



**Advancing NIH Research on the Health of
Women: A 2021 Conference**

The Case of Fibroids as a Female-Specific Chronic Debilitating Condition

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Virtual Meeting

Disclosures

- Editor-in-Chief, Fertility & Sterility – Science
- Board Member, Division of Reproductive Endocrinology and Infertility, ABOG
- Women’s Healthcare Academy, Sponsored by Bayer

The views expressed in this presentation are the presenters, and do not represent the Uniformed Services University of the Health Sciences, the Department of Defense, or the Federal Government.

Defining Chronic Debilitating Disease

Chronic: Lasting over a year, require ongoing medical attention and/or limit activities of daily living.

Debilitating: Causing serious impairment of normal activity

Disease: Disruption of health that induces specific signs and/or symptoms

Chronic Debilitating Diseases

Female Specific

- Gyn Cancers
- Menstrual abnormalities
- Fibroids
- Endometriosis
- Adenomyosis
- Female Infertility
- Miscarriage
- PCOS
- Pelvic Floor d/o
- Menopause
- PID
- Pregnancy

Female Prevalent

- Depression
- Migraine
- Breast Cancer
- Autoimmune
- Rheumatoid Arthritis
- Multiple Sclerosis
- STIs
- Chronic Fatigue
- Fibromyalgia
- Osteoporosis
- Candidiasis

Poorly Understood in Women

- Violence
- Dementia
- Osteoarthritis
- Endocrine d/o
- Metabolic d/o
- Blood d/o
- Immune d/o
- Recurrent UTIs
- HIV
- Neuropathy
- Incontinence
- Chronic pain

Morbid in Women

- Heart Disease
- Low back pain
- COPD
- Drug use d/o
- Stroke
- Diabetes
- Obesity
- Influenza
- Pneumonia



Impact vs Commitment to Female-Specific Health Issues, USA

	Est. Percent Symptomatic	Est. # Impacted (in Millions)	Est. NIH Funding (% , 2020)
Menopause	85%	140	<0.00001%
Menstrual Disorders	50-60%	83	0.00004%
Fibroids	20-25%	33	0.001%
Pelvic Floor Disorder	17-19%	30	0.002%
Vulvodynia	16%	27	0.0008%
Infertility	15%	25	0.007%
Endometriosis	10%	17	0.0009%
Invasive Breast Cancer	9.4%	16	0.3%
Polycystic Ovarian Syndrome	8%	13	<0.00001%
Premenstrual Dysphoric Disorder	7.4%	12	<0.00001%
Pelvic Inflammatory Disease	4.4%	7	0.002%
Endometrial Polyps	3-35%	6	<0.00001%
Endometrial Cancer	2.8%	5	0.01%
Ovarian Cancer	2.5%	4	0.07%

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Poorly Understood in Women

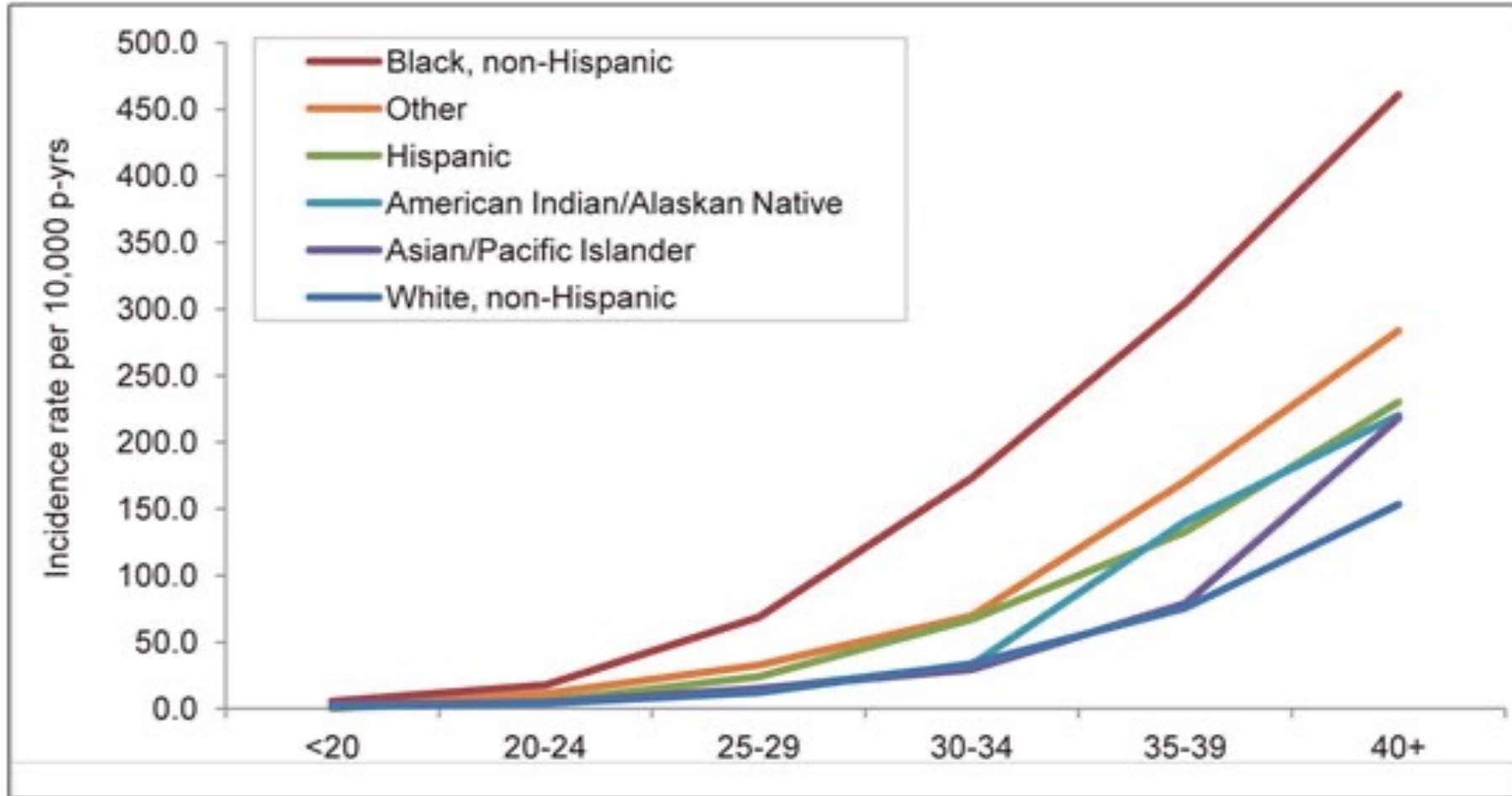
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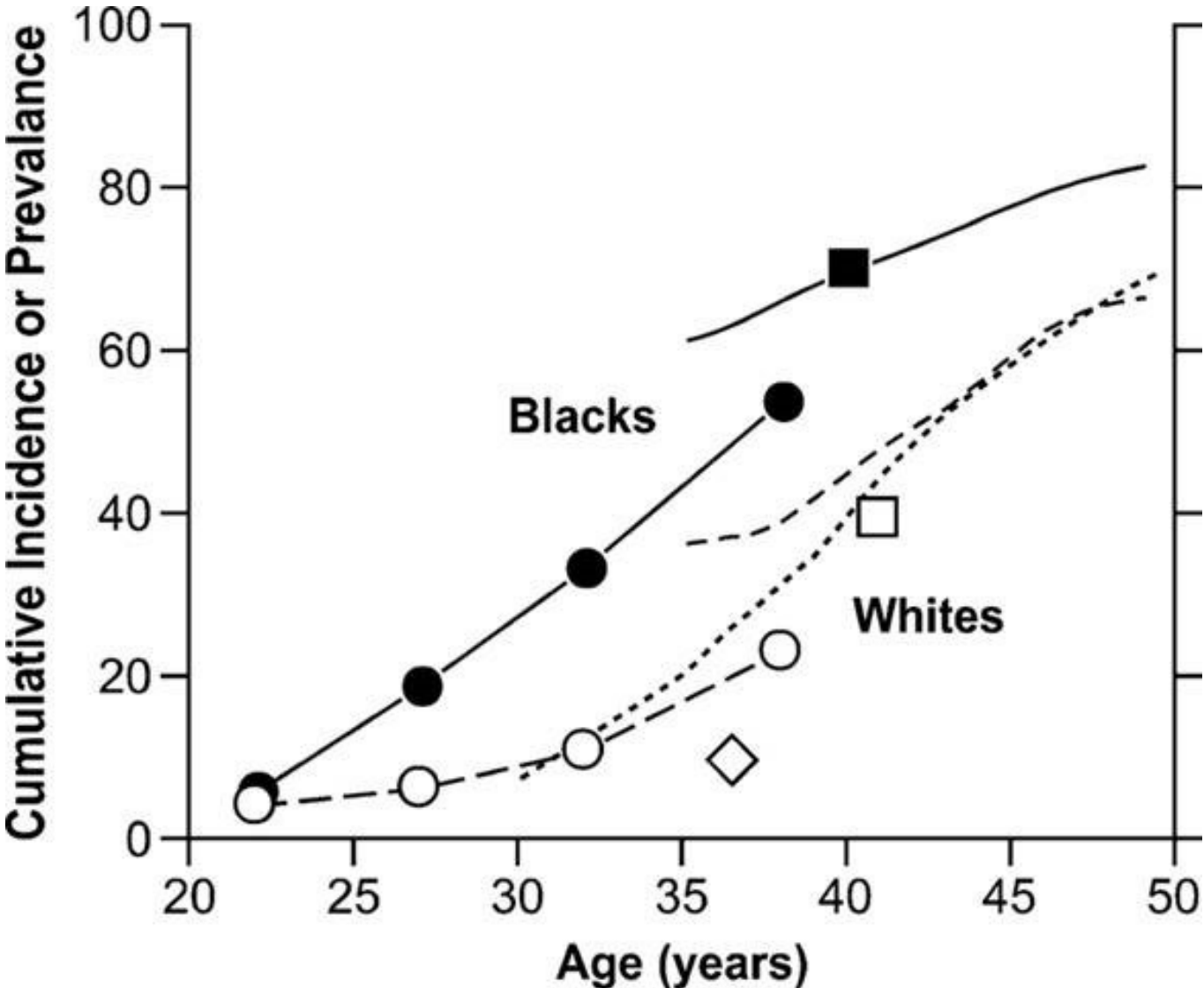


Fibroids in Active Duty Women



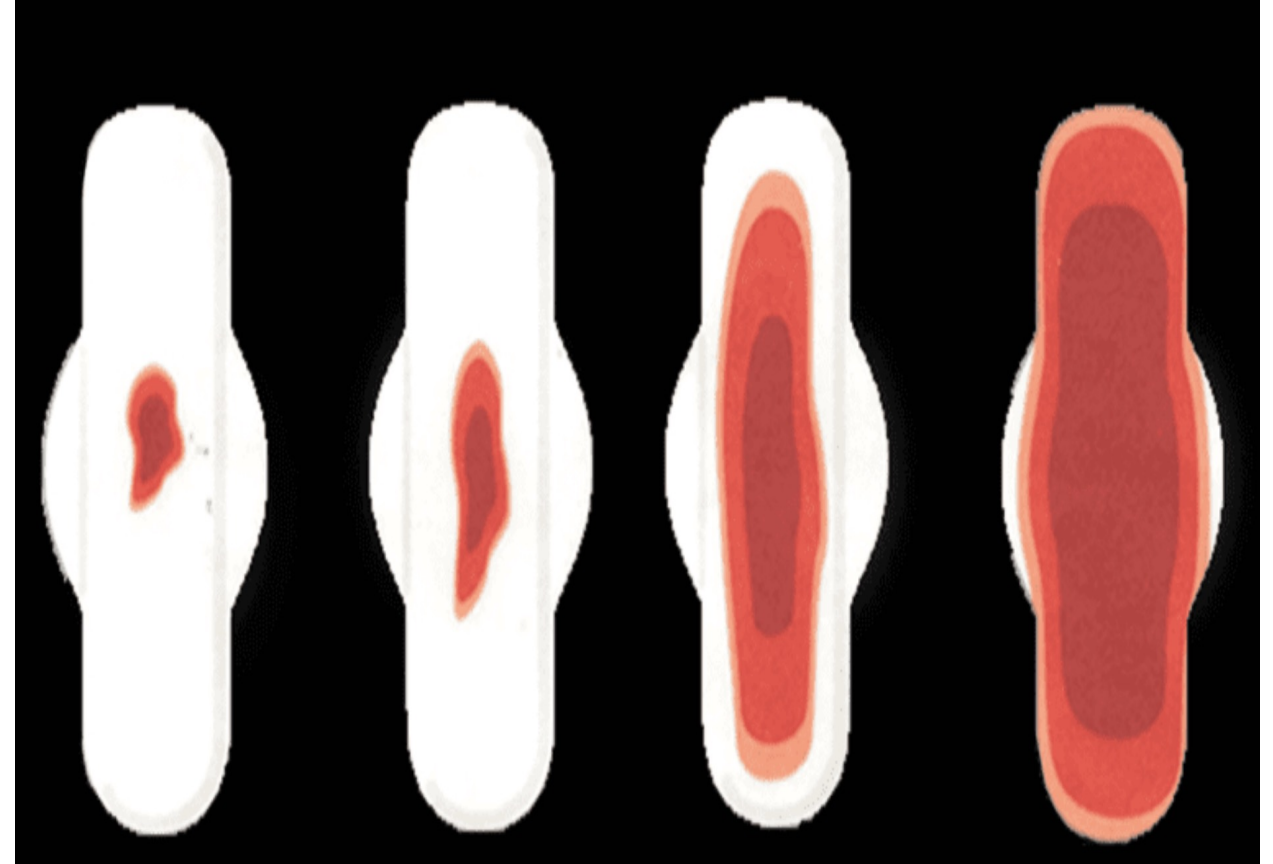
"Incidence rates of uterine fibroids by age group and race/ethnicity, active component, U.S. Armed Forces, 2001-2010"

Cumulative Incidence of Fibroids over Reproductive Lifespan



Heavy Menstrual Bleeding

- Excessive menstrual blood loss that interferes with physical, emotional, social and material quality of life
- Impacts up to 30% of women in their lifetime
- Accounts for 18-30% of gynecologic visits
- Estimated annual direct costs = \$1,000,000,000
- Estimated indirect costs = \$12,000,000,000
 - Lost days of work and quality of life



Farquar and Brown Cochrane Database Syst Rev 2009;4:CD000154
Marret Eur J Obstet Gynecol Reprod Biol 2010;152:133-7
Nicholson Am J Obstet Gynecol 2001;184:523-30
Liu Value Health 2007;10:183-94

Pain

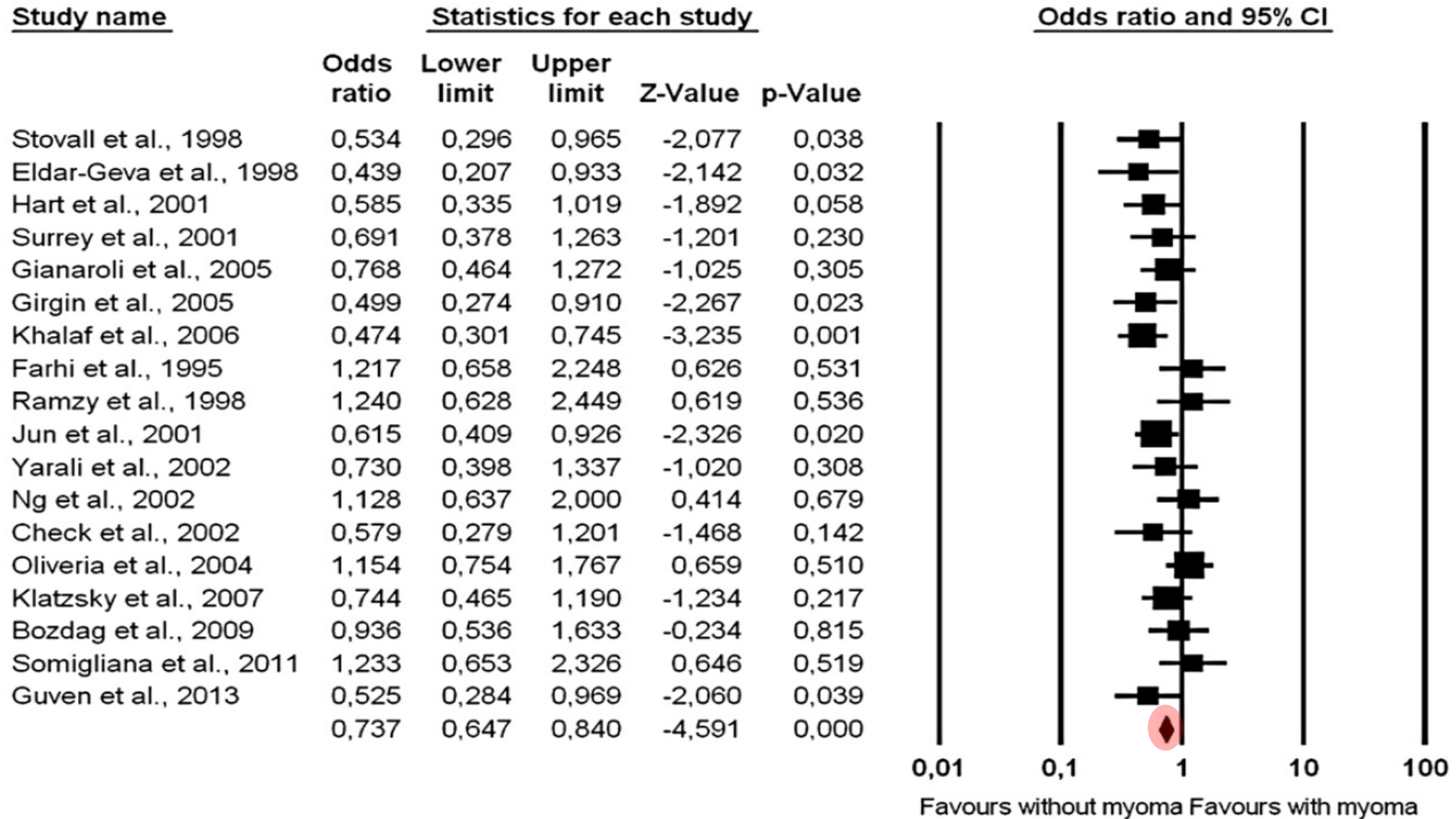
- Most common symptoms:
 - Menstrual pain 51-63%
 - Low back pain 58-65%
 - Pelvic pressure 16-33%
 - Abdominal pain 25%
 - Pain during sex 17-24%

1 in 4 find such symptoms
extremely bothersome



Osuga Fertil Steril 2019;112:922
Fuldeore Int J Womens Health 2017;9:403
Soliman Curr Med Res Opin 2017;33:1971
Zimmerman BMC Womens Health 2012;12:6

Fibroids Increase Miscarriage Rate



Odds of miscarriage decreased with no myoma compared to myoma

Not Impacting the Cavity

OR = 0.737 [0.647, 0.840]

Obstetric Complications of Fibroids

<u>Complication</u>	<u>Fibroid</u>	<u>No Fibroid</u>	<u>OR</u>
Abnormal labor	49.6%	22.6%	2.2
Cesarean Section	46.2%	23.5%	2.0
Preterm delivery	13.8%	10.7%	1.5
Breech position	9.3%	4.0%	1.6
Postpartum Hemorrhage	8.3%	2.9%	2.2
Premature Rupture of Membranes	4.2%	2.5%	1.5
Placenta previa	1.7%	0.7%	2.0
Abruption	1.4%	0.7%	2.3

Biderman-Madar Arch Gynecol Obstet 2005;272:218
 Coronado Obstet Gynecol 2000;95:764
 Navid Ayub Med Coll Abbottabad 2012;24:90
 Stout Obstet Gynecol 2010;116:1056

Ciavattini J Matern Fetal Neonatal Med 2015;28:484-8
 Kramer Am J Obstet Gynecol 2013;209:449.e1-7
 Sheiner J Reprod Med 2004;49:182
 Qidwai Obstet Gynecol 2006;107:376

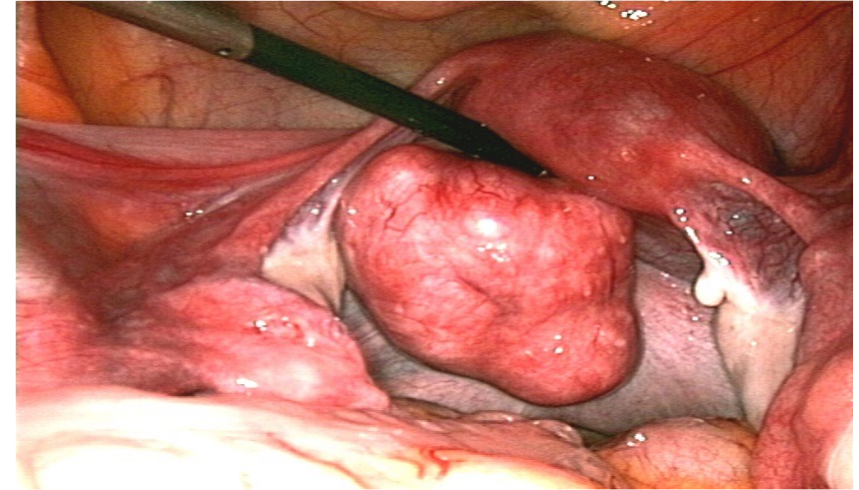
What are Fibroids, and What Can We Do?



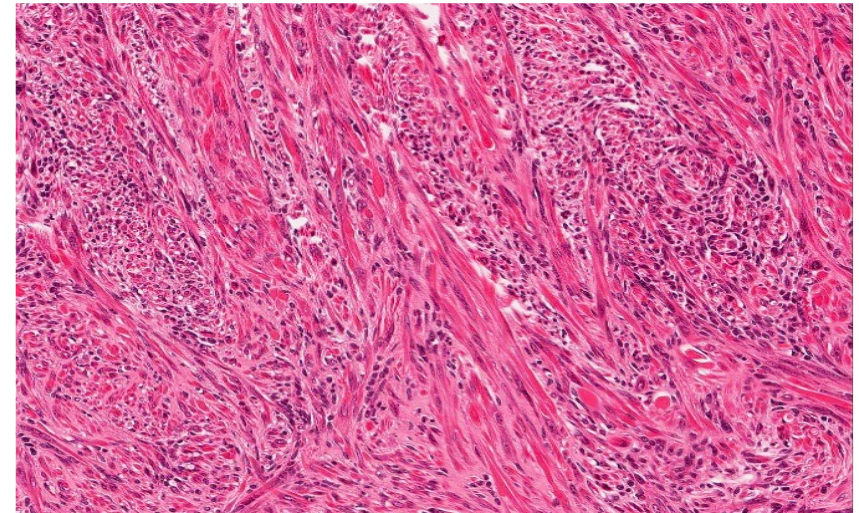
What are Uterine Fibroids?

- Hormonally sensitive benign tumors that produce an abundance of fibrosis
- Account for 50% of all hysterectomy procedures
- Grow in the presence of estrogen and progesterone

Gross



Microscopic



Fibroids Throughout History



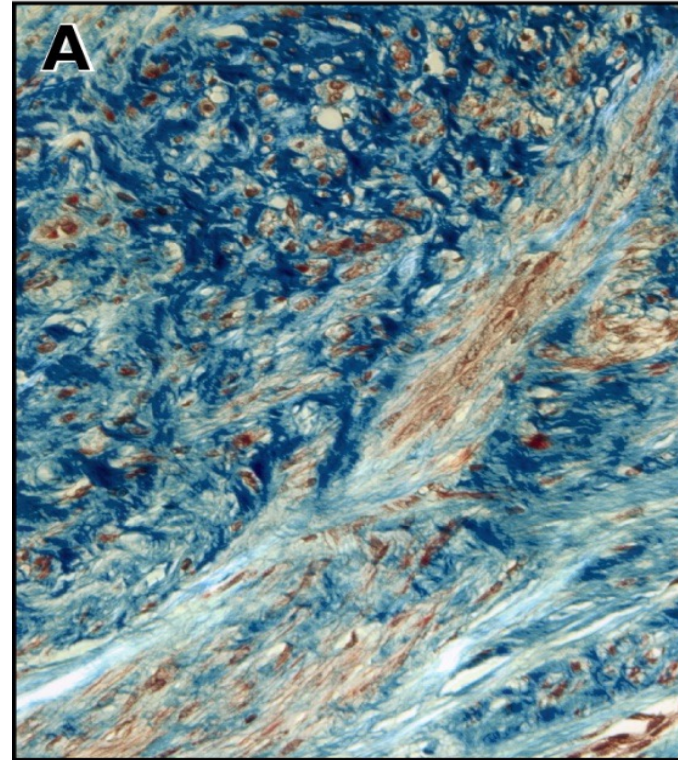
5,000 year old calcified mass from human skeletal remains

Fibroids are Predominantly Scar Tissue

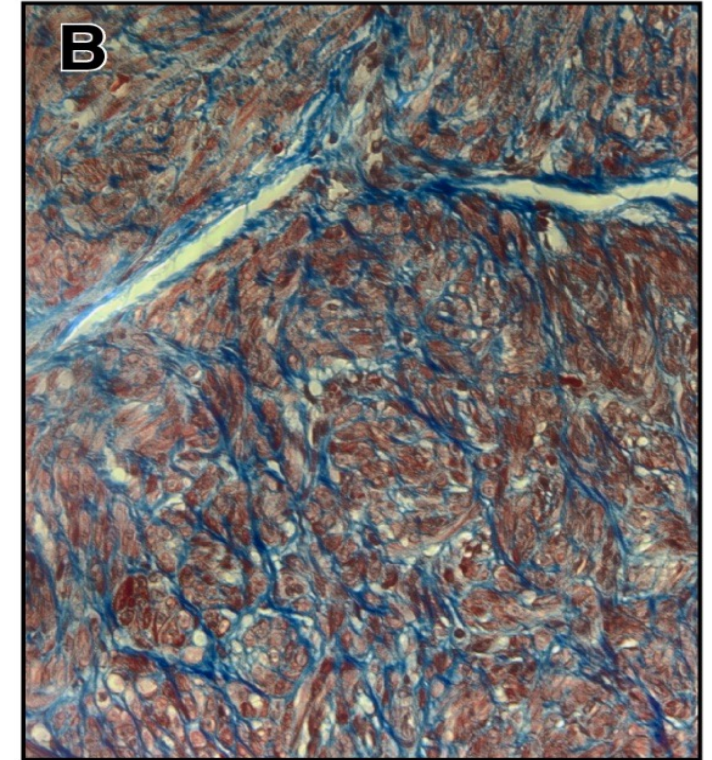
Uterus with Fibroid



Fibroid



Normal Uterus

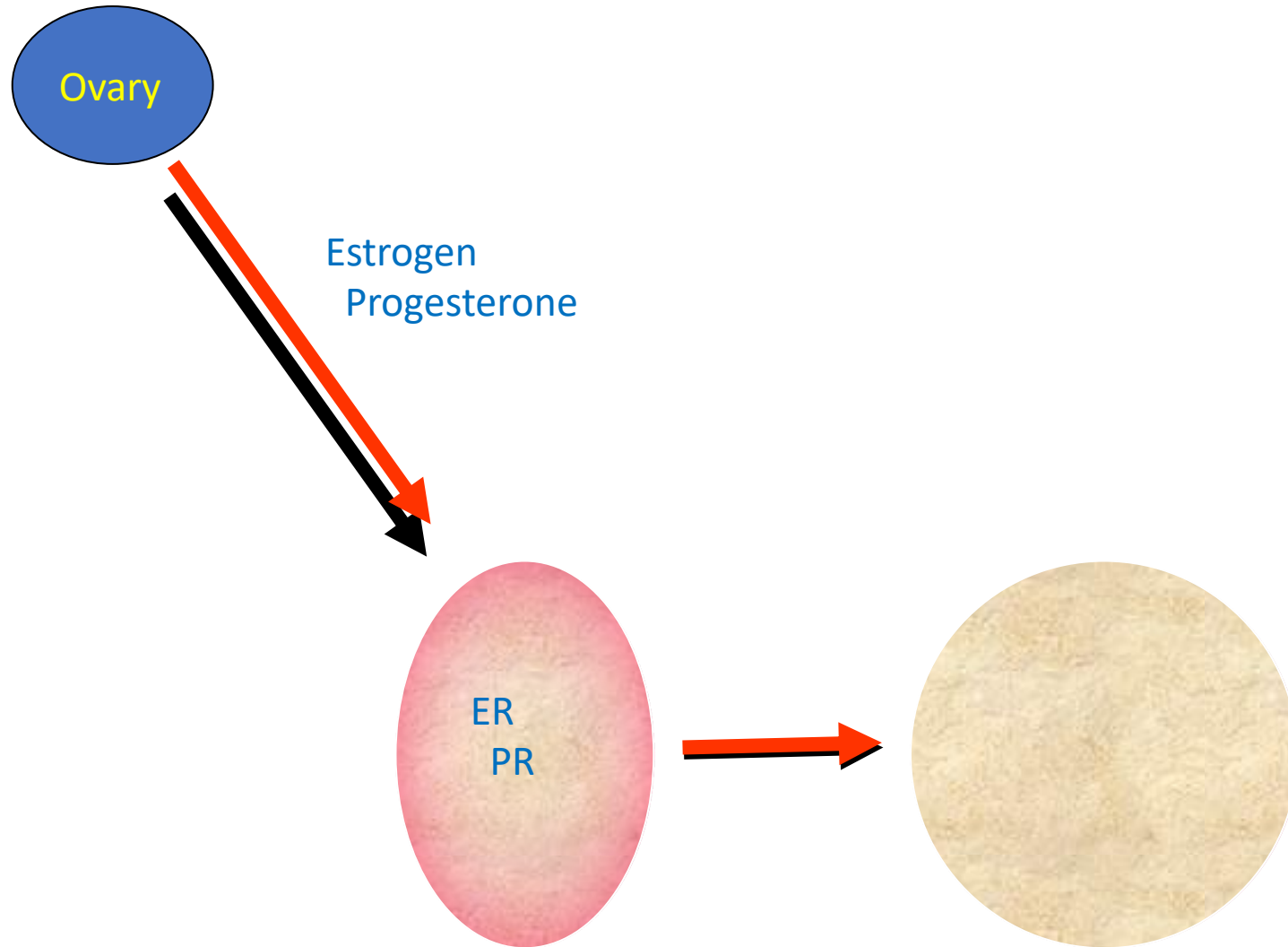


TREATMENT CONCEPT 1: Fibroids Need Blood



- Hysterectomy
- Myomectomy
- Uterine artery embolization
- Uterine artery occlusion
- MRI guided HIFU
- Radiofrequency ablation

TREATMENT CONCEPT 2: Ovarian Hormones Stimulate Fibroid Growth



- Gonadotropin releasing hormone analogues
- Aromatase inhibitors
- Selective progesterone receptor modulators

Treatment options for Uterine Leiomyomas

Surgical

Hysterectomy

Open

Myomectomy L/S

Myomectomy

Robotic Myomectomy

H/S Myomectomy

Radiologic / Minimally Invasive

Uterine Artery Embolization

MRI-Guided HiFU

Endometrial Ablation

L/S Radiofrequency

Ablation Uterine Artery

Occlusion

Damages uterus

Starves uterus

Hormonal

regulation Pain

control

Medical

Oral Contraceptive

Pills NSAIDs

GnRH Analogues

Aromatase Inhibitors

SPRMs

Why Such Poor Options After 150 Years of Study?

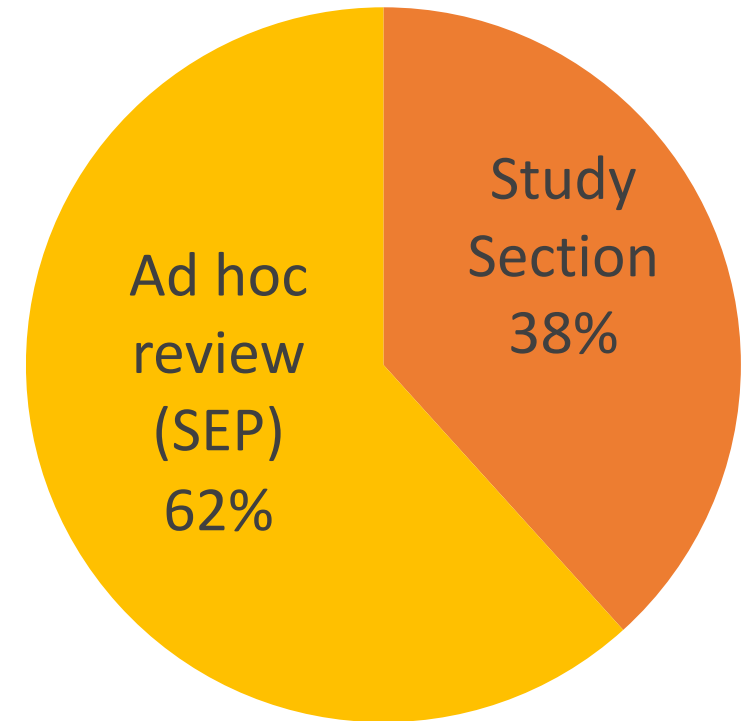
- The disrespected uterus
- Symptom taboo
- Poor models
- Poor focus



Remaining Gaps in Fibroid Knowledge to Improve Women's Care

- Increased Public Awareness
- Diversify Study Populations
- Improved Understanding of Fibroid Growth
- Improved Understanding of Fibroid Impact on Pregnancy
- Identification of Novel Therapies
- Improved Fibroid Classification
- Identification of Environmental Exposures
- Identification of Different Fibroid Phenotypes
- Large-Scale Cohort Studies
- Mechanism of Hormonal and anti-hormonal Regulation

Awarded Fibroids RCDC applications
FY2018-2021



Need for Focused Research in Women's Health

- Adding women to a study is not the same as studying women
- Intermittent research in women's health insufficient
- Diseases unique to women result in life-long disability

- Recommendations
 - Development of a National Institute of Women's Health
 - Specifically address diseases unique or more common in women
 - Collaborate with other institutes regarding diseases that also impact women, with an effort to design trials directly related to the disease experience in women

Societal Benefits for the Investment

- Decreased death
- Decreased disability
- Decreased suffering
- Improved quality of life
- Improved productivity
- Improved care of children
- Improved care of the elderly

Thank You!