

Health Outcomes of ADHD: Impact on Life Expectancy and Implications for Management

Russell A. Barkley, Ph.D.

Clinical Professor of Psychiatry

Virginia Commonwealth University Medical Center
Richmond, VA

Websites:

RussellBarkley.org

Email: drbarkley@russellbarkley.org

©Copyright by Russell A. Barkley, Ph.D.

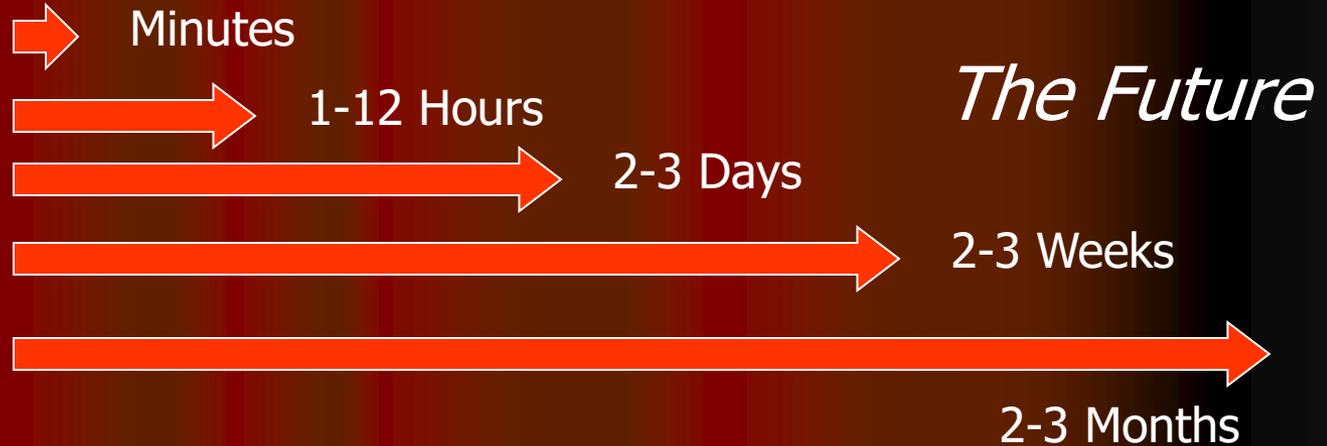
What is the Underlying Nature of ADHD?

- ADHD is more than just a disorder of attention (and inhibition)
- It is a disorder of self-regulation
- This arises due to deficiencies in the executive functions that allow self-regulation
- Self-regulation permits the anticipation of hypothetical future events and the organization of behavior directed at them
- ADHD is therefore a disorder of the cross-temporal organization of behavior so as to optimize longer-term consequences and one's general welfare over more immediate gratification

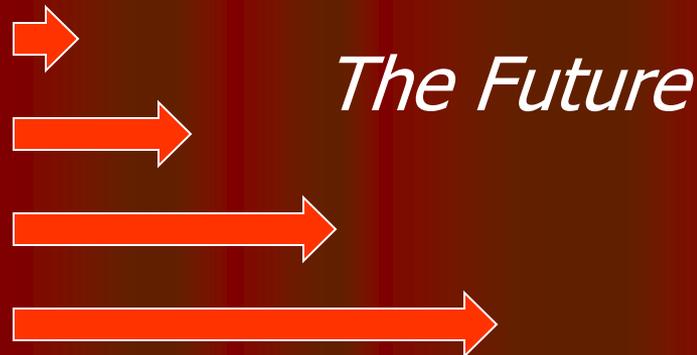
ADHD Disrupts the Development of Foresight: An Emerging Window on Time



Typical Person



ADHD



ADHD thus creates an incredibly **high time preference** or a substantial discounting of the value of future consequences

More on ADHD

- This explains the negative association of ADHD with delay of gratification and the personality trait of conscientiousness
 - The consideration of longer-term consequences for self and others in the decision to act
- Hundreds of times each day, people must invoke self-regulation to make choices that involve conflicts between immediate versus delayed consequences
- ADHD biases decision making in such choice scenarios toward optimizing momentary and smaller consequences over delayed, larger, and more important outcomes
- Such impulsive decisions have both a cumulative impact on risk for impairment and occasionally a singular impact on risk for injury, suicide, and accidental death
- Thus, ADHD predisposes to adverse consequences in nearly every domain of major life activity including risk for substance experimentation and use disorders (SUDs)

Reasons to Expect ADHD to Be Linked to Shortened Life Expectancy

ADHD Related Injury Risks

- Greater risk for traumatic brain injuries
 - Greater driving, motorsports, sports injuries
- Greater risk for accidental injuries of all types
 - Risk extends across childhood into adulthood
- Increased likelihood of violence as both perpetrator and victim due to more
 - reactive aggression, bullying, assaults, and victimization of and by others
- Greater risk for partner violence in intimate relationships
- 4-5 x Greater risk for suicidal ideation, attempts and completions
 - Peak risk is during high school years but remains elevated thereafter
 - Ideation is related to depression generally; in females to low self-concept and in males to high impulsivity. Attempts are related to impulsivity in both.

Risky Sexual Behavior

- Earlier start to sexual intercourse involving shorter relationships and less use of contraception
- Higher risk for teenage pregnancy and for more risk factors during such pregnancies (smoking, excessively low or high body mass index, alcohol or substance use)
 - 32% of males and 68% of females in Milwaukee study (1980s)
 - 15.3 vs. 2.8% risk for teenage girls with ADHD in Sweden (2007-14)
- Higher risk for contracting sexually transmitted diseases by late adolescence and adulthood
 - Puts them at risk for higher HPV infection and subsequent cancer risk by mid-life

Excess Sedentary Activity

- Less exercise, reading, in-person social activities with friends, and engagement in self-improvement activities
- More time watching television, screen time with technology, use of social media, and especially Internet gaming with others or alone – 15-20% have Internet addiction by adolescence
- Internet addiction is also worsened by comorbid depression, anxiety, and social neglect or rejection by others

Greater Health Complaints

- Poorer self-reported general health by young adulthood – headache, fatigue, low back & joint pain, etc.
 - More complaints of vague medical concerns if comorbid anxiety/depression
- Disrupted sleep – 40% of both children and adults
- Higher risk of contracting COVID-19 in adults with ADHD
- Greater risk of contracting respiratory infections disease in children
- Increased risk for fibromyalgia syndrome
 - More so in female than male cases with ADHD
 - Also, 25-30% of cases with fibromyalgia have ADHD, espec. Females
 - Risk of comorbidity is linked to impulsivity and to higher opioid SUD

More Health Risks

- Shared genetic liability between ADHD and gout implies increased risk for comorbidity
- Greater occurrence of asthma in ADHD (OR = 1.92)
 - This is not mediated by ADHD genetic risk; is it a gene x environment interaction?
- Greater occurrence of migraine headaches
 - Risk of migraine arises from shared genetics with ADHD
- Increased risk for gastrointestinal disorders (dyspepsia, constipation, irritable bowel syndrome)
 - Could be further increased by extent of methylphenidate treatment
- Recent population study found adult ADHD linked to 34 of 35 medical disorders, with strongest linkages to pulmonary (asthma, COPD), endocrine (types 1 and 2 diabetes, obesity), and neurological conditions (migraine, sleep, epilepsy, dementia). Most links results from shared genetic risk but neurological ones were also associated with nonshared (unique) environmental effects. (Reitz et al. (2021) *Lancet*.

Greater Use of Health Impairing Substances

- More frequent use of :
 - caffeine (?)
 - tobacco,
 - marijuana
 - alcohol
 - more difficulty quitting substance use
- If Conduct Disorder developed by adolescence, then greater risk of
 - Illegal substance use, prescription drug abuse
 - Diagnoses of substance use disorders
- As a consequence, a possibly greater risk for mid- and late-life cancer ?

High Risk Eating Patterns and Diet

- Greater consumption of “Western style” fast-food, high carb and high sugar foods and beverages
- Possibly more deficient in vitamin D and zinc (children)
- Highly impulsive eating patterns and preferences
- More dental plaque, caries, and trauma; poorer oral hygiene
- 2-3x risk of obesity by adolescence and adulthood
 - shared heritability between ADHD and obesity risk
 - risk increases with age
 - Conversely, ADHD is over-represented in patients treated for obesity at eating disorders clinics (32% vs. 4% population prevalence)
- Higher risk for Type 2 diabetes:
 - teens (2.83x); adults (3.28x)
- 3.5x risk in females for impulse eating disorders & increased eating pathology
 - 10-20% of ADHD females vs. 0-5% of controls
 - Bulimia is most likely type, being 5.6x more likely by age 16
 - Eating Disorders linked to earlier impulsivity, peer rejection & harsh parenting,** and concurrent MDD, anxiety disorders, & ODD/CD*

Growing Risk for Future Medical Conditions

- Greater risk of cardiovascular disease (CHD) by age 27
 - Greater risk for hypertension
 - Lower HDL cholesterol and higher Total/HDL ratio
 - Greater common carotid artery intima-media thickness (risk for atherosclerosis)
 - Higher atherosclerotic risk to coronary arteries due to smoking, alcohol use, & diet
 - Higher Framingham CHD risk percent over next 5 and 10 years
 - For every 1 SD decrease in self-regulation there is 20% increase in coronary heart disease or events. ADHD is the bottom 1.5-2 SDs or 2-7% of self-regulation***
- Higher risk for colorectal cancer (3.46x)
- Greater risk for developing dementia (5.5%)
 - 3.4 times higher risk even when controlling for other factors
- 2.4 x Greater risk of diseases of the basal ganglia (e.g. Parkinsons, 8 vs. 1%) and cerebellum
 - this rises to 8.6x risk if treated with stimulants – probably because treated cases have worse ADHD, not because of stimulants
- Recent genome wide association study found shared genetic risks between ADHD and risk for most of these adverse health and lifestyle factors

Evidence for Earlier Mortality

Suggestive Evidence

- ✓ Freidman et al. follow-up study and many others found that decreased conscientiousness in childhood is associated with earlier death by all causes (<25th percentile = -7 yrs) .
- ✓ ADHD is linked to very low conscientiousness (that includes behavioral disinhibition) and shares genetic heritability with it. Given that ADHD is the bottom 5-7% of the population in disinhibition and hence conscientiousness, it should be linked to an even greater reduction in life expectancy.
- ✓ Those with ADHD often miss scheduled appointments. McQueenie et al. (2019) found that missing 2+ appointments per year in people with mental health disorders increased all cause mortality 8x more than those who do not do so.

More Suggestive Evidence

- ✓ Greater child externalizing behavior has been linked to 1.5-2x greater risk of mortality by age 46 (Jokela et al., 2009)
- ✓ A study by Li et al. (2018) tracked over 120,000 people (nurses health study) for 34 years with 42,167 deaths identifying 5 low risk/health activities:
 - ✓ nonsmoking,
 - ✓ exercise moderately 30+ minutes per day,
 - ✓ keep BMI below 25 (kg/m²),
 - ✓ moderate alcohol intake (6 oz women, 12 for men),
 - ✓ high quality diet (low in fats, red meat, carbs, sugar).
 - ✓ Those doing all 5 had 12-14 more years of life expectancy than those doing none.
 - ✓ People with ADHD often do the opposite in all 5 risk factors (hence may live 12-14 years less).

Direct Evidence

- ✓ Klein et al (2012) found that by age 41 years, there was an increased mortality rate (7.2% vs. 2.8% in controls)
- ✓ London & Landes (2016) found that adults with ADHD have mortality risk 1.8x more within any 4 year period.
- ✓ Dalsgaard et al. (2015) using Danish population found the risk for mortality is nearly double in childhood (1.86) and more than doubles again (4.25) in adulthood. And those with ADHD are 3x more prone (13% vs. 4%) to death by accident.
- ✓ Virtanen et al. (2018) used the Swedish population database for 2001-2010 ages 10-35 yrs and found a 2.54 increased risk for early mortality in ADHD cases (3.93 risk for suicide) [risks for ASD were 2.06 and 3.02, respectively]. In ADHD cases, comorbid disorders further increased risks by 2.4 and 2.8.

More Direct Evidence

- ✓ Chen et al. (2019) study of Taiwan population ages 4-44 yrs shows greater mortality in ADHD linked to accidents (OR = 1.3), suicide (OR = 2.1), and homicide (OR = 2.0)
- ✓ Sun et al. (2019) using a large Swedish database found:
 - ✓ Mortality rates 5x higher in ADHD (11.6 vs. 2.2 per 10,000 person yrs.).
 - ✓ Odds ratios were higher for adults (4.64) than kids (1.41) with ADHD
 - ✓ ORs were markedly affected by number of comorbid disorders (1.4 for ADHD pure) vs. 25.2 for ADHD with 4+ comorbidities.
 - ✓ Death by natural causes in ADHD was mainly due to early onset comorbid disorders (ASD, ID)
 - ✓ While death in ADHDs by suicide was related to later onset disorders (depression, anxiety)
 - ✓ Death due to accidents or other causes was related to ADHD, not comorbidity.
- ✓ Genome wide association study by Demontis et al. (2018) showed shared genetics between ADHD and earlier parental mortality in both mothers and fathers of probands.

Computing the Life
Expectancy of Children with
ADHD Followed to Young
Adulthood

Milwaukee Study Collaborators

- Mariellen Fischer, Ph.D., Co-PI
 - Department of Neurology, Medical College of Wisconsin (MCOW), Milwaukee, WI
- Karen M. Smith, Ph.D. (Genotyping)
 - Dept. of Biology, University of Louisiana - Lafayette
- Research Assistants:
 - Lori Smallish, Lori Bauer (MCOW)
- Health Screeners – Physician Assistants:
 - Hope Schrader, Kent Shiffert (MCOW)
- Data Entry Software Program
 - Kenneth Fletcher, Ph.D., University of Massachusetts Medical School
- Data Entry
 - Peter Leo

Milwaukee Study Methods

- 158 children ages 4-11 years diagnosed as hyperactive child syndrome in 1978-1980
 - Had significant symptoms of inattention, impulsiveness, and hyperactivity as reported by parents
 - Were +2SDs on Conners Hyperactivity Index & Werry-Weiss-Peters Activity Rating Scale, and +1SD (6 or more settings) on Home Situations Questionnaire
 - Onset of symptoms by 6 years of age
 - Excluded children with autism, psychosis, deafness, blindness, epilepsy, significant brain damage, etc.
- 81 control children from same schools and neighborhoods matched on age and obtained via a “snowball” sampling procedure
- Most children re-evaluated at mean ages of 15 (C=78% & H=81%), 21 (C=93 & H=90%), and now 27 years (C=93% & H=85%).
- To be currently ADHD (H+ADHD), participants in this aspect of the study had to have 4+ symptoms on either DSM-IV symptom list and 1+ domains of impairment (out of 8) by self report (N=54). Remainder (N=77) were grouped as H-ADHD. Community Controls = 71
- Groups were 83-94% males

Source: Barkley, R. A., Murphy, K. R., & Fischer, M. (2008). *ADHD in Adults: What the Science Says*. New York: Guilford Press.

14 Life Expectancy Calculator Variables

Goldenson Center for Actuarial Research¹

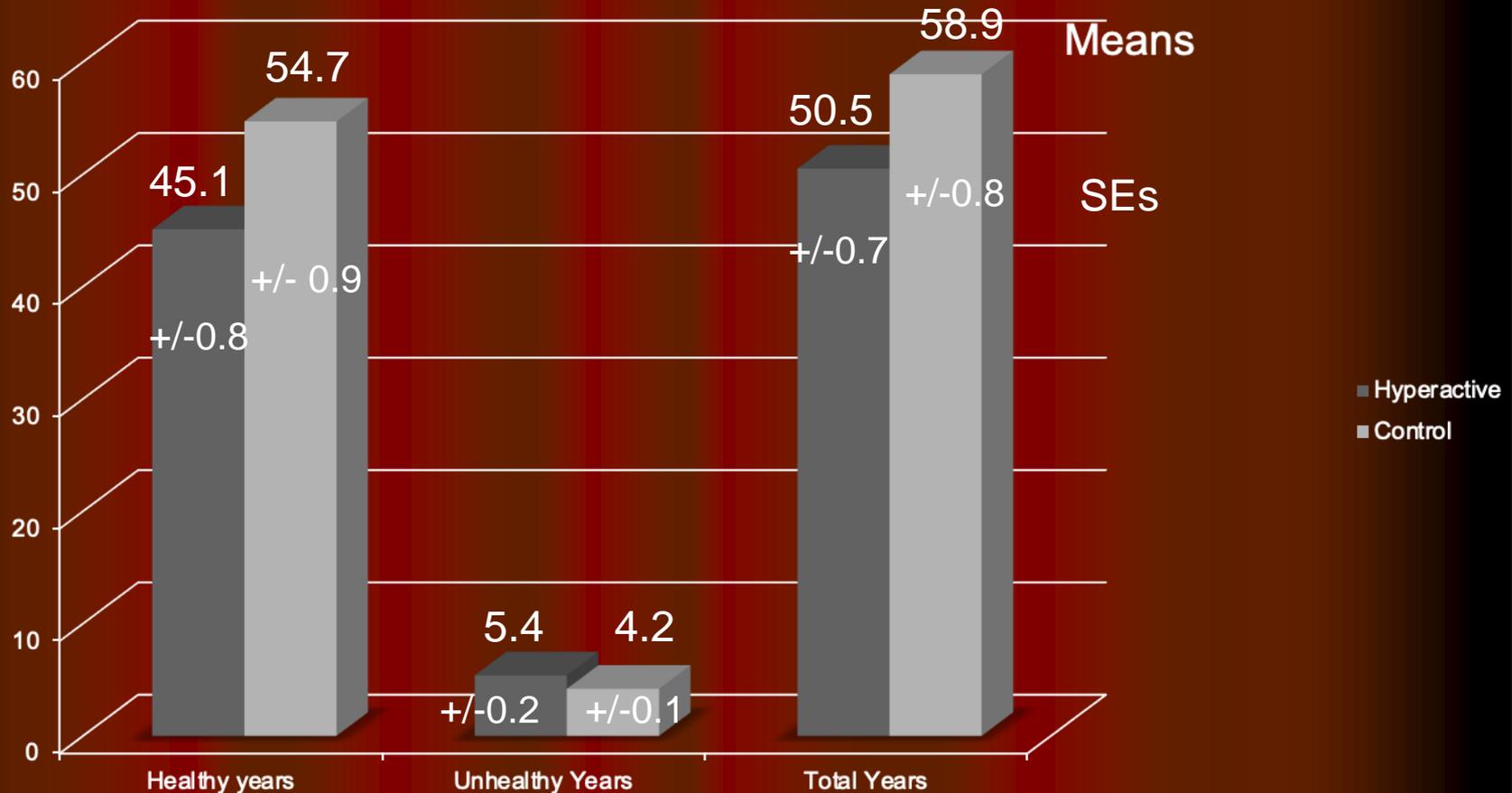
- Sex - 83-94% of all groups were male
- Age - 27 years (mean)
- Height – in cm
- Weight – in kg
- Mean income (always \$25-50K categorization)
- Type 2 diabetes (just 3 cases)
- Current Health (options Poor, Fair, Very Good, Excellent)
- Nutrition (options Poor, Fair, Good, Excellent)
- Exercise (times per week – usually 1-3x)

¹<https://apps.goldensoncenter.uconn.edu/HLEC/>

More Calculator Entries

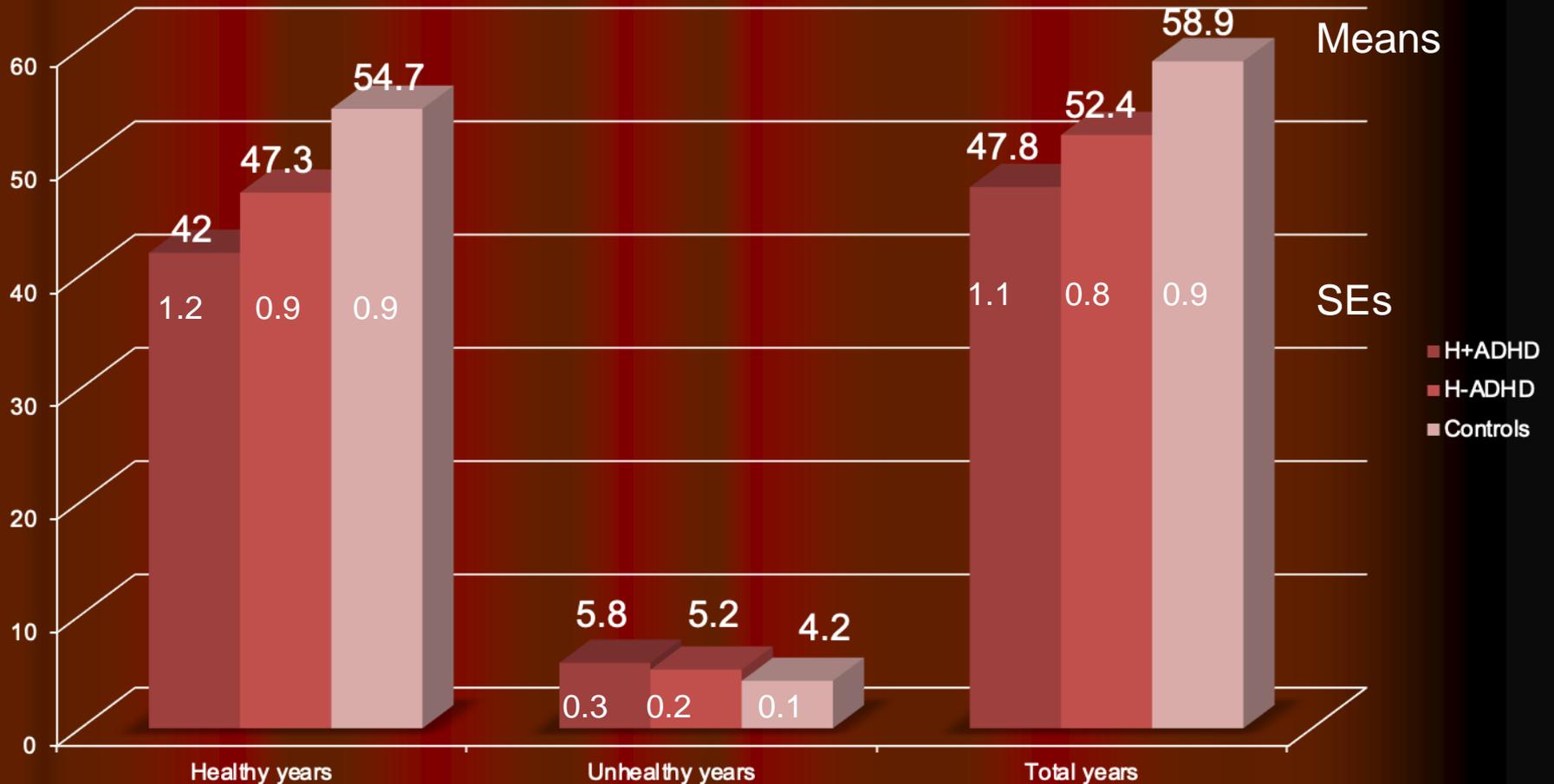
- Sleep (8+ hrs/night, <5 hrs, 5-8 hrs)
- Education (non-HS, HS, college, or graduate school)
 - We adjusted above high school - 11 months added to ELEs per extra year of education
- Driving – 0, 1, 2+ license revocations
 - A proxy for risky driving
- Current Smoker – No or Yes
 - Project added amount smoked per day and adjusted ELE outputs: if 20+/day, then reduced ELEs by 2.4 yrs
- Alcohol Use - (No, 1-2 per day, 3-7 per day, 8+)

Estimated Life Expectancy (yrs. Left) Hyperactive (ADHD-C) Children vs. Controls



Data used to create the graph are from Barkley, R. A. & Fischer, M. (2019). *Hyperactive child syndrome and estimated life expectancy at young adult follow-up: The role of adult ADHD and other potential predictors*. *Journal of Attention Disorders*, 23, 907-923.

Estimated Life Expectancy Persistent vs. Non-persistent ADHD



Data used to create the graph are from Barkley, R. A. & Fischer, M. (2019). *Hyperactive child syndrome and estimated life expectancy at young adult follow-up: The role of adult ADHD and other potential predictors*. *Journal of Attention Disorders*, 23, 907-923.

First Order Calculator Variables Contributing to Group Differences in Life Expectancy

- Less education in both ADHD groups (32-37%+ did not graduate high school)
- Less annual income (\$24-25K vs. \$37K per year)
- Greater frequency of alcohol use per week (H+ADHD)
- More likely to smoke (both ADHD groups)(57-65% vs. 35%)
- More likely to smoke more than 20+ cigarettes per day (H+ADHD)(43% vs. 11%)
- Less likely to be in excellent health (18-36% vs. 69%)
- Less likely to get 8+ hrs. sleep/night (both ADHD groups)(48-67% vs. 86%)
- More license suspensions/revocations ($p = .06$)

Second Order – Background Predictors of Life Expectancy

- Four second order background factors explained 40% of the variance in estimated life expectancy (ELE)
 - Behavioral disinhibition (from EF Rating Scale) – 31% of variance in ELE
 - Verbal IQ – 6%
 - Interpersonal Hostility – 2%
 - Nonverbal fluency (working memory) – 1%

ADHD Risk Gene Predictors

- Three risk genes had been genotyped earlier in the project – DRD4 (7+ repeat), DAT1, and DBH Taq1
- Two of the three genes predicted additional reductions in ELE apart from the second order psychological predictors
 - DBH Taq1 A1/A2 allele polymorphism in heterozygous pairing (-2 yrs.) compared to the homozygous pairings (A1/A1 or A2/A2)
 - DAT1 9/9 allele pair vs. 10/10 pair (-5 years)
 - DAT1 9/9 vs. 9/10 pair (-2 yrs.)
 - DAT1 9/10 vs. 10/10 (-3 yrs.)
- Genes were likely operating via impact on alcohol use (DBH) and education, smoking risk, smoking amount, and exercise (DAT1)

Putting These Findings in Context

Reductions in life expectancy for various adverse health conditions:

- Obesity: - 4.2 years¹
 - - 7 mos. Per unit of BMI over mean
- Smoking: <20 per day, -2.4 years
 - >20 cigs per day = 6.8 years²
- Excessive alcohol use:²
 - -2 yrs for men, 0.4 years for women
- Substance use disorder: - 10 years³
- Elevated blood pressure: - 5 years²
- Education: +11 mos. Per year after high school

Limitations

- Predictive accuracy of online ELE calculators has yet to be established, although internal validity is sound given large actuarial databases followed over time to create regression weights and entry variable adjustments to ELE
- Relatively small sample sizes for inferring risk
- Clinical samples of ADHD cases are more severe than community samples and so may exaggerate differences in life expectancy
- Severely limited number of females restricts results to male cases

More Limitations

- Lack of ethnic and regional diversity restricts results to mainly white populations and Midwest of US
- Under-reporting of symptoms and impairments in young adults with ADHD could yield conservative estimates of ELE
- Some health variables known to impact ELE adversely were not used in the calculator, such as lipid profiles, accidents, etc. making estimates conservative. But low behavioral inhibition may have explained their link to ELE
- ELE risk is not immutable going forward; it may change as risk factors increase or are reduced (by time or intervention)

9 Malleable Factors in the Calculator Can Change ELE

- Years of Education (and hence income also)
- Weight
- Nutrition
- Exercise
- Sleep Duration
- Risky Driving
- Smoking
- Alcohol Use
- Current Health

Lots of advice on the Internet for how to address these and other health risks

Behavioral Inhibition (Conscientiousness)

Families and clinicians cannot just focus on improving these specific first order health concerns but must also address the ADHD symptoms and particularly deficient behavioral inhibition and self-regulation that routinely bias decision-making in daily life related to those concerns

Conclusions

- ADHD is a disorder of self-regulation
- The disorder is associated with numerous and serious impairments in major life activities
- But ADHD is also linked to adverse health and lifestyle risks generally known to negatively impact life expectancy
- More recent research demonstrates an increased risk for earlier mortality in children and especially adults with ADHD, particularly related to accidents and suicide
- Evidence shown here indicates that besides the risk for death by injury or suicide, childhood ADHD may typically shorten healthy life expectancy by nearly 10 years and by nearly 13 years if it is persistent into young adulthood compared to concurrently followed control children
- Why? Recent qualitative research suggests that ADHD causes a decline in health and quality of life because it interferes with daily decision-making around health challenges, thus resulting in daily coping failures in healthy choice situations.

Implications

- ADHD is a serious public health problem; it accounts for greater reductions in ELE than any single risk factor of concern to public health and medical professionals, such as smoking, excess alcohol use, obesity, coronary heart disease, nutrition, sleep, exercise, or risky driving among other widely accepted health risks.
- It is 2.5x worse than even the top 4 above combined.
- Not surprisingly, ADHD is associated with \$26,000+ per patient year in increased costs for health, social care, crime, increased disability and other state benefits in comparison to siblings
- Treating ADHD and especially its behavioral inhibition deficits, such as with medications improves most domains of impairment, reduces many of the associated health risks that may thereby improve estimated life expectancy and improves mortality rates in children.
 - Population wide medication studies show that it reduces risks for driving accidents and citations, accidental injuries in children and adults, suicide attempts, adolescent pregnancies, obesity, antisocial behavior/crime, and arguably substance abuse, as well as all cause mortality in children.

More Implications

- Patients and families need to become aware of such risks so as to encourage more engagement in health risk reduction
- Mental health professionals need to:
 - broaden their evaluations to include health, lifestyle, and other factors related to life expectancy
 - Include recommendations for reducing those first order risk factors as part of their treatment package
- Primary Care Providers need to:
 - recognize the role of ADHD in diminished health, wellness, and life expectancy in their practice
 - recognize that their patients who are failing in typical health improvement programs may have adult ADHD that is undermining their success
 - assess for adult ADHD, and
 - treat it or refer to others more expert in doing so to improve chances of responding to health and lifestyle self-improvement interventions
- Government agencies tasked to deal with public health issues need to be aware of the important role that ADHD plays in these health domains and mediating success or failure in health improvement changes, encouraging screening for and treating it especially when prior efforts at self-improvement have failed.

Final Remarks

- ADHD is among the most treatable psychiatric disorders yet it is not recognized in primary care or by public health officials in their policies and programs as playing a critical role in health and healthy life style choices.
- The greatest problems currently are under recognition and under treatment of teen and adult ADHD, access to evidence-based treatments, reducing costs, and getting patients to remain in treatment through the critical adolescent and adult years.