

September 19, 2025

Longevity Update: Beyond GLP-1s Erectile Function as a Harbinger of Health

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Our deep dive into longevity as the next wave for biotech investors attracted significant attention. Many asked how to get involved now and which companies would benefit. As a natural extension of the obesity therapeutic landscape, we see the two incumbents (LLY, NOVO) as well positioned in addition to two new entrants from our coverage (AMGN, VKTX) by virtue of their potential to provide favorable outcomes benefits associated with weight loss, glycemic control and anti-inflammatory benefits. One area of inquiry is the gender gap associated with lifespan and healthy aging. We believe this gap may provide important clues for biotech investors interested in longevity. Women outlive men by an average of 5.8 years in the US and this gap has grown over time. Heart disease, diabetes and emotional distress are among the leading contributors to the gender gap and erectile dysfunction (ED) is often the first detectable symptom of these.

KEY POINTS

- We're encouraged by [feedback from experts coming out of ARDD](#) that GLP-1 based obesity therapeutics are increasingly being discussed as longevity drugs along with many other applications. As we previously indicated, metformin, shingles vaccines, mTor inhibitors and SGLT2 inhibitors are among the various drugs with alleged longevity benefits. Based on the correlation between ED and other life-threatening outcomes, we're increasingly interested in the potential benefits of PDE5 inhibitors and other ED therapeutics.
- Substantial evidence points to mortality benefits of treating ED, as multiple studies show that ED predicts subsequent cardiovascular events regardless of relevant risk factors including age, body mass index, and prior cardiovascular disease. ED is also implicated in psychological pathologies, with evidence suggesting that ED acts as both a cause and symptom of psychological distress, underscored by the increased likelihood of depressed mood among affected men.
- Given findings linking ED to both cardiovascular and psychological outcomes, we believe early diagnosis and effective treatment can help reduce the gender lifespan gap and work to improve quality of life for men and their partners, thereby narrowing the overall lifespan-healthspan gap. Currently, PDE5-inhibiting drugs dominate the ED treatment landscape, with emerging evidence highlighting their ability to promote longevity.
- Importantly, PDE5 inhibitors, specifically sildenafil (Viagra) and tadalafil (Cialis), have been shown to significantly reduce the risks of mortality, cardiovascular disease, and dementia, with tadalafil providing slightly greater benefits than sildenafil likely due to its longer half-life and multi-day duration-of-action.
- While we underscore the utility of ED therapies in promoting longevity, real-world usage of PDE5 inhibitors is limited by side effects and ineffectiveness. We believe novel, non-PDE5 drugs could address highly-prevalent ED while delivering critical lifespan-healthspan benefits: Dicot Pharma's lead asset LB-01 is particularly interesting given its multi-week efficacy and competitive safety profile.

We will virtually host Dicot Pharma at our [Private Company Showcase on Sept. 25th, 2025](#). Please contact your Oppenheimer representative to register.

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Longevity Update: Erectile Function as a Harbinger of Health

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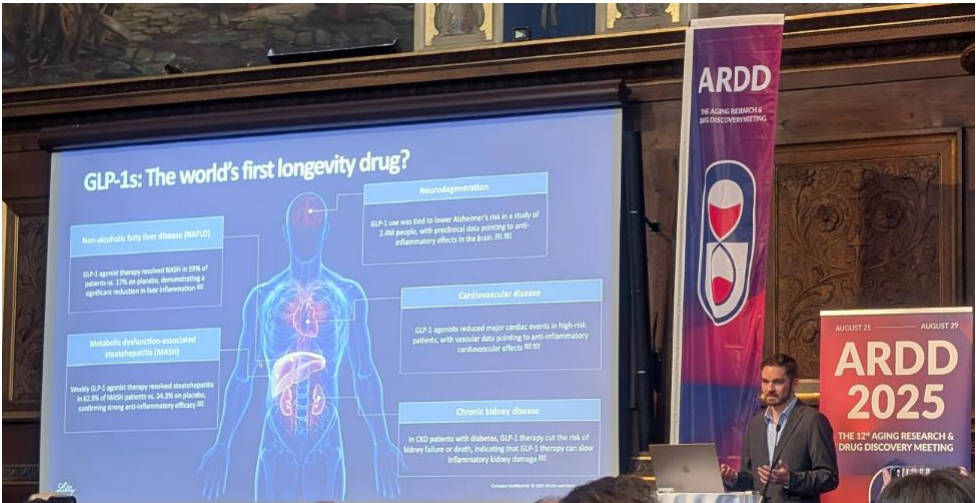
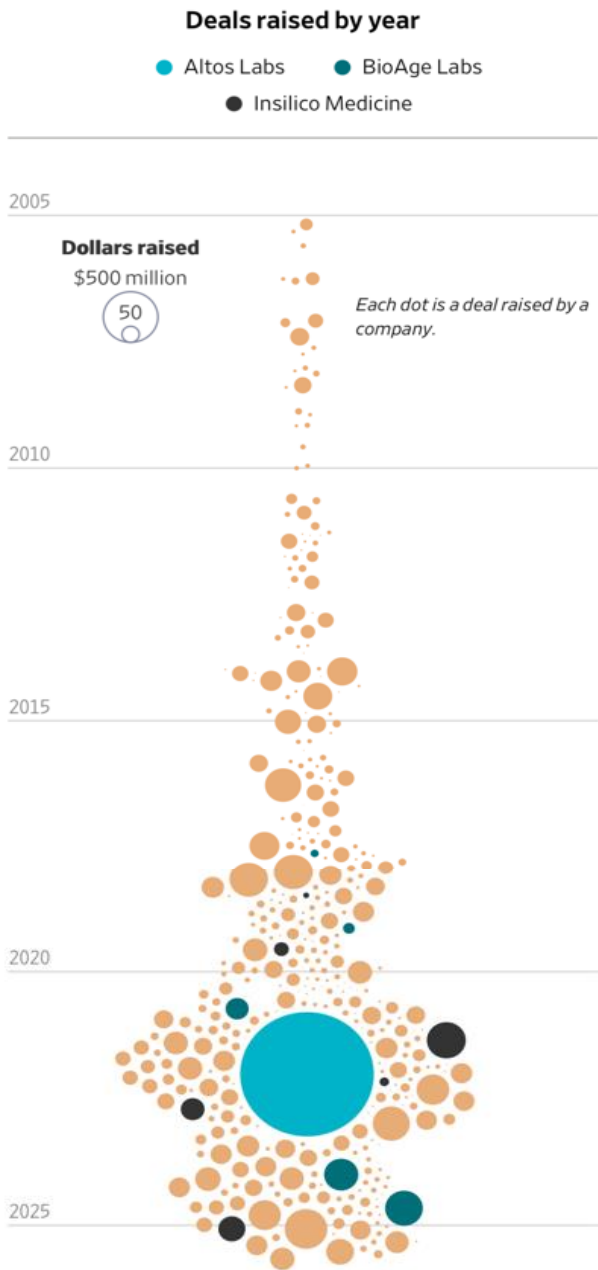
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01

Recent Developments in Longevity Support Our Enthusiasm

1 | Recent Developments in Longevity Support Our Enthusiasm

Since our 7/7/25 Report: Longevity Gaining Mainstream Attention



- In a Sept. 7 report titled “The Billionaires Funding the Quest for Longer Life”, the WSJ indicates “there is no consensus on what make something a longevity company” and describes categories based on corporate missions.
- The WSJ highlights 3 companies (Altos Labs, BioAge Labs and Insilico Medicine) that have successfully raised capital and describes how longevity has increasingly attracted funding from wealthy investors.
- Phil Newman and other longevity experts highlight how **Eli Lilly scientist Andrew Adams described GLP-1s as “The World’s First Longevity Drug?”** at the AARD
- **Novo Nordisk’s Lotte Knudsen** also gave a presentation at AARD, titled **“Semaglutide as a Proven Longevity Medicine”**.



While the exact terminology is yet to be defined, longevity is a clear therapeutic target of interest to investors and Large Pharma

Source;; WSJ.com, Alex Zhavoronkov (X), Acquired Podcast

These Recent Dynamics Support our Longevity Thesis

- Longevity will be an important theme for biotech and generalist investors, potentially larger than obesity, and we want to get in front of it before it takes off.
- Current obesity therapeutics are dominated by drugs that were originally designed to treat diabetes and only after serendipitously finding those diabetes drugs also cause weight loss did they become successful obesity drugs. It turns out those same obesity drugs, and other drugs for different diseases, also improve longevity.
- The link between obesity and longevity is well established and GLP-1 based drugs are now recognized by LLY and NVO for their longevity benefits.
- While we believe longevity is the next wave of growth for biotech investors to focus on, we recognize that it may not be known as longevity but instead referred to as preventive medicine.
- We see preventive medicine as an especially attractive strategic opportunity for AMGN and VKTX in our coverage and global demographic dynamics overwhelmingly support growing interest from multiple large and small cap companies.

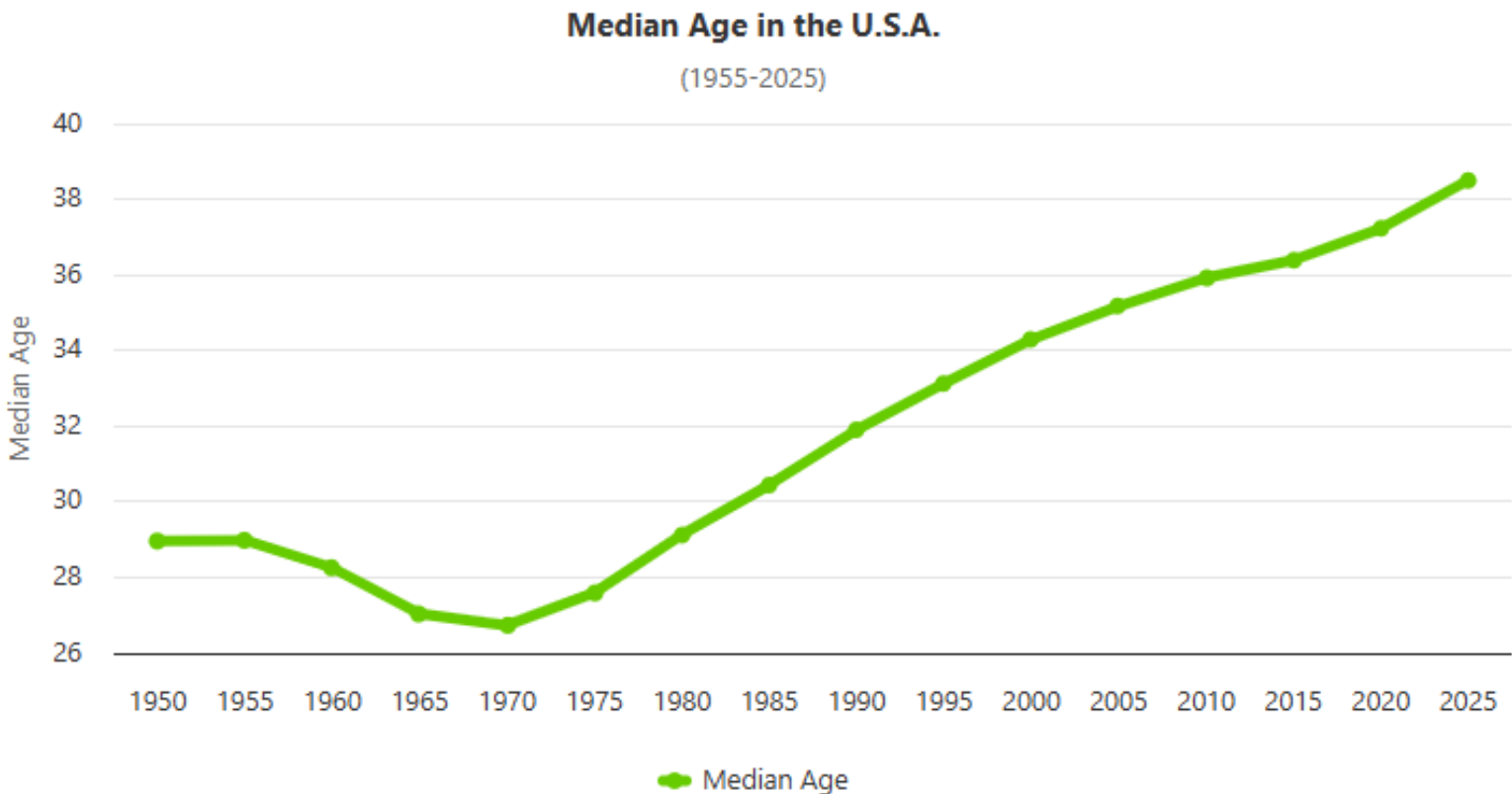


**The aging population will drive a longevity opportunity
that we see as the next wave for biotech investors**



Longevity Market is Large and Growing Based on a Rapidly Aging Population

The **median age** in the United States is **38.5 years** (2025).



- The current life expectancy in the US is 79.6 years which includes 82.1 years for females and 77.2 for males
- The median age in the US is now 38.5 years and has been increasing relatively linearly at a rate of 1 year every 5 years since 1970
- The increasing median age is driven by a slowly increasing life expectancy, slowly decreasing fertility and offset by the impact of migration
- Gains in life expectancy across global populations are recognized as a societal achievement



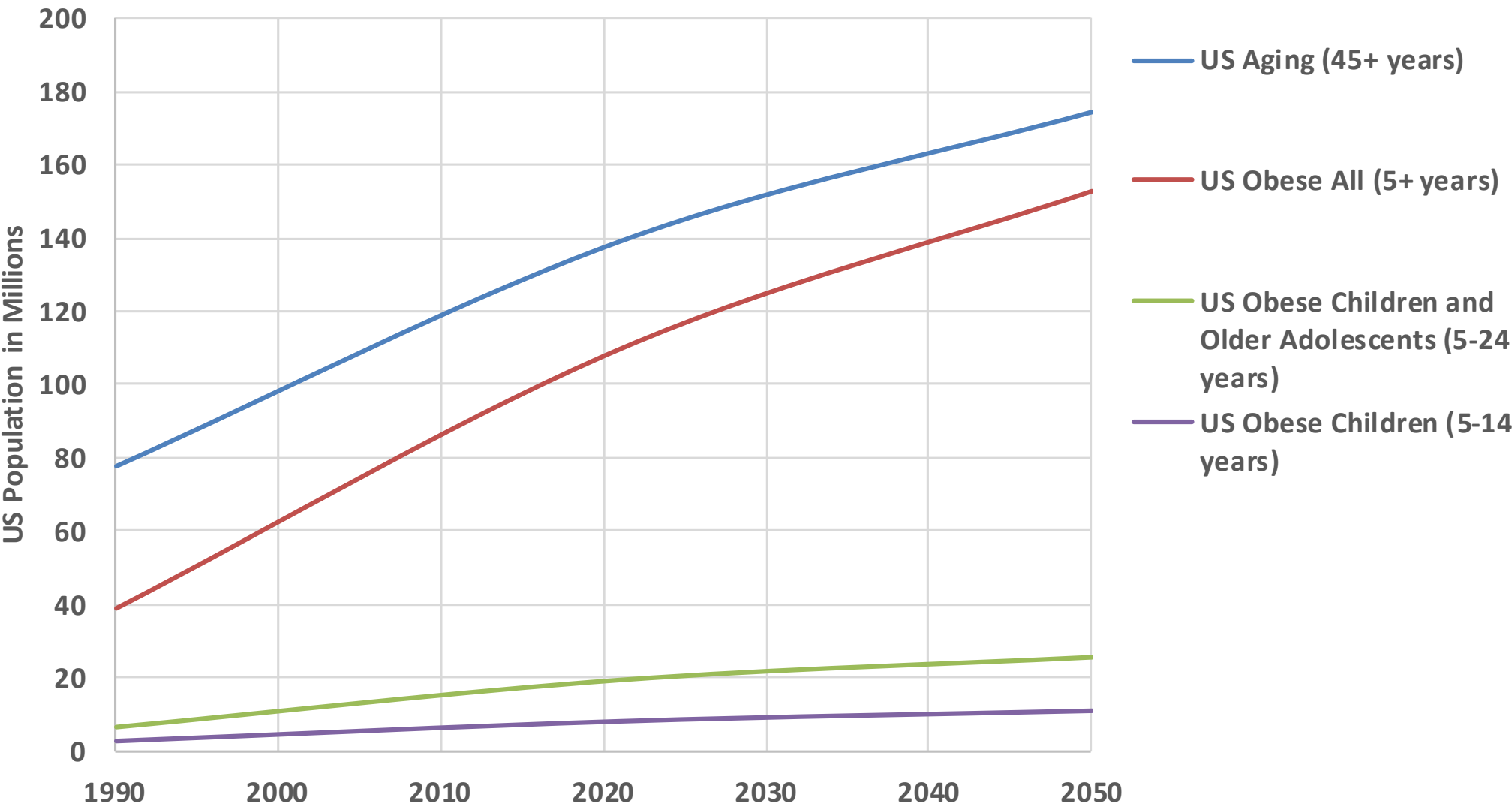
Increased lifespan, however, does not necessarily mean a longer healthy life

Source: <https://www.worldometers.info/demographics/us-demographics/#median-age>

US Population is Aging, Potentially Greater Opportunity than Obesity



Aging (45+) US Population Exceeds Obesity



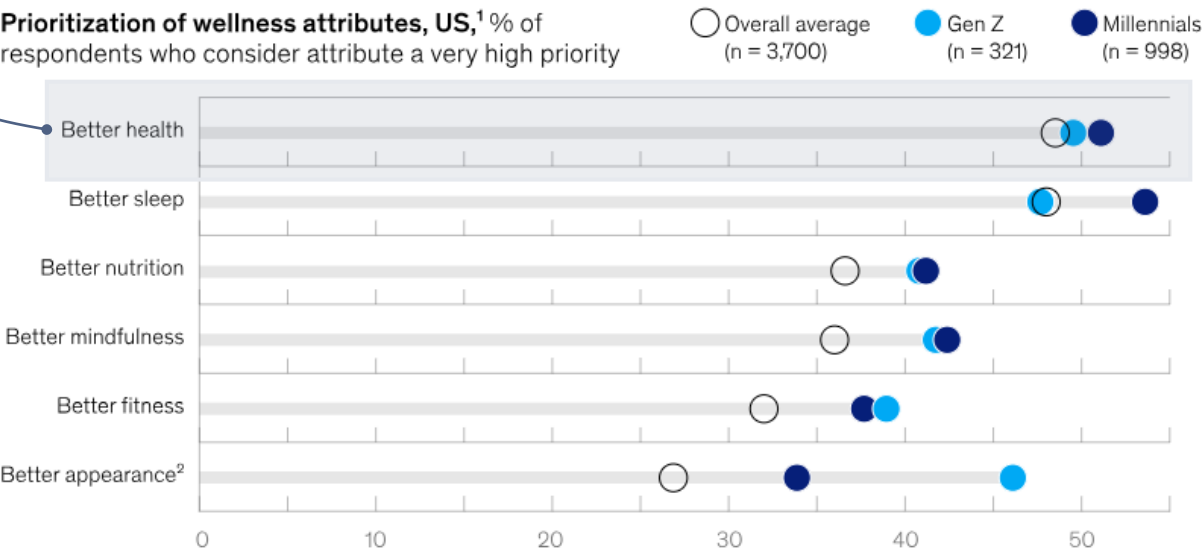
1 | Recent Developments in Longevity Support Our Enthusiasm

Health & Wellness Trends Back Projected Growth in Longevity Products



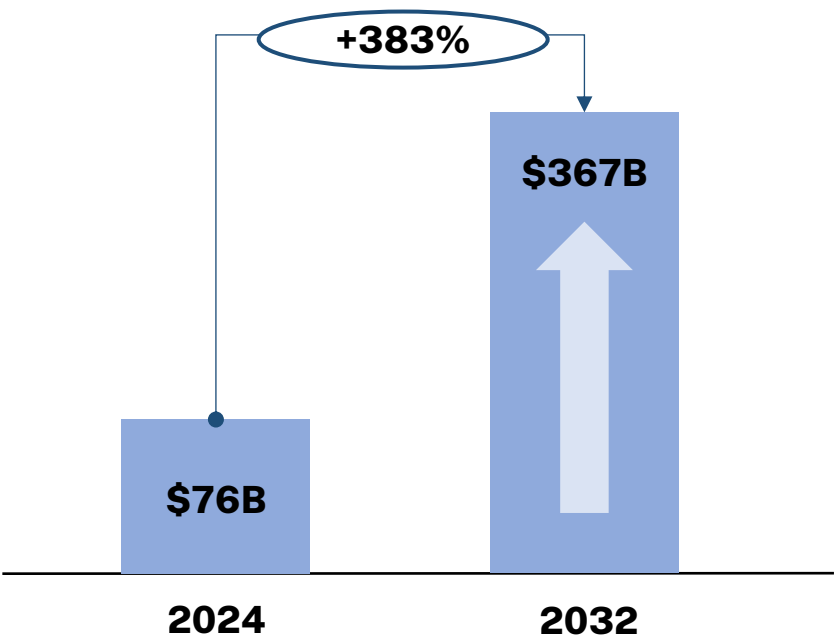
Alignment in wellness goals across generations, with better health as a top priority, sets a strong foundation for the growth potential of the evolving longevity market, which is expected to nearly quadruple by 2032.

Gen Z, Millennial Survey of Wellness Priorities¹



¹Question: How high of a priority do you place on the following attributes?
²Through skin care, makeup, and other cosmetic enhancements.
Source: McKinsey Future of Wellness Survey, Nov 2024

Complementary and Alternative Medicine for Anti-Aging Market Projections²



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**21.7%
CAGR**

Current projections for the H&W longevity market alone reveal vigorous growth in global demand within the next decade, comparable to initial expectations for obesity's 2019-2032 CAGR (~23%)³. Given that these H&W market projections are not pharmaceutical-inclusive, we expect the introduction of longevity-focused therapeutics to drive further growth beyond 2032.

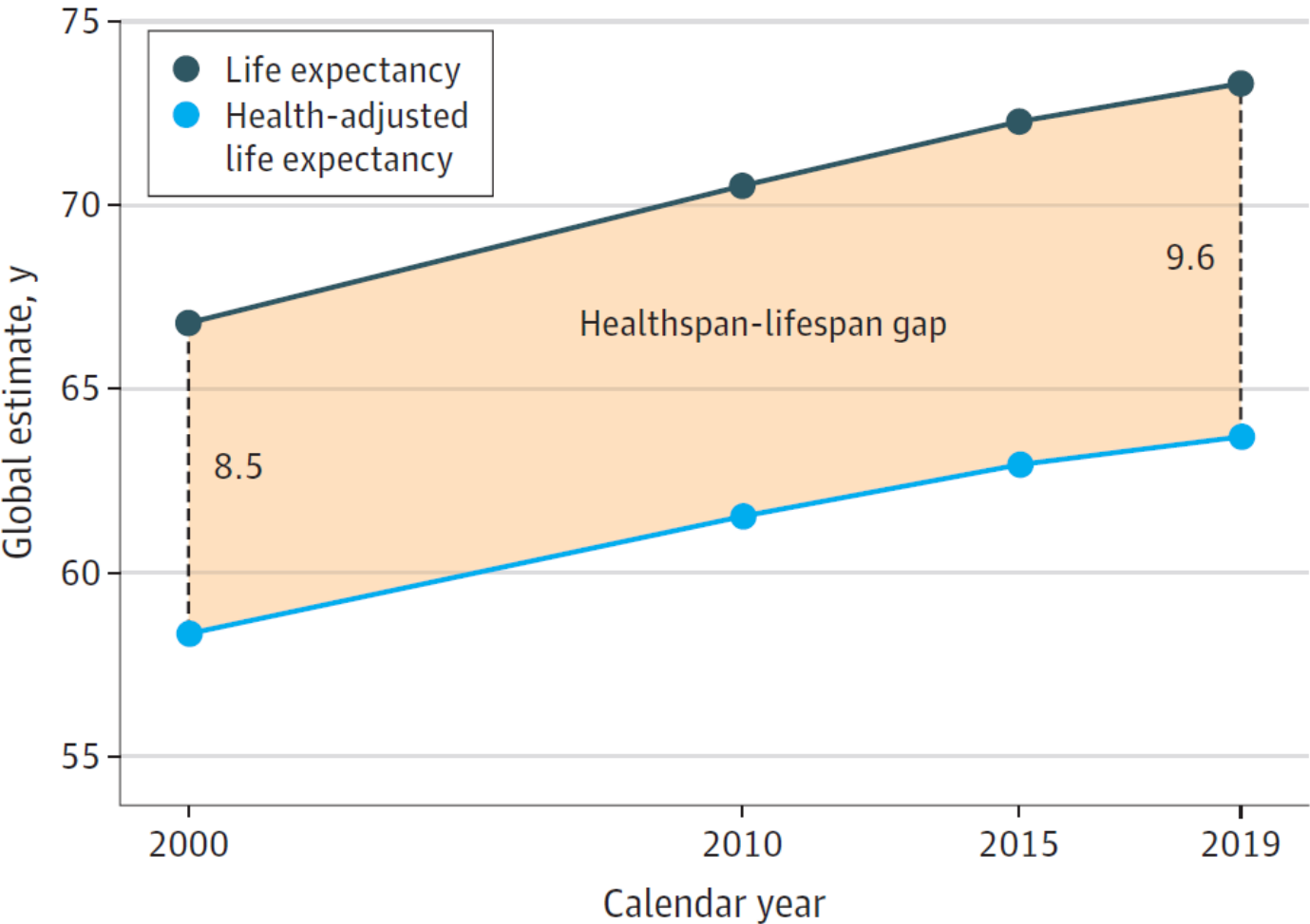
Source: 1. [McKinsey – Future of Wellness Trends, April 2025](#); 2. Adapted from Phil Newman XPrize Presentation, [Polaris Market Research](#); 3. [Obesity Market to Showcase Robust Growth at a CAGR of 23% by 2032 | DelveInsight](#)
H&W: Health and Wellness

02

Addressing the Gender Gap in Lifespan and Healthspan

The Gap Between Healthspan and Lifespan is Large and Growing

Globally, an unequal rise in life expectancy compared to health-adjusted life expectancy resulted in a growing healthspan-lifespan gap climbing from 8.5 years in the year 2000 to 9.6 years in the year 2019, a 13% increase over the past 2 decades.



Over the last 2 decades, global life expectancy increased 6.5 years compared with the 5.4-year increase in health-adjusted life expectancy

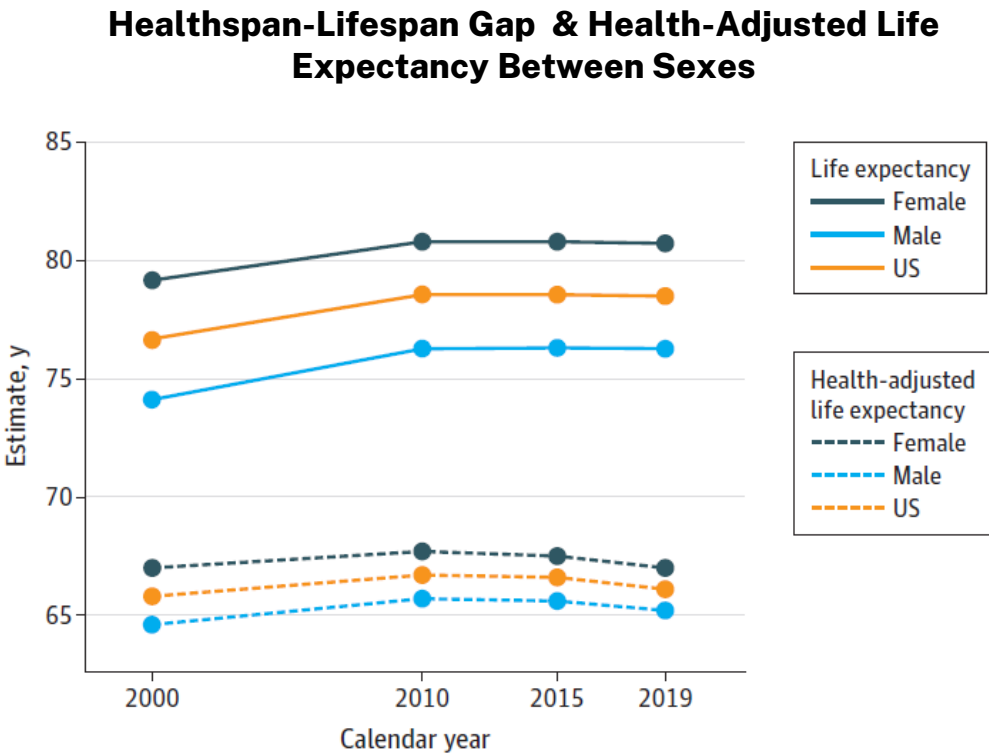
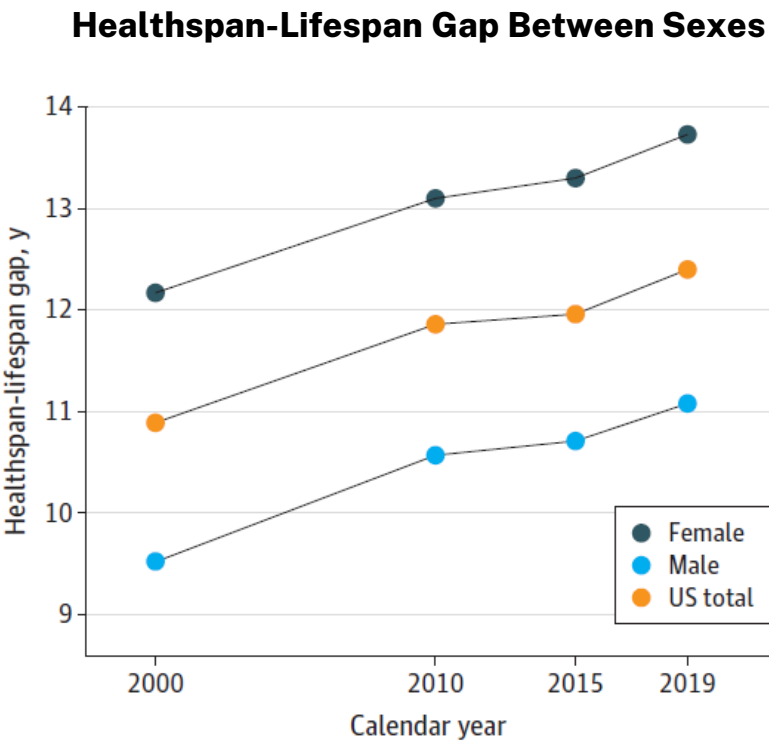
The difference in life expectancy and health-adjusted life expectancy (i.e., healthspan-lifespan gap) represents the number of years lived with disease or disability

Source: Garmany and Terzick, JAMA Open Network 2024

Frailty and Sarcopenia are Important Therapeutic Targets, especially for Women



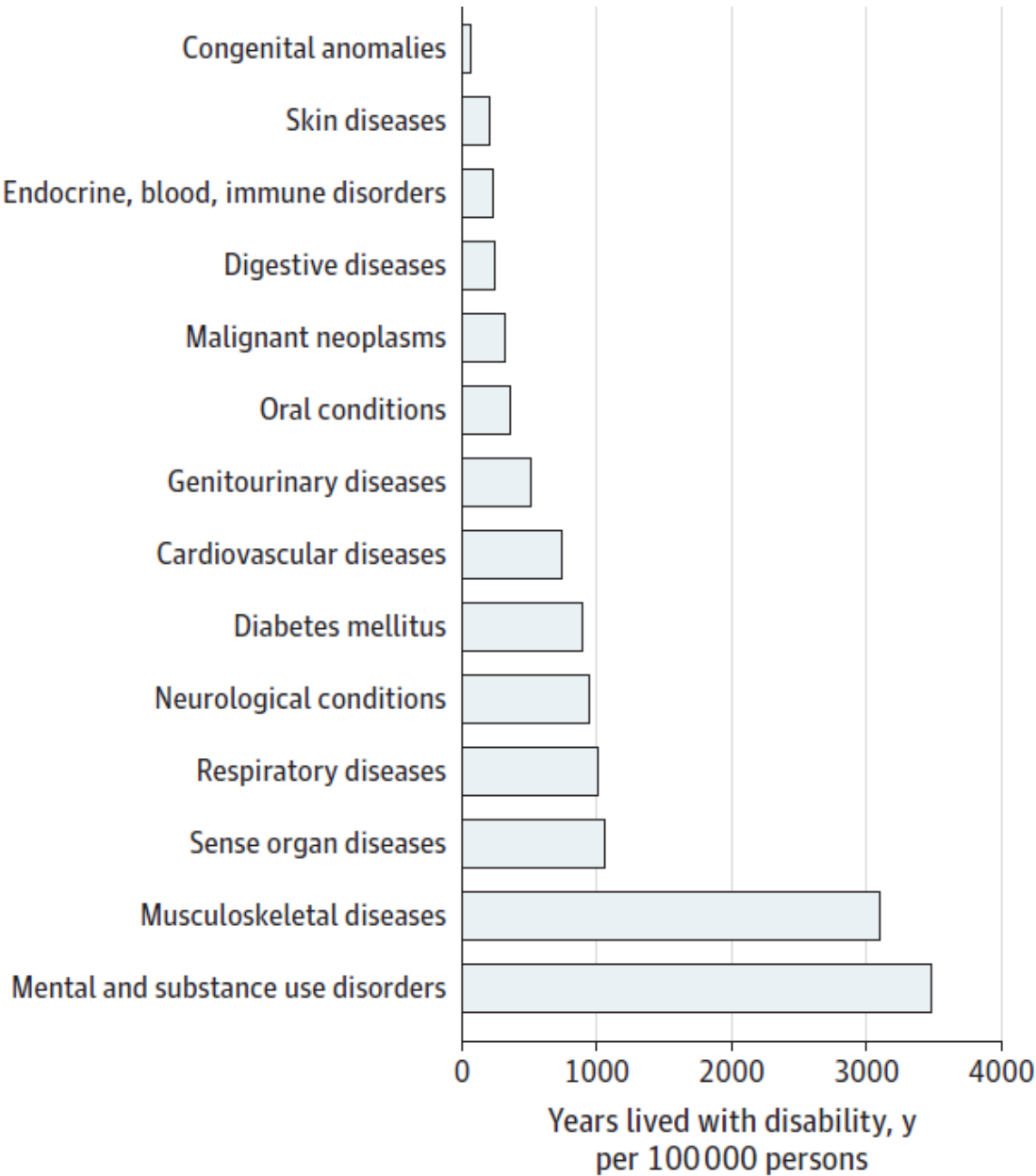
A sex disparity in the healthspan-lifespan gap was identified at global scale, partly underpinned by the higher life expectancy in women and higher noncommunicable disease burden including much higher musculoskeletal disease burden globally in women



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★ This finding suggests that things like frailty and sarcopenia, especially among women, should be important therapeutic targets for reducing the healthspan-lifespan gap

In Addition to Musculoskeletal, Neurological Disease Burden is High in Women



Mental and substance use disorders, along with musculoskeletal diseases, contributed most to years lived with disability in the US, whereas musculoskeletal, genitourinary, and neurological diseases contributed most to the differential burden in women.

- This study reported life expectancy and health-adjusted life expectancy trends over the past 2 decades and found healthspan-lifespan gaps for each of the 183 WHO member states
- The mean healthspan-lifespan gap across WHO member states was 9.2 years
- The US stands out with the largest healthspan-lifespan gap (12.4 years) and the greatest noncommunicable disease burden
- Gender disparities in healthspan-lifespan gaps and association with longevity and disease burden are also reported
- The risk to healthspan is found amplified by longevity and is here recognized to be more pronounced in women

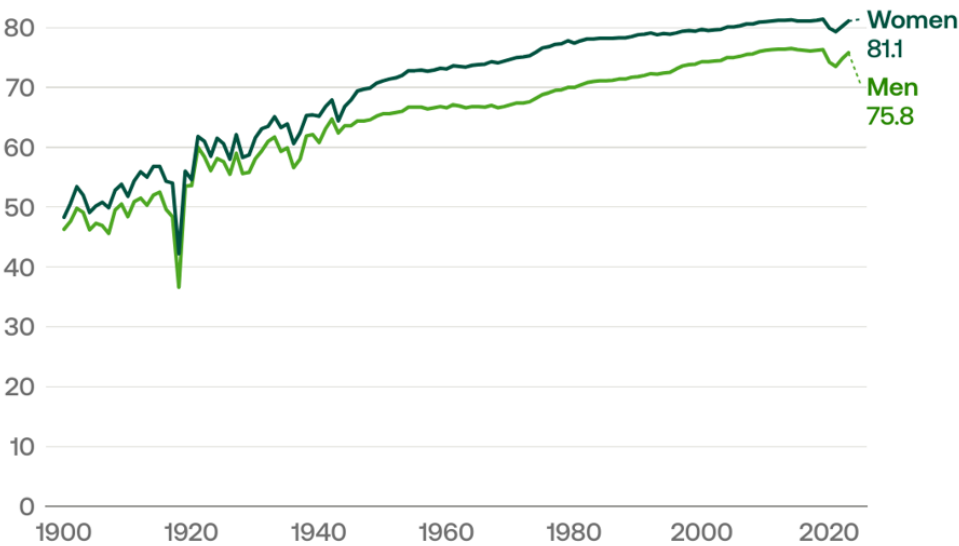
Source: Garmany and Ierzick, JAMA Open Network 2024

Women Outlive Men in both Lifespan and Healthspan



Women are expected to outlive men by 5.3 years as of 2023.

Life expectancy at birth by sex, 1900–2023

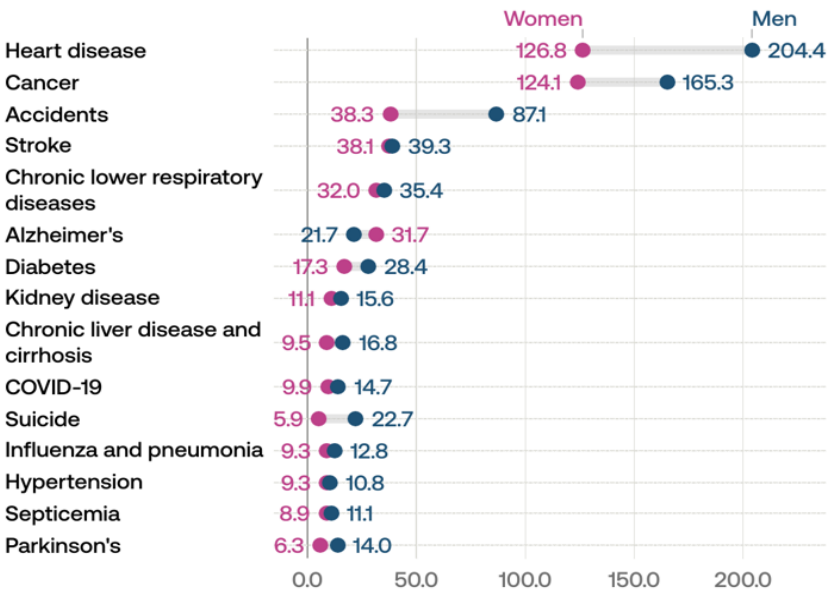


Source: Centers for Disease Control and Prevention



Men die at a higher rate than women for all but one leading cause of death.

Age-adjusted deaths per 100,000 people, top 15 overall causes of death, 2023



Sorted by overall crude death rate.

Source: Centers for Disease Control and Prevention



- Heart disease, cancer, stroke and most other diseases kill men at higher rates than women
- Alzheimer's disease is the only leading cause of death that kills women at higher rates than men

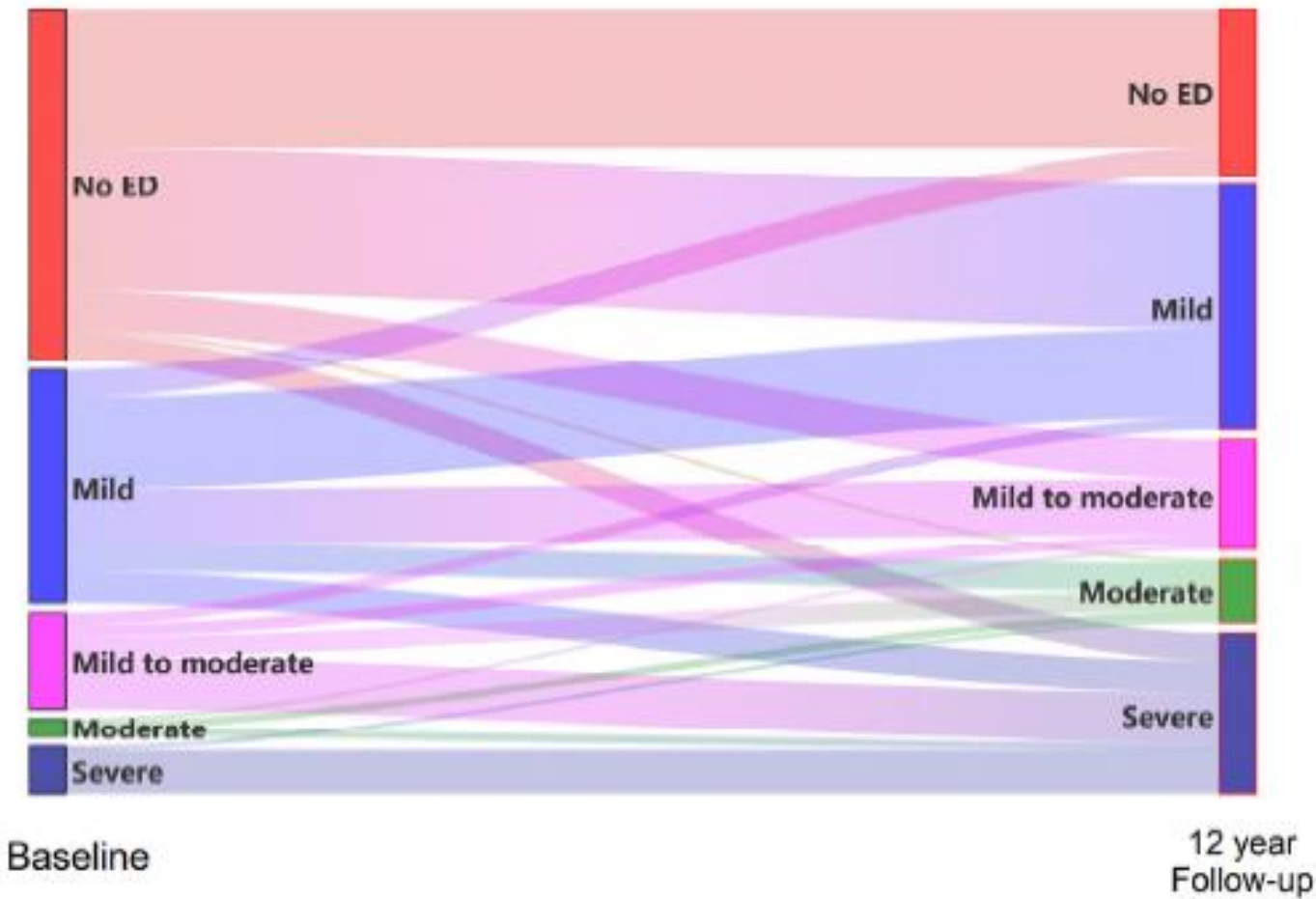
03

The Link Between Erectile Dysfunction and Aging

Erectile Function May Provide a Proxy for Aging

Aging is the greatest risk factors for erectile dysfunction based on a 12 year study conducted by Saramies et al.

The mean age of participants was 62.0 years at baseline. The prevalence of ED was 62% at baseline and 79% at the 12 year follow-up, and the prevalence tended to increase with age. All of the men aged 75 years or more had at least mild ED. **A total of 55% of the men experienced ED progression, while 39% reported no changes in erectile function, and 6% experienced ED regression during the 12-year study. The likelihood of ED progression increased with age.**



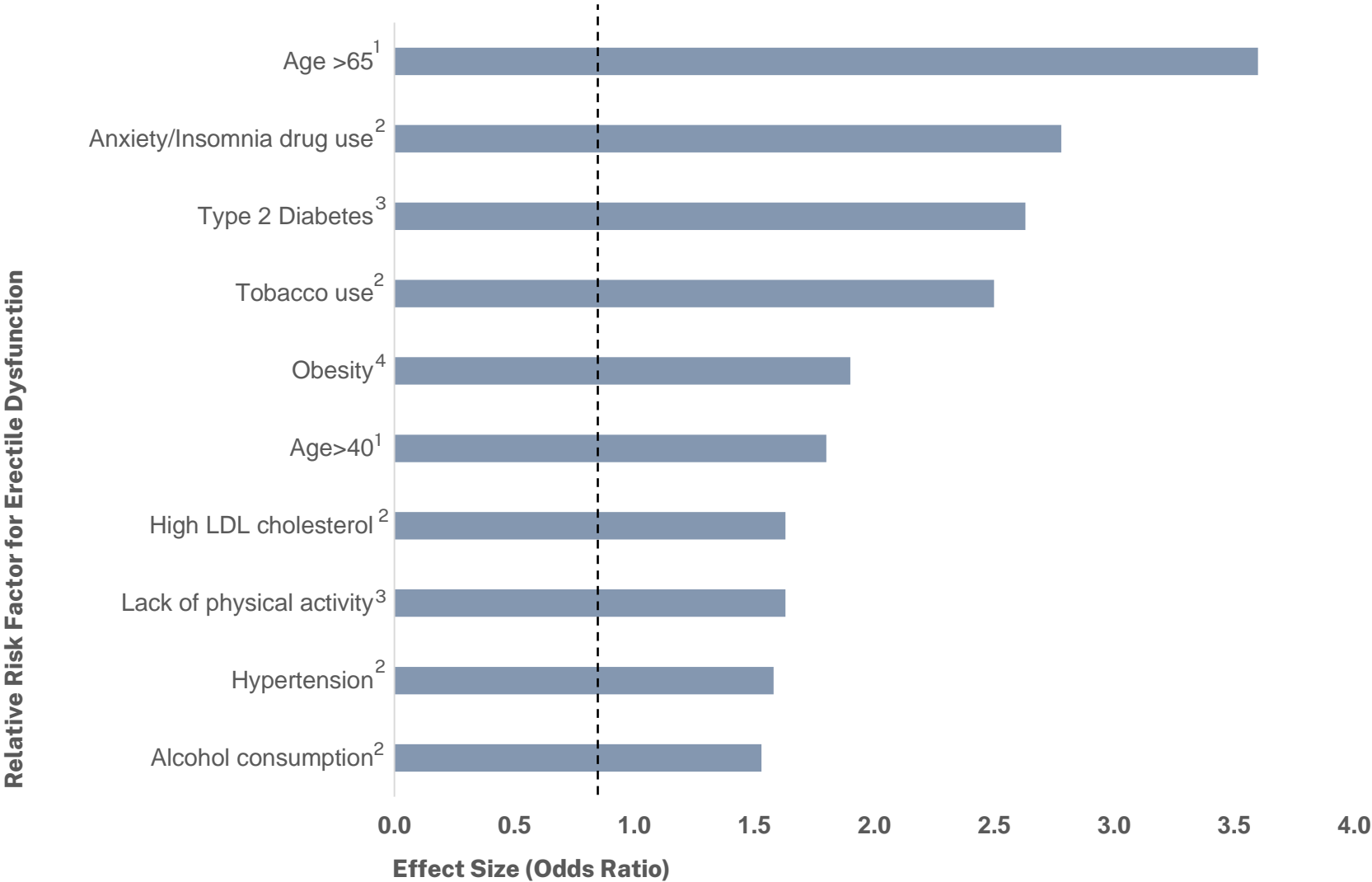
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Aging is one of the greatest risk factors for erectile dysfunction. Erectile function declines with age and does not generally improve without therapeutic intervention.



Erectile Dysfunction Risk Factors Highlight Link to Lifespan

Leading Risk Factors for Erectile Dysfunction Validated by Multiple Observational Studies



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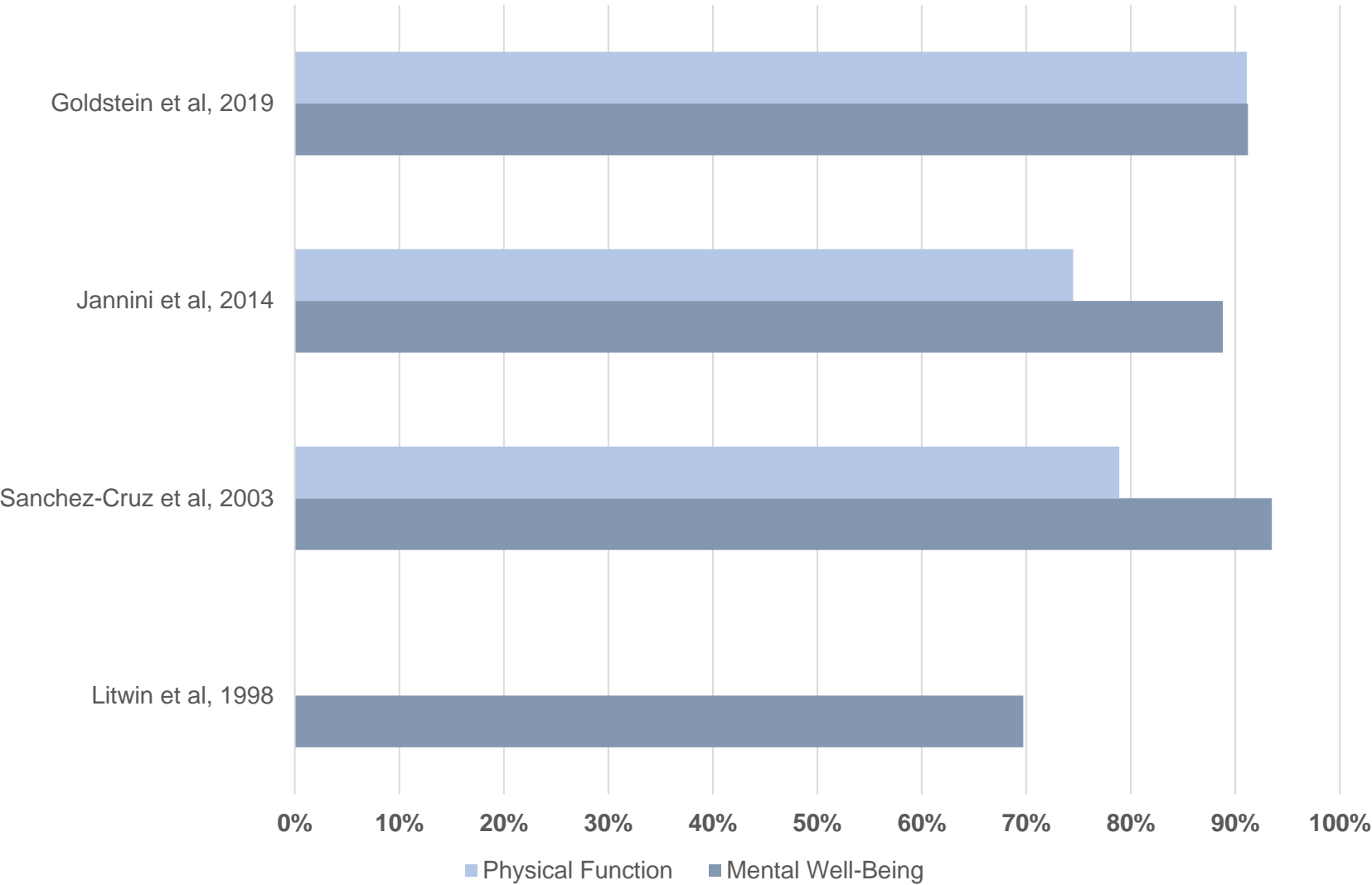
The risk factors for erectile dysfunction are many of the same risk factors impacting lifespan and healthspan. While the greatest risk factor, age, is not yet modifiable, the other major risk factors are readily modifiable once identified.

Source: 1) Saigal et al, 2006; 2) Martin-Morales et al, 2001; 3) Shiferaw et al, 2020; 4) Bacon et al, 2006, Oppenheimer Research

Erectile Function and Quality of life – Direct Impact on Healthspan



Impact of ED on Mental and Physical QoL Validated by Multiple Studies



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ED reduces mental well-being by an average of 14% and physical function by an average of 18% compared to matched controls without ED across the published studies surveyed. We see ED as a major contributor to the gender gap in lifespan and healthspan.

Source: Publications cited above, Oppenheimer Research

04

Diagnosis of ED as a Driver of Preventive Medicine



Erectile Dysfunction: Canary in the Coal Mine for Men at Risk of CVD

Study	Study population	Study design/data collection	Main findings
Thompson 2005 ²⁰	Placebo treated men >55 years of age (n=9500) in U.S. prostate cancer prevention trial.	Longitudinal assessment of ED, labs with clinical follow-up from 1994 to 2003.	Men with incident ED have higher risk of CV events comparable to smoking or family history of MI.
Montorsi 2006 ¹⁸	Italian community sample of men (N=285) with ED and CAD.	Cross-sectional comparison of CAD risk in men with and without ED.	In patients with observable CAD, ED onset precedes CAD by approximately 2-3 y.
Schouten 2008 ¹⁹	Dutch, community sample (n = 1248) of men aged 50-75 years of age without CVD during baseline period (1995-1998).	Longitudinal follow-up up to 8 y. Extensive annual data collection.	Men with ED at baseline predicts cardiac events at follow-up. Dose-response effect—more severe ED predicts more CV events irrespective of age and other risk factors.
Gazzaruso 2008 ¹⁶	Italian men with T2DM (n = 291) with silent CAD.	Longitudinal follow-up to 48 mo.	ED associated with increased MACE (HR, 2.1). PDE5 use associated with lower rates of MACE.
Inman 2009 ¹⁷	Olmsted County longitudinal study of U.S. men aged 40-70 years of age from 1996 to 2005 (N = 1402).	Longitudinal study of male health in the general population.	ED associated with an approximately 80% higher risk of later CAD—a stronger effect in younger men.
Chew 2010 ¹⁵	Western Australian men with ED (N=1660) and without CVD at baseline, 45-70 years of age.	Retrospective linked data design health records for follow-up.	Incidence of atherosclerotic CV events in men with ED were twice the rate observed in general male population (SIRR, 2.1; 95% CI, 1.9-2.4)
Banks 2013 ¹⁴	Australian men in national health survey from 2006-2009 (N = 95 038).	Proportional hazards modeling of ED on CV outcomes.	ED strongly predictive of subsequent CV events and death in men with and without prior CV history.
Uddin 2018 ²¹	Subsample (n = 1914) of U.S. men in the MESA study from 2000 to 2012.	Proportional hazards modeling of ED effects on CV outcomes.	Strong, independent effects of ED on subsequent CV events after multiple controls for other potential causes.
Adam 2020 ¹³	Male participants (N = 573) of mixed ages in epidemiological studies in 4 European countries.	Systematic review and meta-analysis of pooled data from 4 separate studies.	ED is highly significant harbinger of CV events after controlling for all other risk factors.

Abbreviations: CAD, coronary artery disease; CI, confidence interval; CV, cardiovascular; CVD, cardiovascular disease; ED, erectile dysfunction; HR, hazard ratio; MACE, major adverse cardiovascular events; MESA, Multi-Ethnic Study of Atherosclerosis; MI, myocardial infarction; SIRR, standardized incidence rate ratio.

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According to the Princeton Consensus,* ED precedes the clinical symptoms of cardiovascular disease (CVD) by 2-5 years, **“making the diagnosis of ED especially useful as a marker of probable subclinical CVD.”** A diverse group of independent, multinational studies have consistently shown that ED predicts subsequent CV events and cardiac deaths, regardless of age, body mass index, prior CVD, and other relevant risk factors.



Erectile Dysfunction: Bidirectional Marker for Psychological Distress

Study	Study population	Study design/data collection	Main findings
Thompson 2005 ²⁰	Placebo treated men >55 years of age (n= 9500) in U.S. prostate cancer prevention trial.	Longitudinal assessment of ED, labs with clinical follow-up from 1994 to 2003.	Men with incident ED have higher risk of CV events comparable to smoking or family history of MI.
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“Men with ED were more than twice as likely to report depressed mood compared with controls, regardless of age and other confounding factors. There is compelling evidence that the direction of causality is bidirectional (psychological distress is implicated as both a cause and consequence of ED).”

We believe these findings and the CVD link underscore the importance of routine ED screening.

Source: Kloner et al, The Journal of Sexual Medicine, 2024, Vol 21, Issue 2

05

Treatment of ED and Clinical Benefits

We Believe ED Treatments Have a Role in Longevity, Similar to Other Therapies



Development for longevity-specific therapeutics is still nascent. However, reaping healthspan and lifespan benefits of pharmaceuticals is not entirely out of reach, as some approved and available agents already demonstrate clinical benefit for promoting human longevity (e.g., GLP-1s, SGLT2s, shingles vaccines, and metformin)



GLP-1s

The landmark SELECT trial showed that semaglutide reduced the incidence of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.¹



SGLT-2s

A systematic review and meta-analysis of 92,920 patients shows that SGLT2 inhibitors significantly reduce morbidity and mortality from cardiovascular and renal diseases.²



Shingles Vaccination

Live and recombinant Shingles vaccines (Zostavax and Shingrix, respectively) have both been associated with lower risk of dementia and cardiovascular disease.^{3,4}



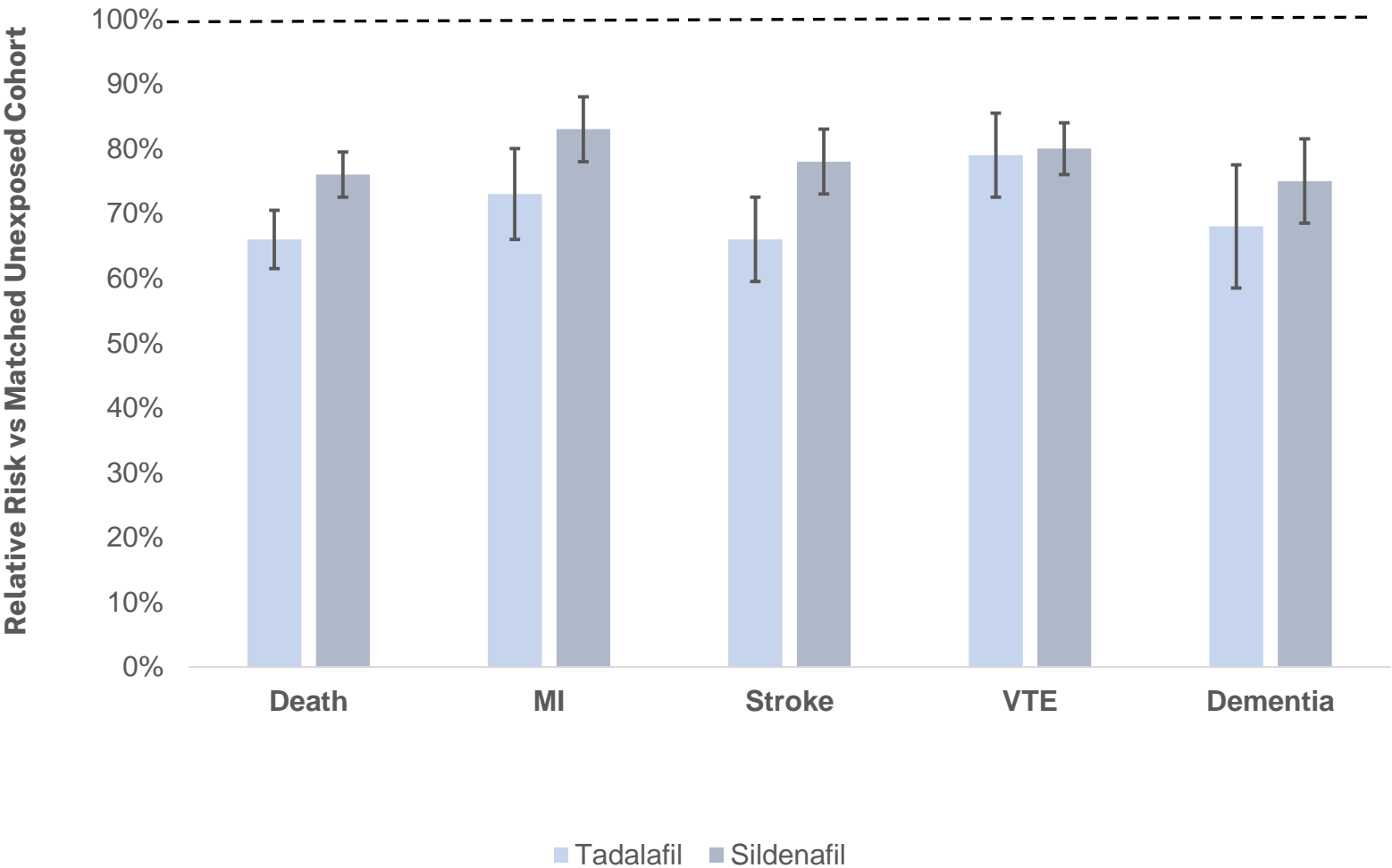
Metformin

FDA-approved metformin increases healthspan and lifespan in mice and has demonstrated preliminary benefits in T2DM, obesity, cardiovascular, and neurodegenerative settings.^{5,6}

Source: Oppenheimer Research; 1. Lincoff et al., NEJM, 2023; 2. Haider et al., Cardiology, May 2025; 3. Taquet et al. Nat Med 30, 2777–2781 (2024); 4. Eytting et al. Nature 641, 438–446 (2025); 5. Martin-Montalvo et al., Nat Commun. 2013;4:2192 (2013); 6. Mohammed et al., Front Endocrinol, 2021 Aug 5;12:718942.

Preventive Medicine: The Longevity Benefits of ED Treatment are Growing

Benefits of PDE5i Treatment on Men with ED (95% CI)



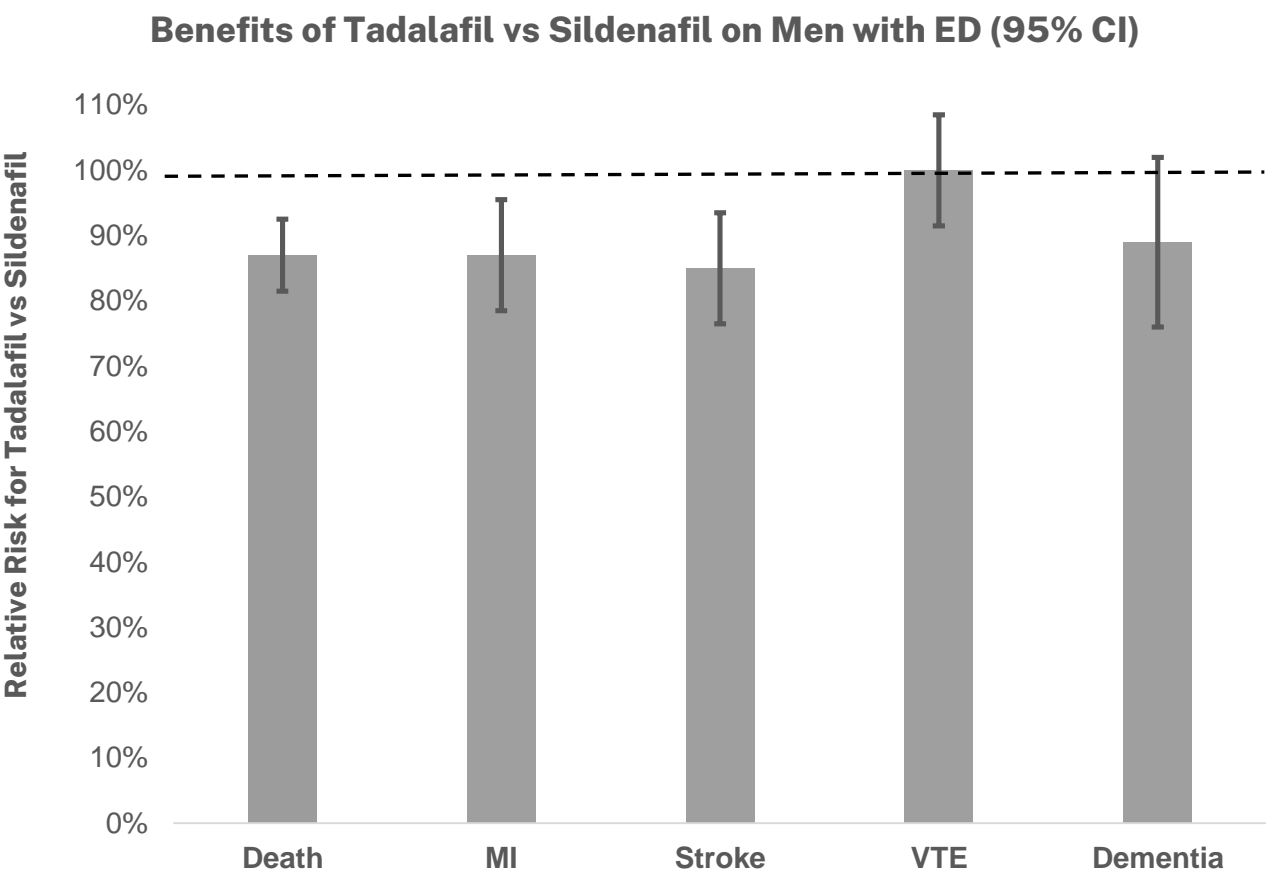
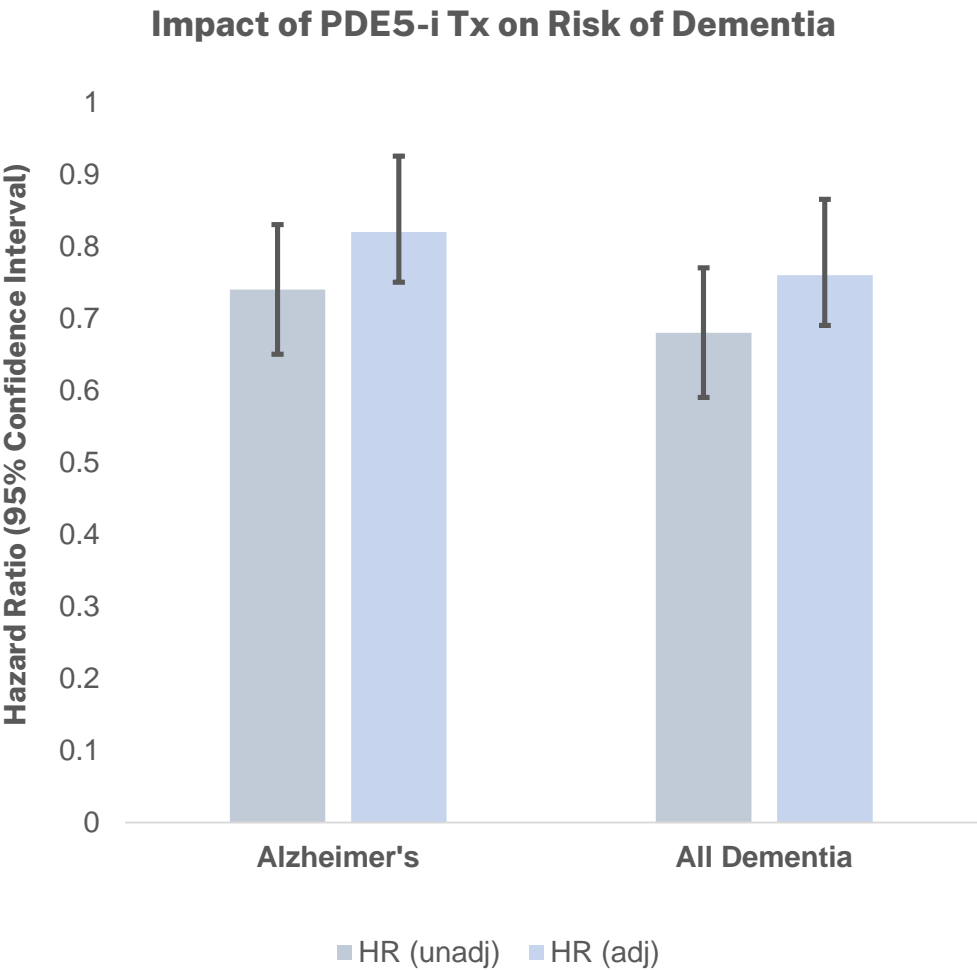
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The use of two leading PDE5 inhibitors, tadalafil and sildenafil, significantly reduce the risks of mortality, cardiovascular disease, and dementia, with tadalafil providing slightly greater benefits than sildenafil.

We believe these findings will become increasingly more recognized over time with longer observational studies.



Preventive Medicine: ED Treatment Significantly Reduces Risk of Dementia



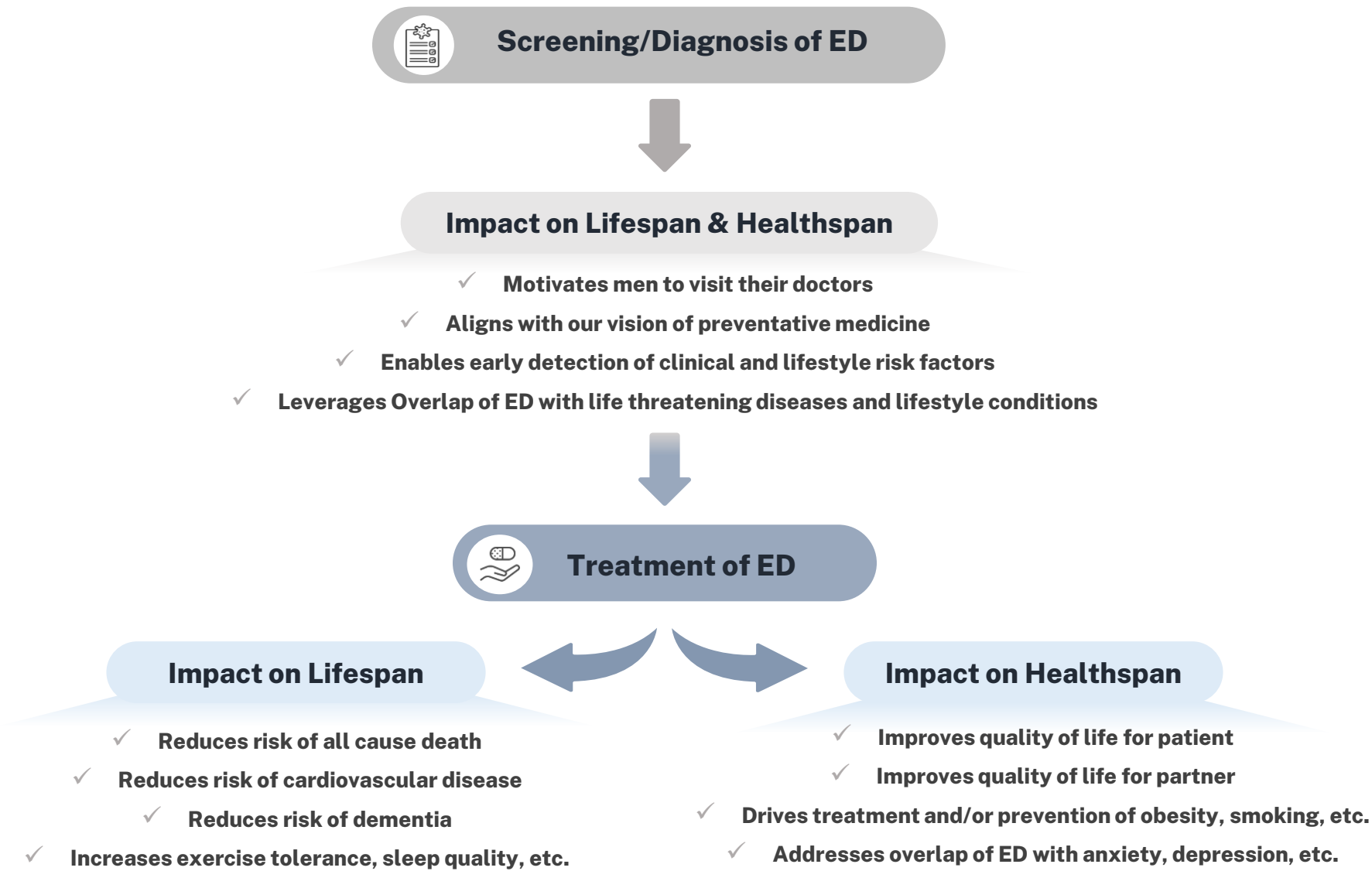
- The use of tadalafil and sildenafil, significantly reduce the risks of Alzheimer’s and other forms of dementia
- **With tadalafil providing greater benefits than sildenafil, perhaps as a result of its longer half-life**

Source: Oppenheimer Research, Jehle et al, The American Journal of Medicine 2024

06

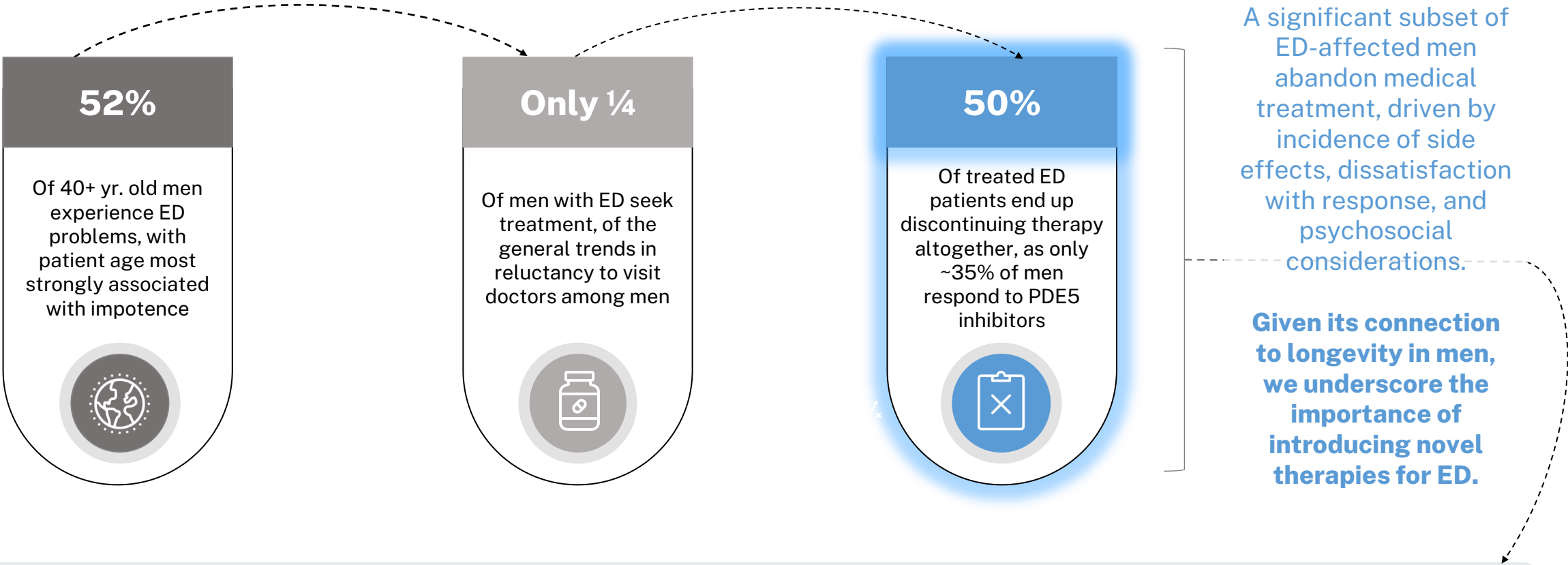
A Novel Approach to Treating ED

Our Research Outlines the Role of PDE5 inhibitors in Longevity Dynamics



Beyond PDE5 Inhibitors: What's Next?

PDE5 inhibitors like sildenafil (Viagra), tadalafil (Cialis), vardenafil (Levitra), and avanafil (Stendra) have dominated as mainstay treatments for ED, despite their dated development and FDA approvals: Viagra being the oldest, with approval nearly 30 years ago in 1998. Based on our landscape analysis, the majority of clinical-stage ED programs in development in the US continue to revolve around PDE5 inhibition.



We highlight Dicot Pharma as one of the few companies exploring non-PDE5 mechanisms for ED, with demonstrated proof-of-concept and an emerging clinical profile that appears highly competitive with incumbent PDE5 inhibitors in our view.

LIB-01: Dicot’s Novel Approach to Pharmacologic ED Treatment

With growing evidence highlighting the link between ED and male longevity, the shortcomings of current PDE5 inhibitors represent a critical unmet need for innovation, and we are particularly interested in Dicot Pharma’s lead asset LIB-01, which employs a non-PDE5 mechanism to potentially address the limitations of current treatments.

Overview of Lead Asset LIB-01

Mechanism

Semi synthetic analog of phragmalin-type limonoids found in root bark, with preclinical evidence suggesting differentiation from PDE5 mechanism given lack of NO-cGMP recruitment

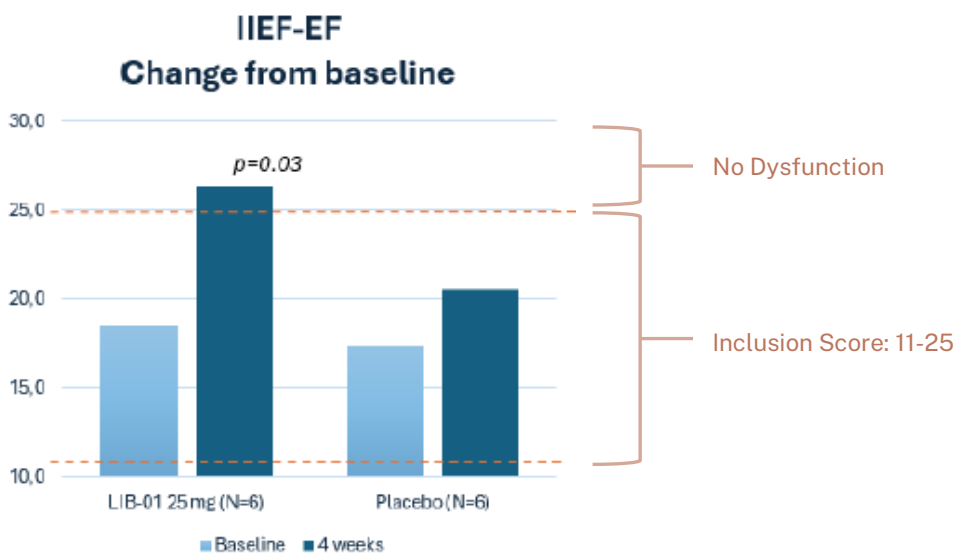
Dosing

In Phase 1, dosed orally either once- or twice-daily over 3-days.

Clinical Status

Phase 2a randomized, double-blind, placebo-controlled trial conducted in the EU evaluating 3 dose levels of LIB-01 with primary endpoint of IIEF-EF at week-4.
Results expected in Oct/Nov 2025.

Phase 1 Results of LIB-01 in ED Patients at 28-Days



Oppenheimer Insights

4-wks LIB-01 demonstrated pro-erectile effect through day-28, or week-4, despite dosing only on days 1-3. Given this observation, the duration of action of LIB-01 is significantly larger scale than PDE5s (weeks vs. hours, respectively).



Phase 1 safety also appeared competitive, with 1) no serious adverse events (AEs) or dropouts due to AEs; 2) most common gastrointestinal AEs occurred with the 1st dose and resolved within 24 hr; and 3) no clinically significant findings on vital signs, hematologic metrics, or electrocardiogram.

Source: Dicot Pharma Company Information; Oppenheimer Research



Questions? Let's be in touch.

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Disclosure Appendix

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Stock Prices as of September 19, 2025

Amgen, Inc. (AMGN - NASDAQ, \$275.83, OUTPERFORM)

Viking Therapeutics, Inc. (VKTX - NASDAQ, \$26.04, OUTPERFORM)





All price targets displayed in the chart above are for a 12- to- 18-month period. For more information about target price histories, please write to Oppenheimer & Co. Inc., 85 Broad Street, New York, NY 10004, Attention: Equity Research Department, Business Manager.

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			Count	Percent
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