

MONDAYS WITH PMARK & PMICHAEL Monday, November 25, 2024 | 1:00 – 1:45PM

TOPIC #34 Are Men an Endangered Species?



Guest speaker:



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LONGEVITY GAP

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Men as an endangered species



Everywhere in the world,

women tend to live longer than men, even as a species



Understanding the longevity gender gap is exceedingly complex. There are several theories, including:

1. Females have two X chromosomes while males have an X and a Y.

The theory is that the extra X in women has a protective effect against harmful mutations and that this holds true in other species.

2. Women produce more estrogen and less testosterone than men ; Estrogen provides protection against a range of diseases, such as cardiovascular disease.

3. Risky behavior and occupational hazards of young and middle-age males partially account for the longevity gender gap, but the primary reason for it is the better somatic fitness of women than men.



Survival difference between sexes

As life expectancy has increased with improvements in living conditions during the last century, there has consistently emerged a survival difference between the sexes, with **women living longer**

- United Kingdom: estimated life expectancies for women and men from birth (2012) are 82.4 and 78.0 years, respectively
- Russia: 73.1 years women & 60.1 years men
- France: 84.7 women & 78.3 years for Men



Top All Cause Mortality for Women vs Men

Women

1. Heart Disease

2. Cancer

3. Chronic Lower Respiratory diseases

4. Stroke

5. Alzheimer's Disease

6. Unintentional Injuries

Men

1. Heart Disease

2. Cancer

3. Unintentional injuries

4. Chronic Lower Respiratory diseases

5. Stroke

6. Diabetes

Men are 3-4x more likely to commit suicide than women



Lemaître et al. 2020 Study

A new study (Lemaître et al. 2020) that looks at **lifespan** in wild mammals shows that females live substantially longer than males. The research finds that, on average, **females live 18.6%** longer than males from the same **species**. This is much larger than the well-studied difference **between** men and **women**, which is **around** 8%

The magnitude of lifespan and ageing across species is probably an interaction between environmental conditions and sex-specific genetic variations



Aviv et al. 2005 study: Are Telomeres the Explanation?

What is a telomere?

• A telomere is the end of a chromosome

Their function is to protect the ends of the chromosomes from deterioration or fusion to other chromosomes during cell division. With every cell division, telomeres shorten.

- Theoretically, the ability of **estrogen to up-regulate telomerase and at the same time reduce oxidative stress could account for the longer telomeres observed in women as compared with men**. This effect of estrogen on telomere dynamics may be attenuated or disappear altogether in older women, but its premenopausal influence could set telomere attrition at a trajectory that maintains longer telomeres in women throughout the entire human life span.
- Such a possibility can readily be tested in the future by longitudinal studies of telomere attrition rates in men versus women, and in premenopausal versus postmenopausal women.



Aviv (2007) study: Cardiovascular diseases, aging and the gender gap in the Human longevity

- Potential of the role of the estrogen and the X chromosome in the longer life span of women than men
- Estrogen exerts numerous effects among which is its ability to attenuate oxidative stress.
- Oxidative stress and inflammation figure centrally in the biology of aging and in aging-related diseases
- Diminished susceptibility of women to these diseases may therefore arise from gender-related differences in the systemic burden of oxidative stress and inflammation.
- However, these differences are not uniform throughout the human life span.
- Though pre-menopausal women are relatively protected against CVD, post-menopausal women exhibit a considerable increase in the risk for CVD, presumably due to the fall in circulating ovarian steroid hormones, particularly estrogen.
- Having two X chromosomes may also account for the better somatic fitness in women than men and its lasting effect is exerted not only during the pre-menopausal but also the post-menopausal period.



Gopalakrishnan et al., 2013 Medaka Fish Study and Longevity

- Medaka fish exhibits longevity gender gap
- Medaka fish is advantageous for studying the direct effect of increased estrogen on telomere length and longevity without the breast cancer complications reported in rodents.
- The results of this study demonstrate for the **first time in teleost that sex differences (female>male)** in telomere length and longevity also exist in fish and a natural 'menopause' -like decline of plasma estrogen was evident in females during aging.
- Estrogen levels significantly correlated with telomerase activity as well as telomere length in female organs (not in males) suggesting estrogen could modulate telomere length via telomerase activation in a sex-specific manner



Gems (2014) Evolution of Sexually Dimorphic Longevity in Humans study

• the current pattern of human aging is the result of three key factors:

1) Increased late-life reproduction by men has increased human longevity relative to other higher primates (the patriarch hypothesis)

2) the design of the ovary has constrained the evolution of longer reproductive lifespan in women

3) antagonistic pleiotropy acting on testicular function has decreased male lifespan

Pleiotropy:

A given gene can exert multiple effects on phenotype (i.e., eye color) at different points in the life history. Such
pleiotropy means that a given gene may, in principle, exert beneficial effects early in life, but deleterious ones later in life
(antagonistic pleiotropy). Because early life traits are more important to fitness, such genes can accumulate in
populations, leading to aging



Gems (2014) Evolution of modern pattern of human aging





Prostate hyperplasia as a model for the evolution of aging

- The evolution of late-life BPH is likely explained by the principle of antagonistic pleiotropy, where increased androgen levels and/or altered prostatic response to it increased early life fitness but in later life gave rise to hyperplasia
- Thus, BPH is a good model for investigating the proximate biological mechanisms of the evolution of aging.
- At the molecular and cellular levels, androgens may orchestrate trade-offs between early life sex-related fitness traits and late-life pathologies.



Good news:

Gender longevity gap is decreasing

Why?

Increase in access to care

Early intervention, screenings



Bottom line:





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- Aviv A. Cardiovascular Diseases, Aging and the Gender Gap in the Human Longevity. *J Am Soc Hypertens*. 2007;1(3):185-188. doi:10.1016/j.jash.2007.02.002
- Gems D. Evolution of sexually dimorphic longevity in humans. *Aging (Albany NY)*. 2014;6(2):84-91. doi:10.18632/aging.100640
- Iorga A, Cunningham CM, Moazeni S, Ruffenach G, Umar S, Eghbali M. The protective role of estrogen and estrogen receptors in cardiovascular disease and the controversial use of estrogen therapy. *Biol Sex Differ*. 2017;8(1):33. Published 2017 Oct 24. doi:10.1186/s13293-017-0152-8
- Oksuzyan A, Brønnum-Hansen H, Jeune B. Gender gap in health expectancy. *Eur J Ageing*. 2010;7(4):213-218. Published 2010 Nov 4. doi:10.1007/s10433-010-0170-4





Questions

Upcoming NEBGH events:

- December 12 30th Annual Tribute to Leadership
- December 16 Mondays with Dr. Mark and Dr. Michael

2025 SAVE THE DATES!

- March 27 Women's Health Conference
- June 5 14th Annual Health & Wellness Benefits Conference

