



Sex as a Biological Variable: Current Successes and Future Needs

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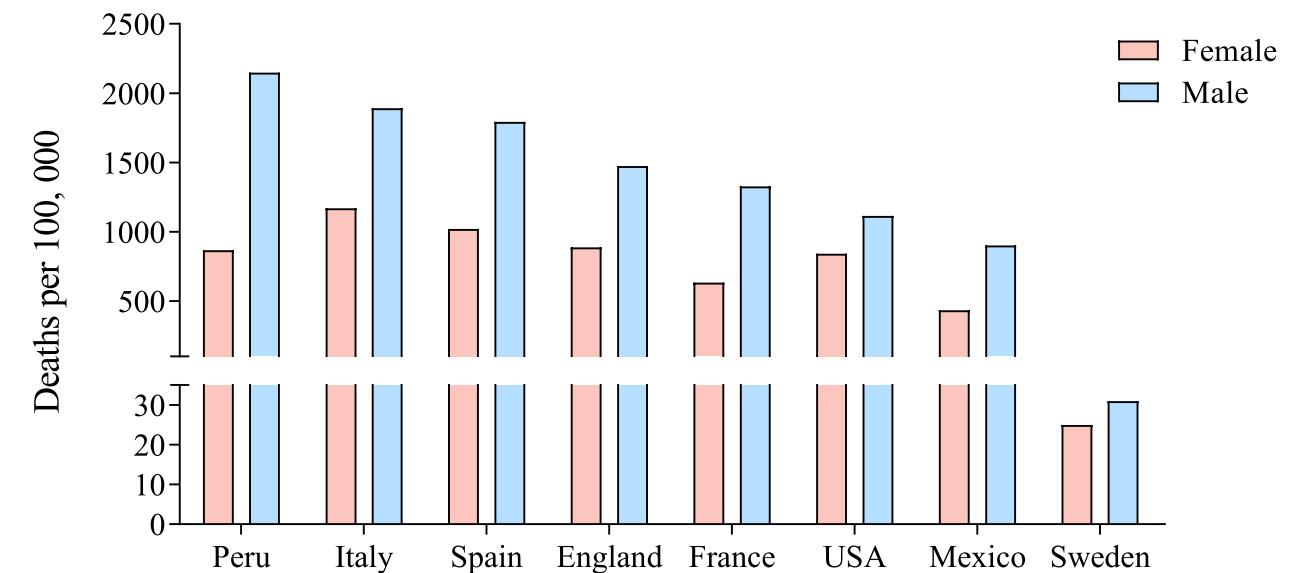
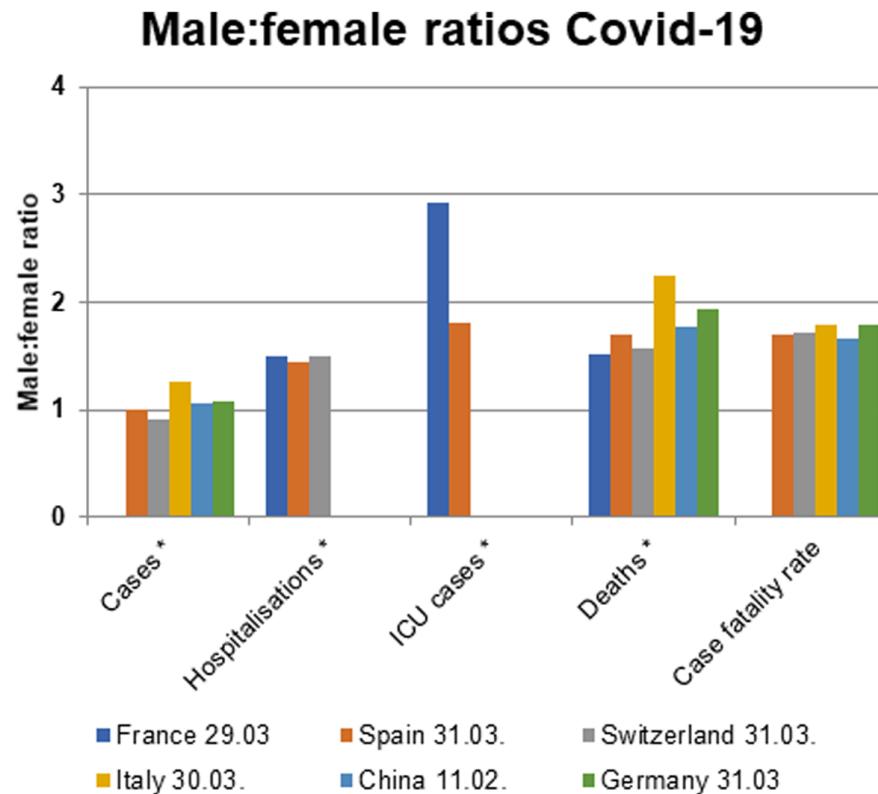


Why should *you* care about Sex as a Biological Variable?

- + Infectious Diseases: COVID-19 and other infectious diseases vary by biological sex.
- + Biological sex affects gene expression and its genetic regulation throughout the body.
- + Neural mechanisms for pain and mental health disorders vary by biological sex.

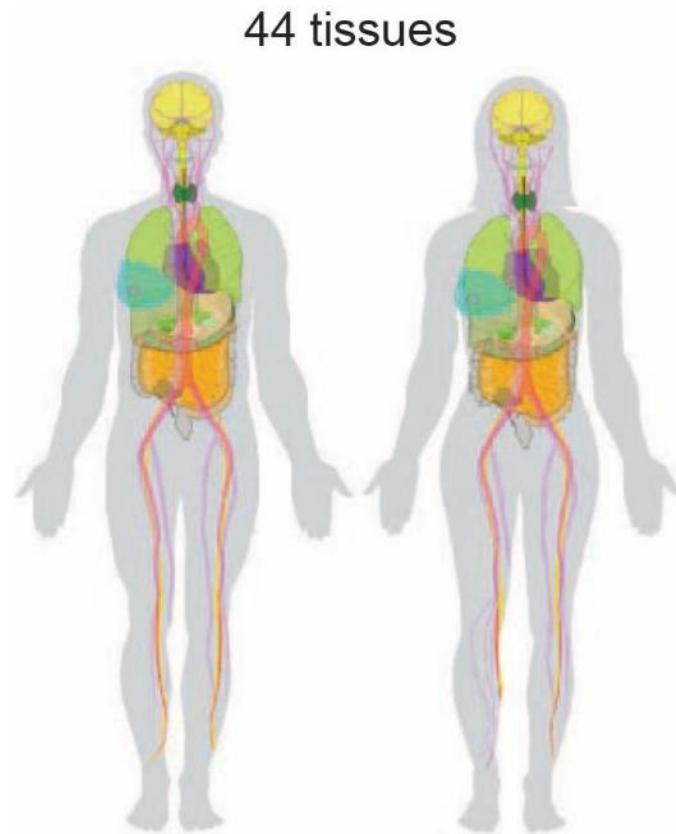
COVID-19

- + Sex-specific Risk Factors.
- + Sex Differences in Disease Presentation and Disease Progression

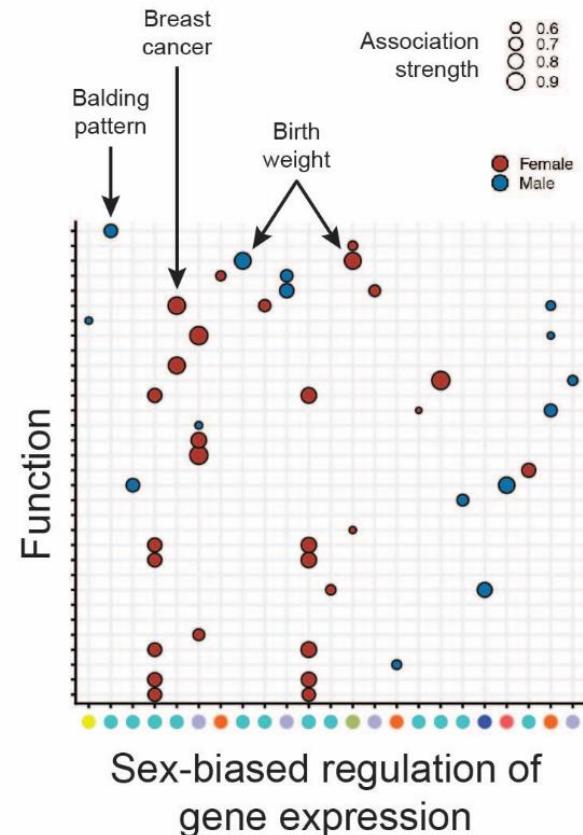


Sex affects gene expression and its genetic regulation throughout the body

Disease	% women:% men
Rett syndrome	100:0
Postoperative hyponatremic encephalopathy with permanent damage or death	96:4
Anorexia nervosa	93:7
Lymphocytic hypophysitis	90:10
True (central) precocious puberty	90:10
Hypnic headache syndrome	84:16
Bulimia	75:25
Senile dementia of the Alzheimer type	74:26
Multiple sclerosis	67:33
Anxiety disorder	67:33
Posttraumatic stress disorders	66:34
Dementia	64:36
Unipolar depression, dysthymia	63:37
Whiplash	60:40
Severe learning disability	38:62
Substance abuse	34:66
Stuttering	29:71
Schizophrenia	27:73
REM sleep behavioral disorder	24:76
Male-to-female versus female-to-male transsexuals	28:72
Dyslexia	23:77
ADHD	20:80
Autism	20:80
Sleep apnoea	18:82
Kallmann syndrome	17:83
Rabies	13:87
Gilles de la Tourette	10:90



Oliva et al., *Science* **369**, 1331 (2020)

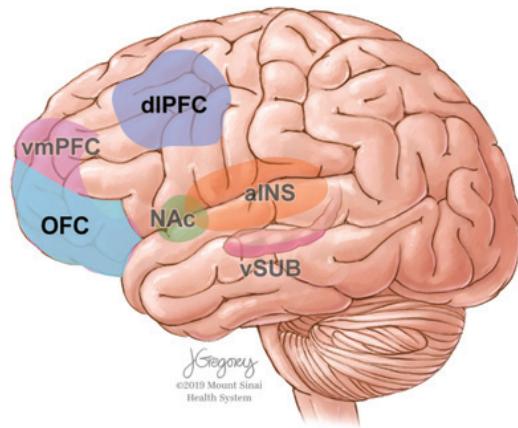


GTEx found sex differences in >13K genes

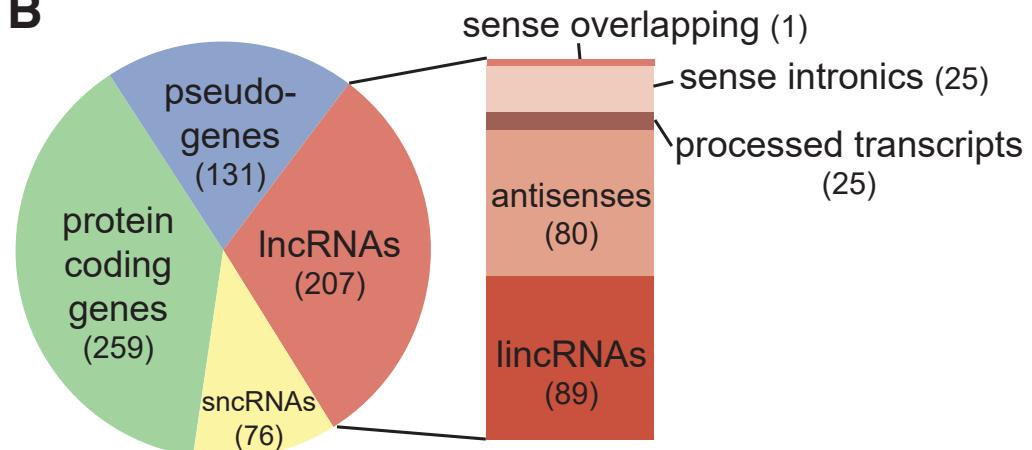
A total of 37% of all genes exhibit sex-biased expression in at least one tissue. 58 gene-trait associations are driven by genetic regulation of gene expression in a single sex.

Depression affects women at twice the rate of men

A



B

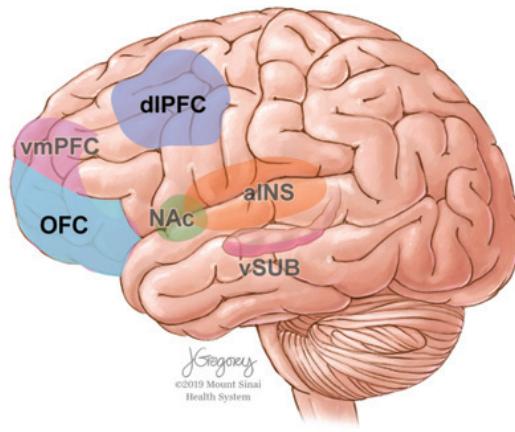


Pie chart illustrates the proportion of RNA biotypes that are differentially expressed in depression across brain regions and sexes. Issler et al., 2020, Neuron 106, 912-926

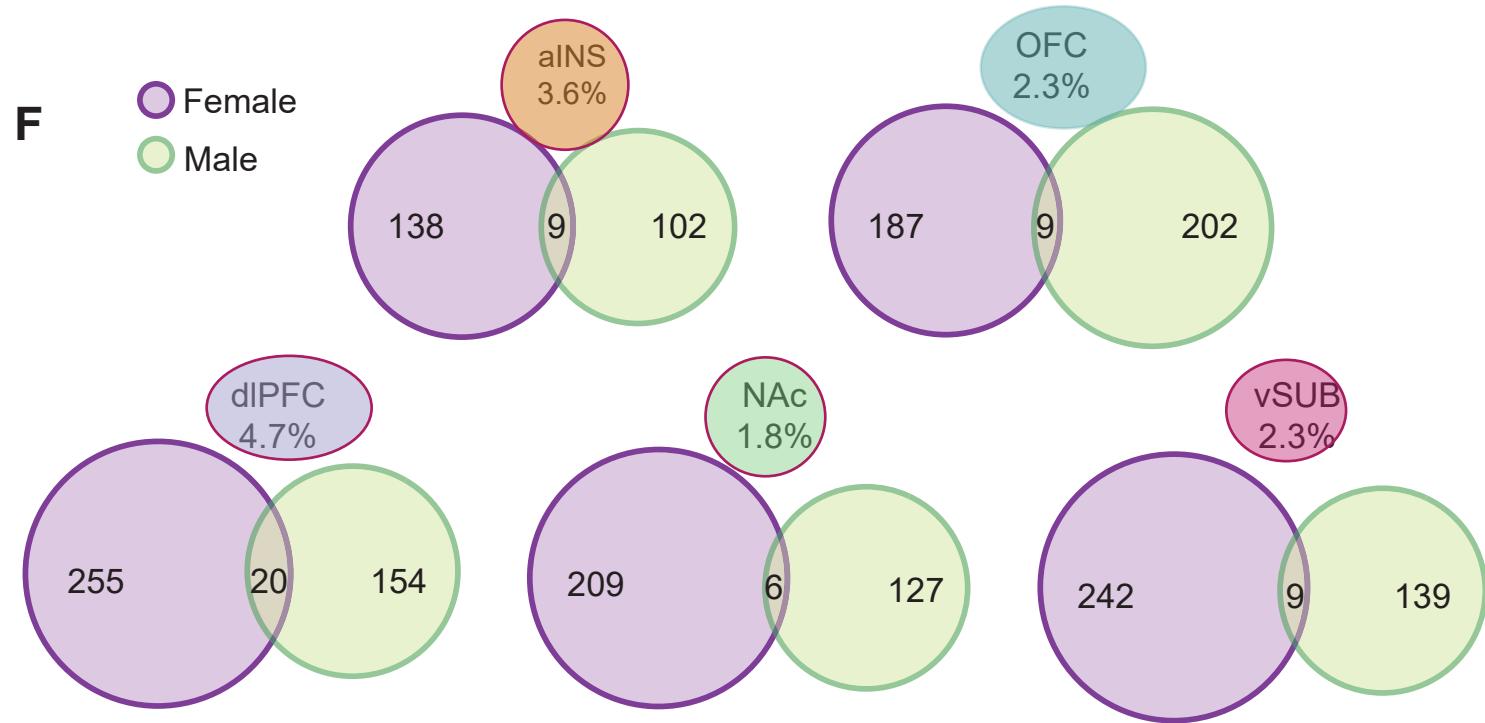
Depression looks the same in men and women

Male and female depressed brains use different genes

A

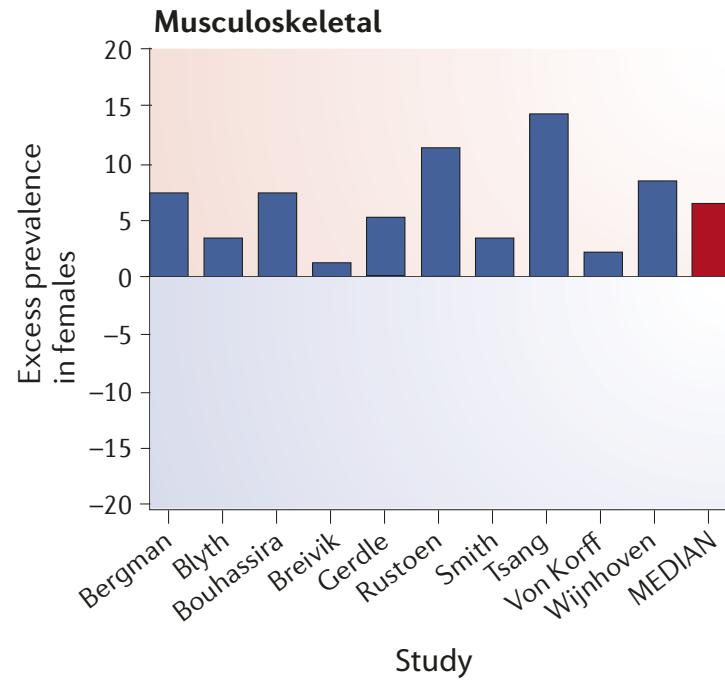
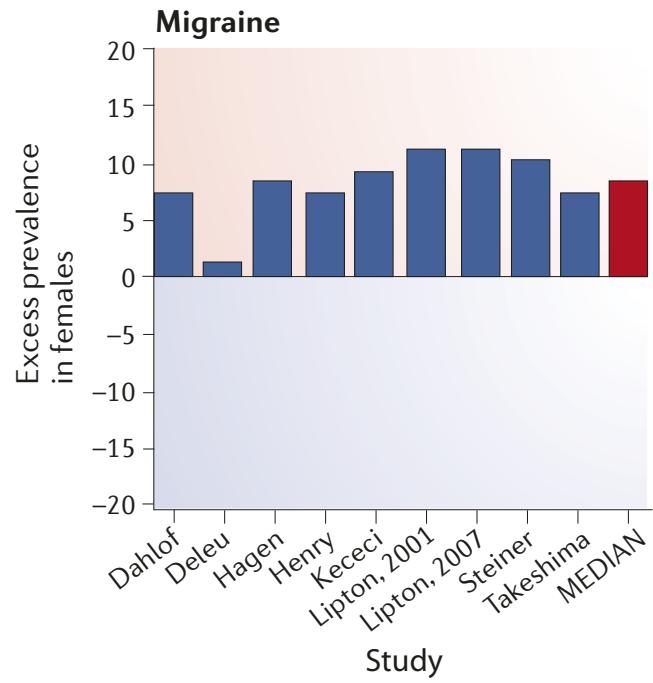
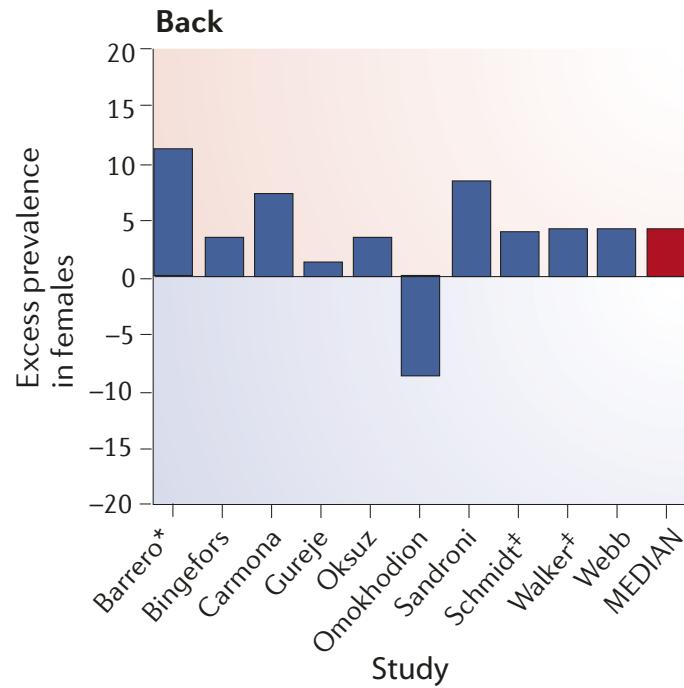


F



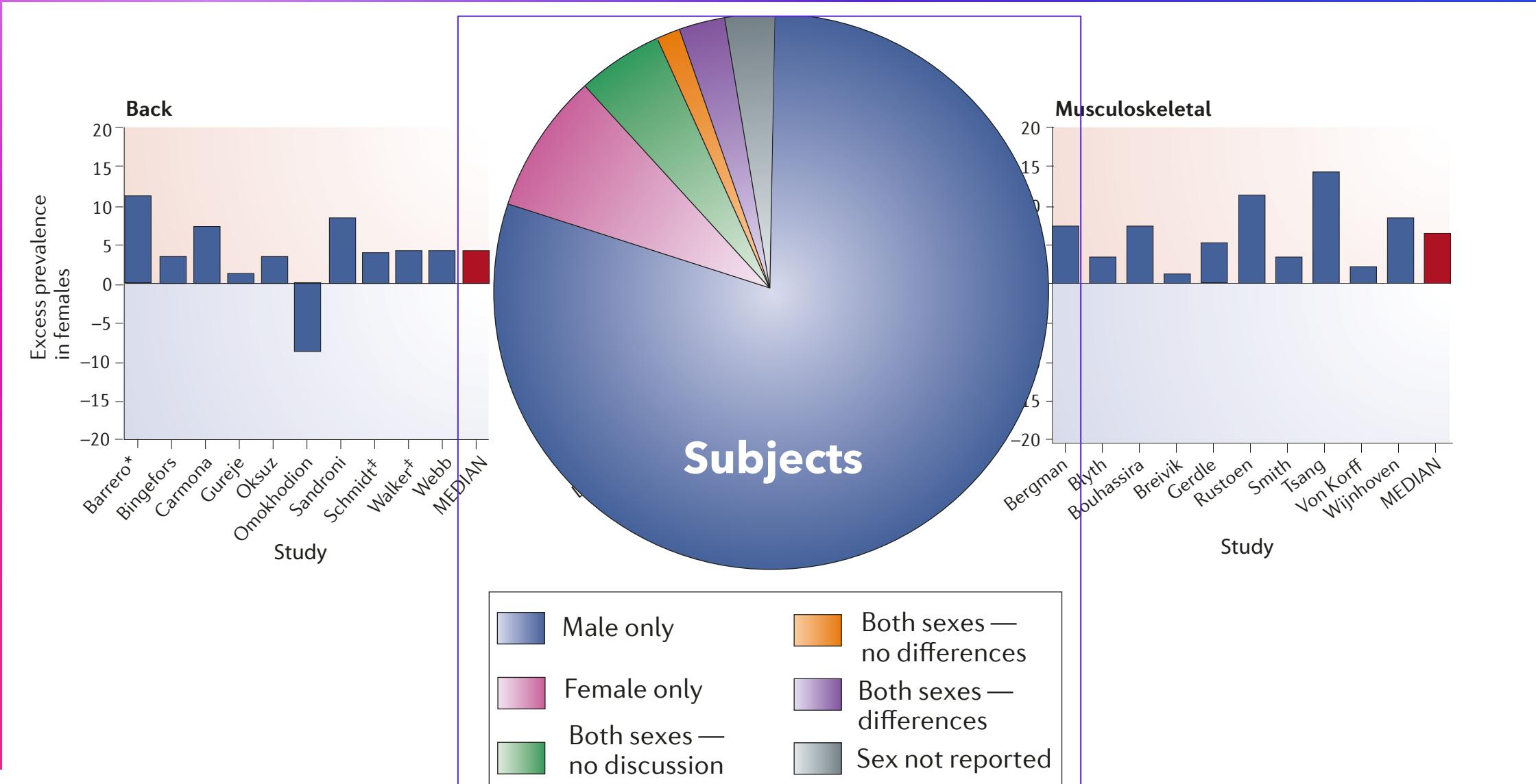
Studies identify a female-specific driver of stress resilience that is aberrant in female depression.

Sex Differences in Chronic Pain



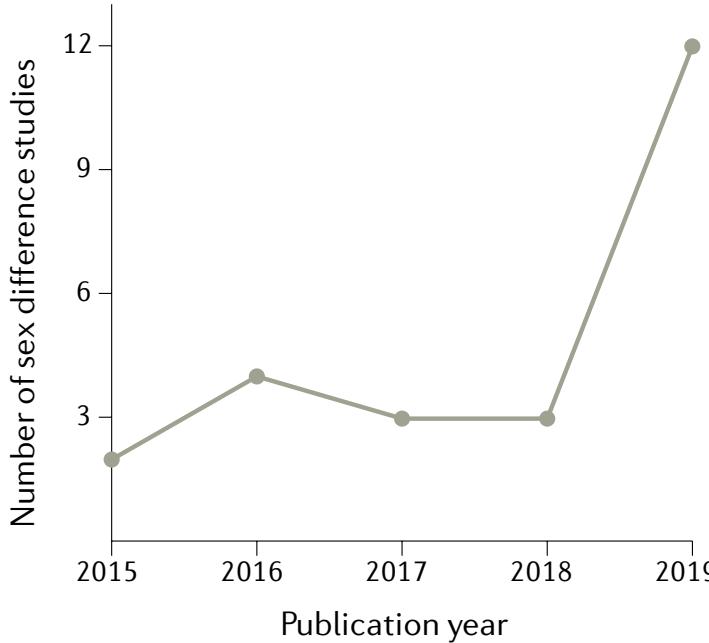
Mogil (2012) Nature Reviews Neuroscience

Sex Differences in Chronic Pain

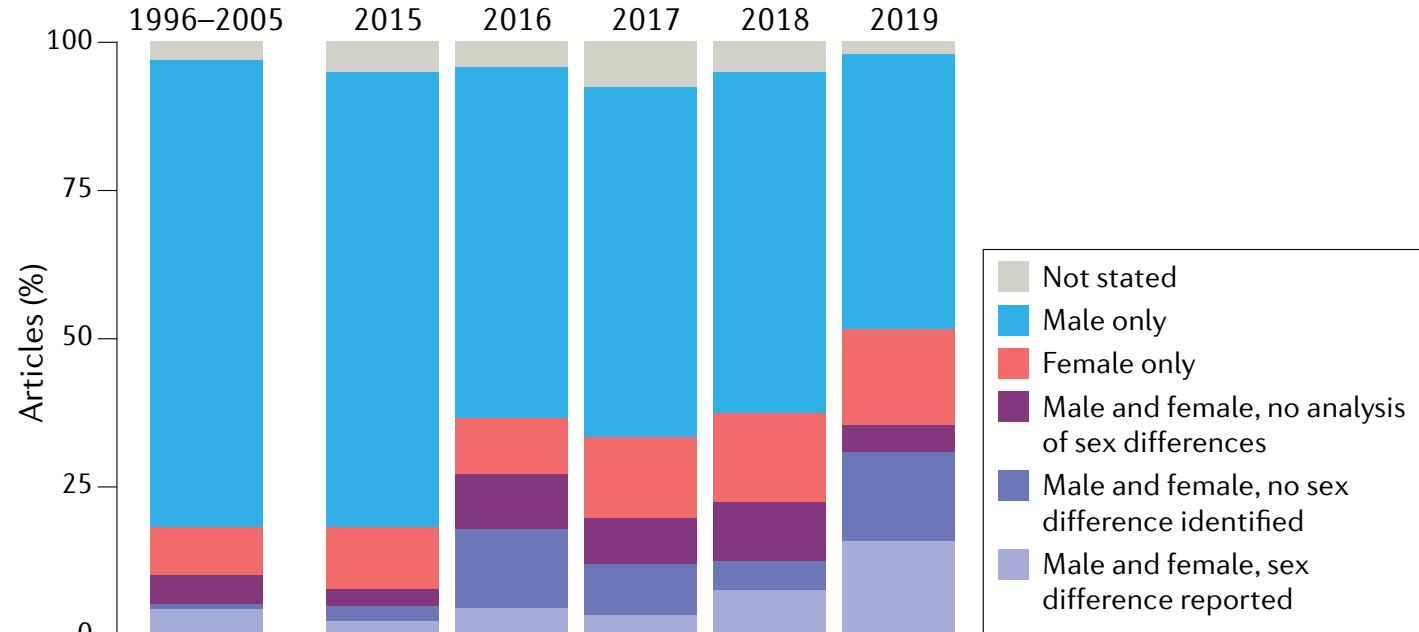


SABV is having an effect

a Sex difference studies published in the journal *Pain*



b Choice and reporting of animal subjects in the journal *Pain*

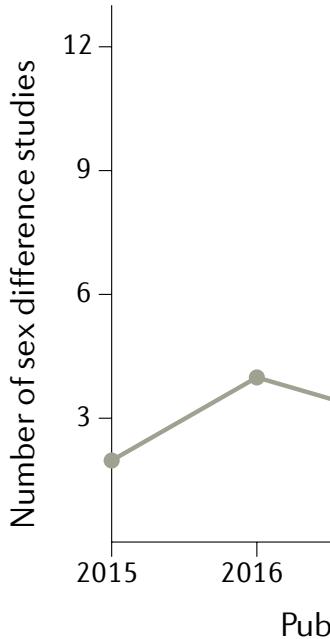


Mogil (2020) Nature Reviews Neuroscience

Studies published in the journal ‘Pain’
Since 2016 more sex differences studies published and
more studies include female subjects.

SABV is having an effect but policy needs to follow the science

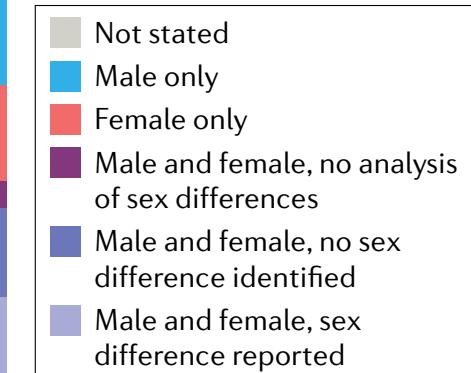
a Sex difference studies published in the journal *Pain*



b Choice and reporting of animal subjects in the journal *Pain*



The federal plan for health science and technology's response to the opioid crisis: understanding sex and gender differences as part of the solution is overlooked



Becker and Mazure *Biology of Sex Differences* (2019) 10:3
<https://doi.org/10.1186/s13293-018-0215-5>

Studies published in the journal *Pain*'

Since 2016 more sex differences studies published and more studies include female subjects.

Future Research Needs for SABV

- + Computational approaches for Sex X gene X trait analyses
- + Systems level analysis and analyses across systems
- + Interdisciplinary and transdisciplinary teams
- + Prioritize translational studies that test mechanistic hypotheses
- + Gender-centered treatments