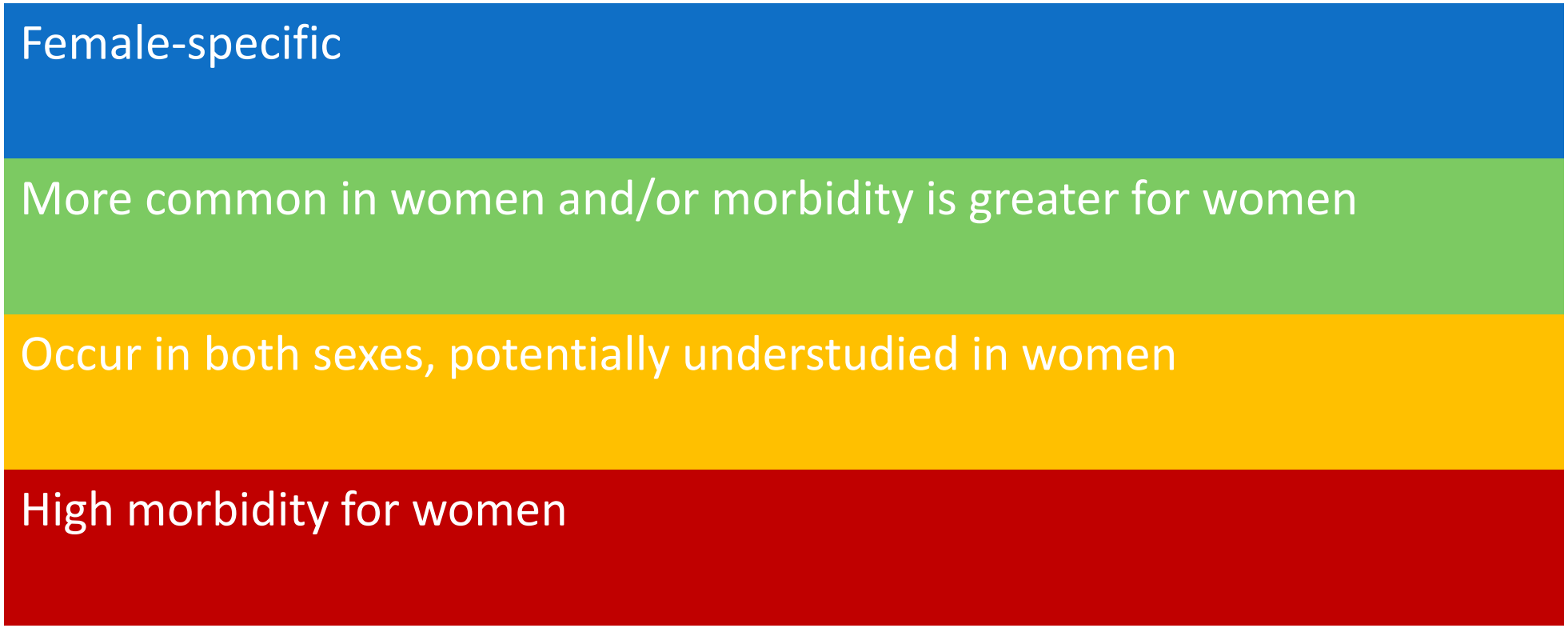
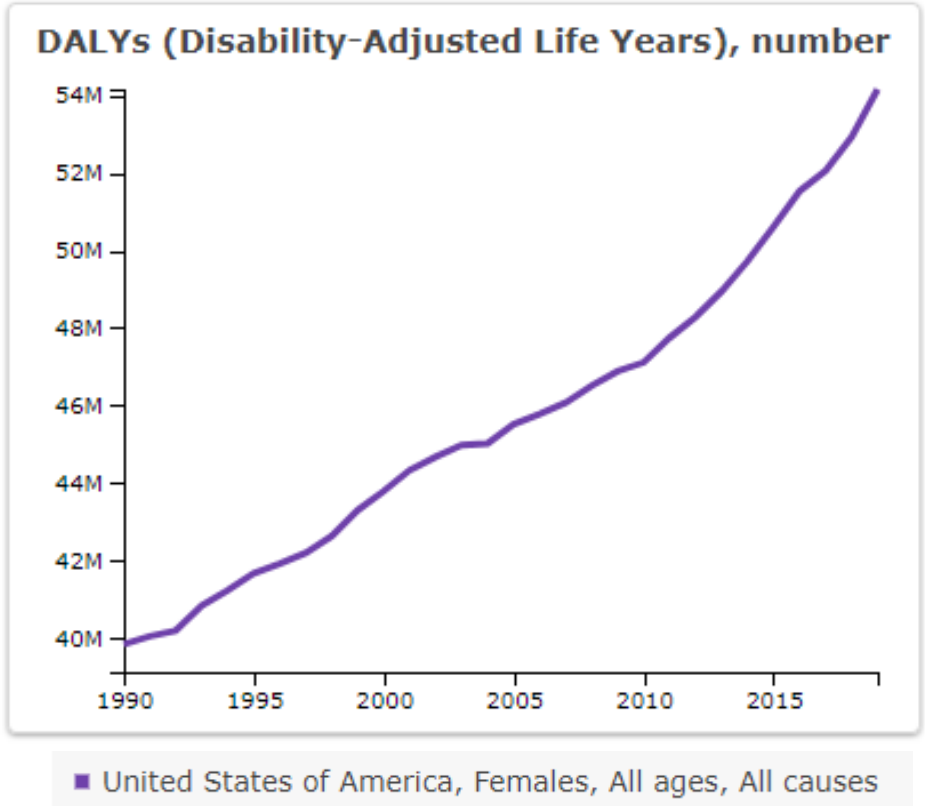
Categorizing Chronic Debilitating Conditions in Women



Rising Rates of Chronic Debilitating Conditions in Women



DALYs Definition:

DALYs = Disability Adjusted Life Years
The sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability.

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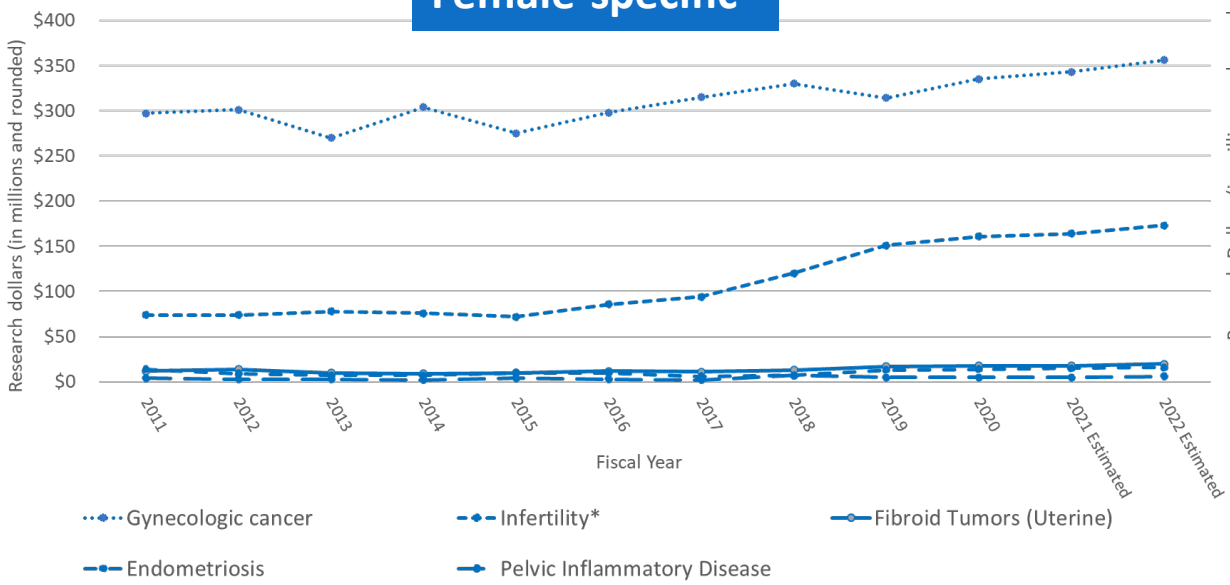
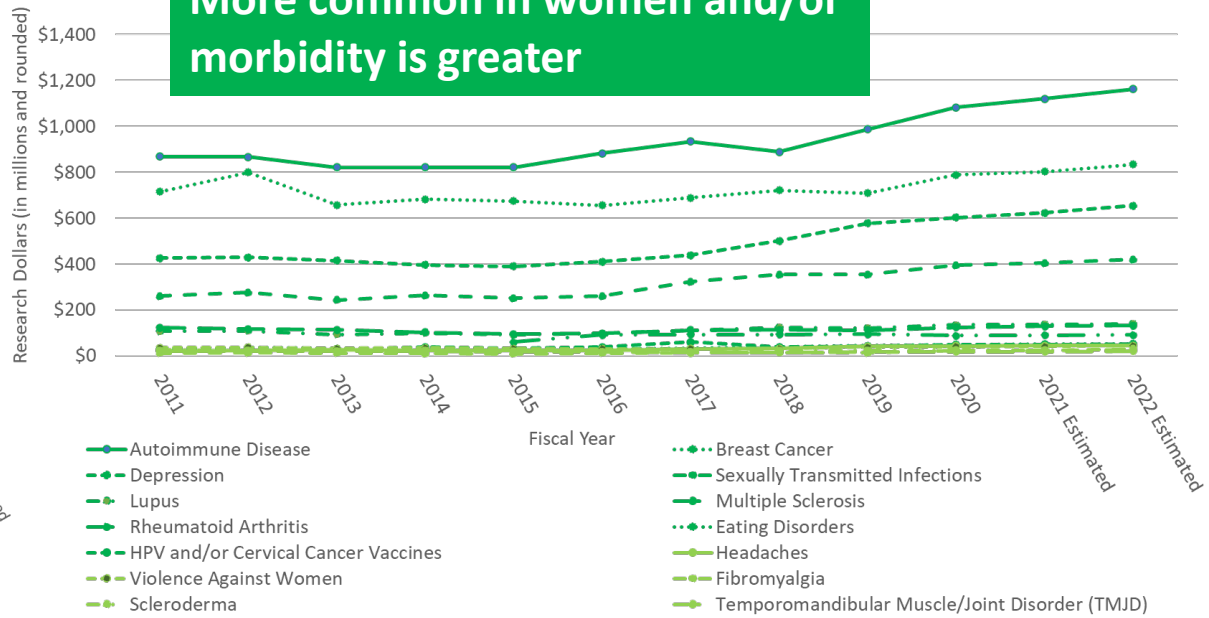
Condition Type	Condition (FY 2020 spending/2019 DALY)							
Female specific	Cancers of the female reproductive tract*	Dys-menorrhea/ Abnormal menses	Fibroids*	Endometriosis * and Adenomyosis	Infertility*/ Early Pregnancy Loss	Polycystic Ovarian Syndrome	Pelvic floor disorders, Organ prolapse	Menopausal symptoms Pelvic Inflammatory Disease* Vulvodynia/Chronic gynecologic pain disorders – pelvic and vulvar Vaginosis
More common in women and/or morbidity is greater for women	Depressive Disorders	Migraine/ Headache	Breast cancer*	Autoimmune diseases (*including RA) •SLE* •Sjögren's Syndrome* Scleroderma*	Rheumatoid Arthritis*	Multiple Sclerosis	Sexually transmitted infections	Temporomandibular Muscle/Joint Disorder (TMJD)* Chronic Fatigue Syndrome* Fibromyalgia* Candidiasis Post-traumatic stress Irritable Bowel syndrome Interstitial Cystitis* HPV infection* Osteoporosis* Eating Disorders
Occur in both sexes/ Potentially understudied in women	Unintentional Injuries (including violence against women*)	Alzheimer's/ Dementia	Osteo-arthritis	Endocrine, metabolic, blood, and immune disorders	Recurrent UTI/ Interstitial Nephritis	HIV	Exogenous hormone use- Neuropathy Overactive bladder/Incontinence Chronic pain including chronic pelvic pain	
High morbidity for women	Heart Disease	Lower back pain	COPD	Drug Use Disorders	Stroke	Diabetes	Obesity/metabolic disease Influenza and pneumonia	

*Per MCS-WH reporting guidance, the following RCDC disease categories are particularly relevant to women's health

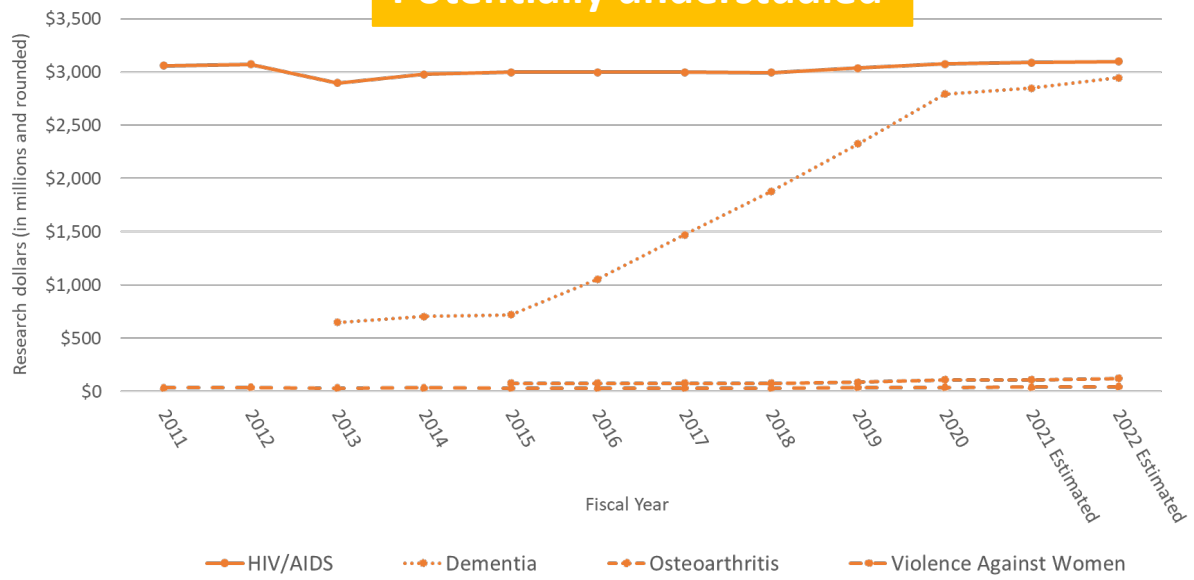
Female-specific



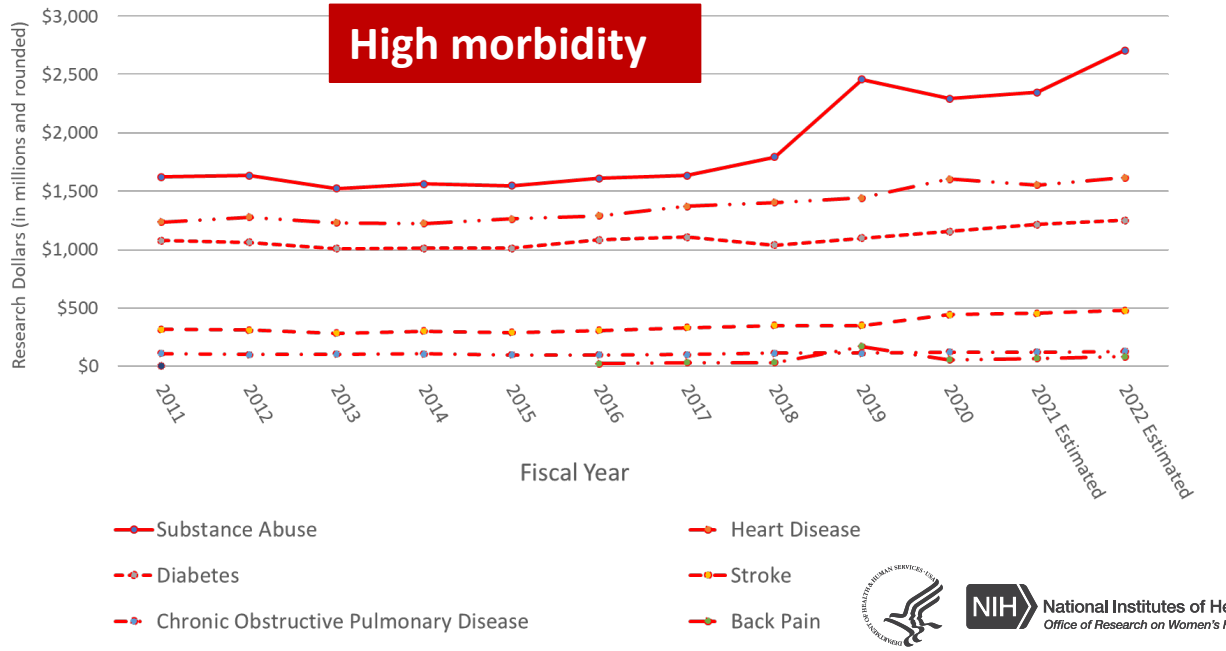
More common in women and/or morbidity is greater



Potentially understudied



High morbidity



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Condition Type	Condition (FY 2020 spending/2019 DALY)							
Female specific	Cancers of the female reproductive tract* **$372**	Dys-menorrhea/ Abnormal menses	Fibroids* **$281**	Endometriosis * and Adenomyosis **$260**	Infertility*/ Early Pregnancy Loss **$6108**	Polycystic Ovarian Syndrome	Pelvic floor disorders, Organ prolapse	Menopausal symptoms Pelvic Inflammatory Disease* Vulvodynia/Chronic gynecologic pain disorders – pelvic and vulvar Vaginosis
More common in women and/or morbidity is greater for women	Depressive Disorders **$353**	Migraine/ Headache **$27**	Breast cancer* **$568**	Autoimmune diseases (*including RA) •SLE* •Sjögren's Syndrome* Scleroderma*	Rheumatoid Arthritis* **$463**	Multiple Sclerosis **$866**	Sexually transmitted infections	Temporomandibular Muscle/Joint Disorder (TMJD)* Chronic Fatigue Syndrome* Fibromyalgia* Candidiasis …umatic stress … Bowel syndrome …ial Cystitis* …ection* …rosis* …isorders
Occur in both sexes/ Potentially understudied in women	Unintentional Injuries (including violence against women*)	Alzheimers/	Osteo-	Endocrine,	Recurrent UTI/ Interstitial Nephritis	HIV **$25,936**	Exogenous hormone use- Neuropathy Overactive bladder/Incontinence Chronic pain including chronic pelvic pain	
High morbidity for women	Heart Disease **$472**	Lower back pain **$17**	COPD **$449**	Drug Use Disorders **$967**	Stroke **$210**	Diabetes **$574**	Obesity/metabolic disease Influenza and pneumonia	

HIV $25,936

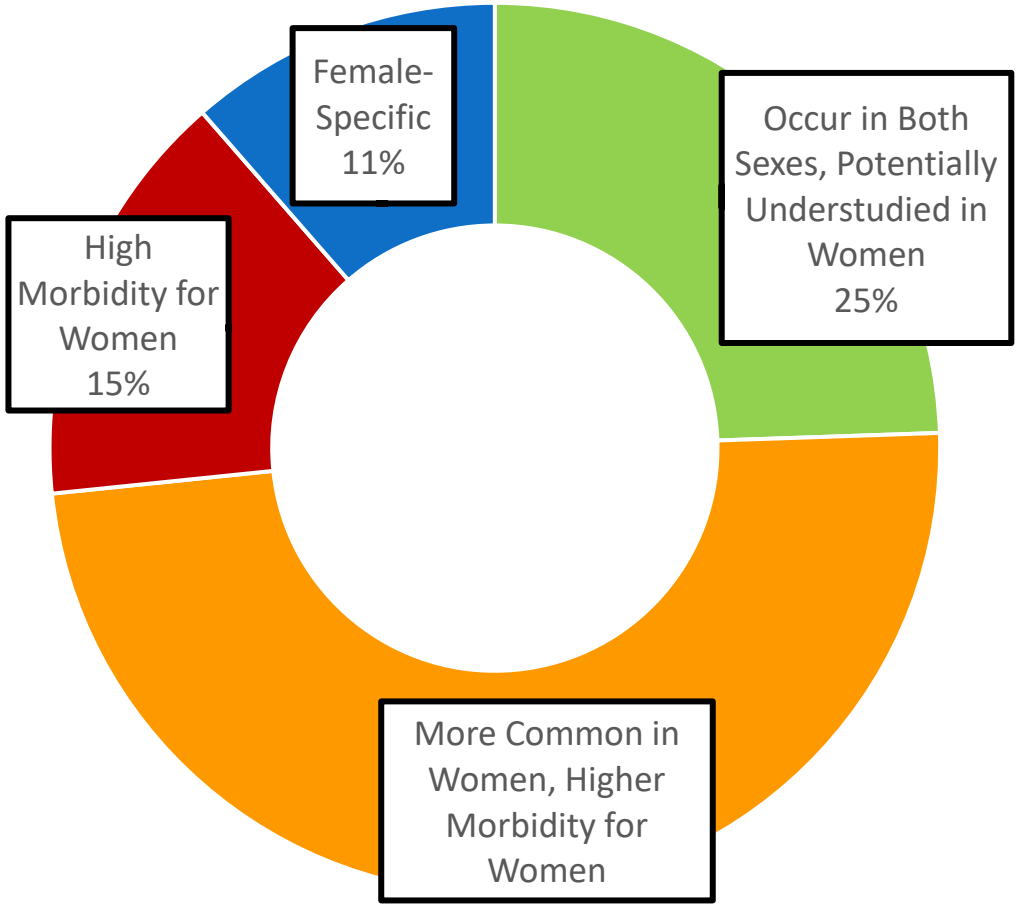
Lower back pain $17

*Per MCS-WH reporting guidance, the following RCDC disease categories are particularly relevant to women's health

Portfolio Analysis: Data and Methods

- ICs were asked to submit their three highest-funded projects related to **chronic debilitating conditions in women** from FY 2018, 2019, 2020.
  - ICs could submit more or fewer projects if desired
- ICs provided: Category (female-specific, higher morbidity for women, etc.), fiscal year, state, funding mechanism, and funding amount
  - Chronic debilitating conditions cluster manually coded projects for clinical/translational elements
- 184 projects submitted from 11 ICOs: NCI, NHLBI, NIAID, NICHD, NIDA, NIDCR, NIDDK, NIMH, NIMHD, NINR, SGMRO
- Limited & non-exhaustive snapshot, provides insights into NIH priorities

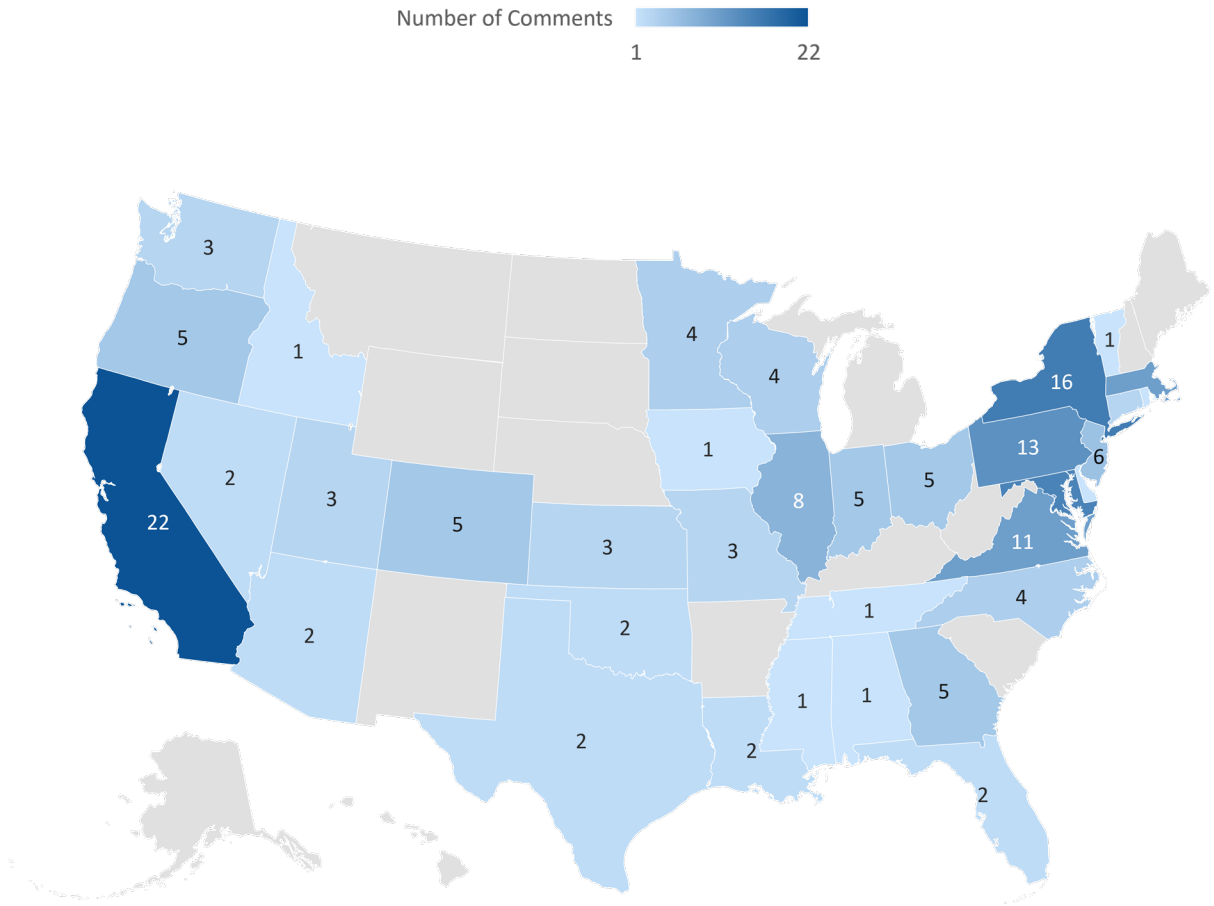
Chronic Debilitating Conditions Snapshot: Distribution of Projects Submitted by ICs



- Multiple IC-supported research on chronic debilitating conditions in women
- Few studies on multimorbidity
- A measured by Disability Adjusted Life Years (DALYS) among the U.S. female population, NIH spending varies widely
  - $17 per DALY for lower back pain to $25,936 per DALY for HIV at either extreme

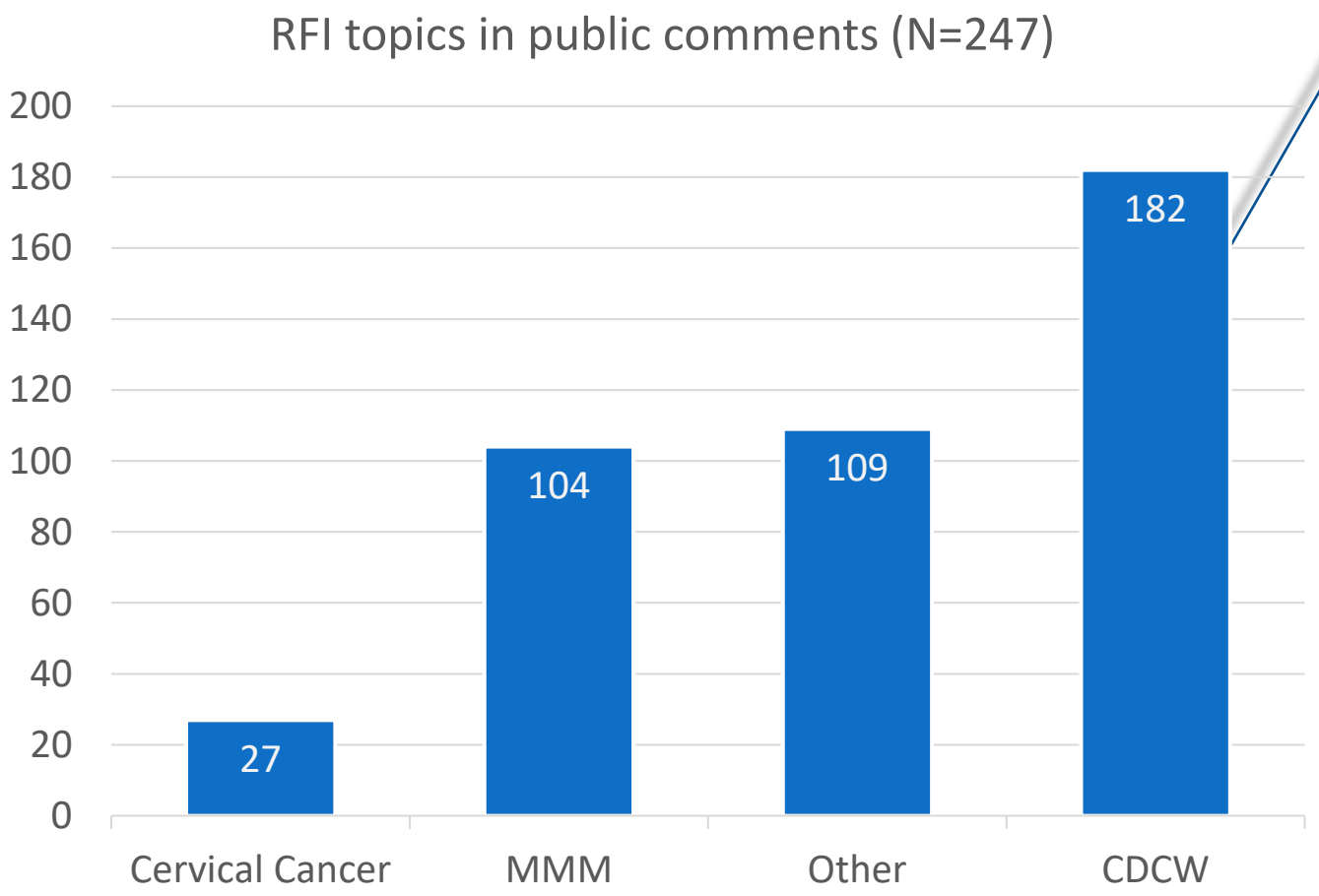
Contributing ICOs: NCI, NHLBI, NIAID, NICHD, NIDA, NIDCR, NIDDK, NIMH, NIMHD, NINR, SGMRO
(Unofficial ORWH analysis)

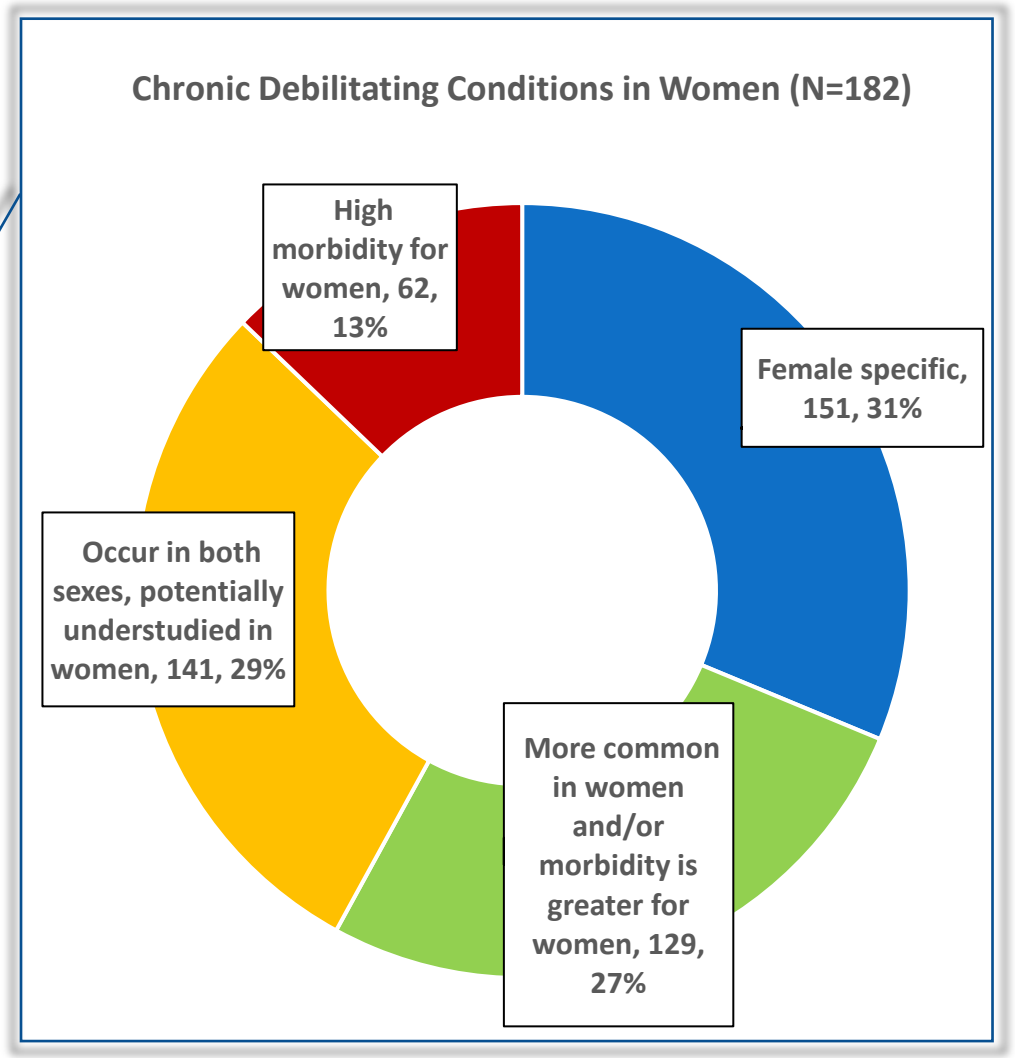
Public Comments
Federal Register Notice (FRN 2021-14151)



- 247 comments received
- Comments were submitted by researchers or research groups (N=56), members of the public (N=49), awareness and advocacy groups (N=36), patients (N=40), and healthcare professionals (N=34).
- The 10 most frequently identified keywords were as follows: (1) maternal morbidity and mortality, (2) racial disparities, (3) access to care, (4) healthcare professional training, (5) mental health, (6) Black or African American women, (7) screening, (8) quality of care, (9) time to diagnosis, and (10) social determinants of health.

Request for Information (RFI) Topics in Public Comments (N=247)





Barr E, et al. J Womens Health (Larchmt). 2023 Apr 11. doi: 10.1089/jwh.2022.0488.

Crosscutting Themes Identified: Where Research is "Urgently Needed"

1. **Implementing best practices** – evidence-based and more holistic, patient-centered care
2. **Addressing care inequities –** especially among populations with overlapping identities
3. **Intentional research** – two components:
   - Historic overreliance on male clinical research subjects left significant gaps regarding disorders and diseases that occur in women
   - Despite Sex as a Biological Variable (SABV) policy, gaps remain in basic and translational understanding of sex differences

https://orwh.od.nih.gov/about/newsroom/events/55th-meeting-advisory-committee-research-womens-healthconsensus-conference

ACRWH Identified Opportunities in Chronic Conditions Research

- **Consider partnering with the National Academy of Science (NAS) to develop a framework specific to women**
- Granular and comprehensive evaluation of NIH-wide research portfolio dedicated to the health of women
- Align clinical research with the needs of women (e.g., study objectives and endpoints)
- Encourage research through the development of funding opportunities around multimorbidity in women

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Questions?