Lifestyle Interventions and Men’s Health

Y. Reisman MD, PhD, FECSM, ECPS
Urologist & Sexologist
Flare-Health, Netherlnads
ESSM President
Life expectancy in 2025 of the man, like of the woman in 1988.

In 2025 life expectancy of the man, like of the woman in 1988.
Why men die earlier?

We don’t know!
Risico factoren

Endothelial dysfunction

CVD

Erectile dysfunction

The Deadly Quartet – Metabolic Syndrome

Diabetes  Obesity  Hypertension  Dislipidemia
ED Shares Common Risk With Other Conditions

Prevalence of ED in co-morbidity

Comorbidities Are More Common in Men With ED

Prevalence of co-morbidity in ED patients

Based on a 2001 survey of nearly 28,000 men in 8 countries, including the US.

Effect of MetS components on penile Doppler ultrasound parameters in patients (n=803) with MetS-associated sexual dysfunction.

Odds ratio (95% CI) for pathologic Vpmax (<30 cm/s)
Androgen levels according to the number of metabolic syndrome factors

- Total-T (nmol/L)
  - p<0.0001

- Free-T (pmol/L)
  - p<0.0001

- c-Free-T (nmol/L)
  - p<0.0001

- c-Bioavailable-T (nmol/L)
  - p<0.0001

- LH (mU/L)
  - p=NS

- ANDROTEST score
  - p<0.0001

Metabolic syndrome factors (#)

Corona et al., Int J Androl. 2009;32:587-98
HR of hypogonadism (decreased testosterone <11 nM and at least 3 sexual symptoms in men with ED) and MetS factors

- Elevated glycaemia
- Elevated BP
- Elevated waist
- Reduced HDL cholesterol
- Elevated triglycerides

Mets is associated with secondary (central) hypogonadism

Corona et al., J Endocrinol Invest 2011 Jul-Aug;34(7):557-67
Predictors of incident secondary HG
Referent Persistent Eugonadal

Rastrelli et al., J Clin Endocrinol Metab 2015;100:3172-82
Male hypogonadism and ED

- Male hypogonadism has been correlated with decreased vascular NO production\(^a\) and with the metabolic syndrome, and testosterone replacement not only improves ED\(^b\), but gathering evidence has shown that it also improves various components of the metabolic syndrome, including a reduction of central adiposity and decreased insulin resistance\(^c\).

\(^a\) Akishita: Hypertens res 2007;30:1029-34,
\(^b\) Traish: J Androl 2009;30:10-22,
\(^c\) Stanworth: Clin Interv Aging 2008;3:25-44
Metabolic syndrome

- ↑ glycaemia
- ↓ HDL
- ↑ triglycerides
- ↑ visceral obesity
- ↓ testosterone
- hypertension

Increased cardiovascular risk
Erectile dysfunction risk
Increased metabolic risk
Life Style Erection Enemies

**Smoking**
Evidence has found a link between smoking and erectile dysfunction through a process called atherosclerosis.

- This is a build up of plaque and fatty materials against the walls of your arteries.
- The longer you smoke for, and the more regularly you smoke, the more pressure you're putting on your arteries.
- And as they become more clogged, the blood flow is restricted to areas you really want blood to get to.

**Alcohol**
Even small amounts of alcohol can have a depressive effect on the body's nervous system. Signals from the brain to the blood vessels in the penis are inhibited.

- As a result, you may experience decreased sexual desire or, if you manage to achieve an erection, you might find it won't last.
- This is because alcohol keeps the blood vessels wide, making it easier for the blood in your penis to drain out. Heavier drinking and alcohol abuse can even damage the nerves in your penis, causing permanent impotence.

**Drugs**
Heavy or prolonged use of many illegal drugs can cause a variety of long term health issues related to erectile dysfunction.

- These include heart problems, irregular blood pressure or mental health issues such as paranoia.
- Amphetamines restrict blood vessels and direct blood flow to the muscles and away from the pelvic area.
- Depressants and certain prescription drugs can change your blood pressure and cause a loss of libido.

**Stress**
Stress can affect the circulatory system and restrict the blood flow to the penis. This is due to the body releasing cortisol and adrenaline into the bloodstream, which causes blood vessels to constrict.

- High blood pressure brought on by stress can cause damage to the lining of the arteries, restricting blood flow.
- Stress can also lead to depression, which may alter the biochemistry of the body and reduce libido. This means you may struggle to achieve and maintain an erection.

**Obesity**
Obesity has direct links with the formation of fatty deposits in the arterial system and atherosclerosis (hardening of the arteries).

- The cavernous artery that supplies the penis with blood is the smallest artery in the body and is typically the first to experience reduced blood flow.
- Testosterone levels also decrease, as fatty tissue produces aromatase which converts testosterone into oestrogen.

Testosterone is very important and this lowered production can have direct consequences on men's sexual health.
Lifestyle as a risk factor for ED

- Smoking
- Fatty diet
- Obesity
- Alcohol abuse
- Recreational drugs
- Sedentary life style

Table 3. Literature sample of studies reporting pre and normal-weight men

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feldman et al</td>
<td>513</td>
<td>Erectile dysfunction</td>
</tr>
<tr>
<td>Fillo et al</td>
<td>216</td>
<td>Erectile dysfunction</td>
</tr>
</tbody>
</table>

Table 4. Literature sample of studies reporting obese men

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esposito et al</td>
<td>55</td>
</tr>
<tr>
<td>Khoo et al</td>
<td>68</td>
</tr>
</tbody>
</table>

NR = not reported
*Based on questionnaires
†Assessed using clinical data

Comorbidities:
- Insulin resistance
- Type II diabetes mellitus
- Dyslipidemia
- Chronic inflammation (e.g., TNF-α)
- Deteriorated blood vessel health
- Cardiovascular disease (CVD)

Psychological Variables:
- Perceived fear of hurting partner
- Self-esteem and body image issues
- Effects of media/thin culture
- Ridicule from partner, peers, or society
- Performance anxiety and/or depression

Sexual desire:
- Overweight: 43.7 ± 5.3, lo-cal diet
- Extreme Obesity: 51.9 ± 6.6, hi-prot diet

Sexual Function:
- Erectile Dysfunction
- Premature Ejaculation
- Inhibited/Delayed Ejaculation
Erectile Dysfunction
Type 2 diabetes m.

Lifestyle
- Lack of physical activity
- Overnutrition
- Smoking
- Stress

Other interventions

Erectile Dysfunction
Type 2 diabetes m.

Cardiovascular events
- Myocardial infarction
- Stroke

Are lifestyle intervention effective in improving SD incl ED?
Cigarette smoking

Stopping smoking can improve ED in a considerable proportion of smokers

40-50% increased risk of ED

Similar in current and past smokers

Stopping smoking can improve ED in a considerable proportion of smokers

Physical activity and erectile dysfunction (univariate)

<table>
<thead>
<tr>
<th>Study name</th>
<th>Odds ratio</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>ZValue</th>
<th>pValue</th>
<th>Relative weight</th>
<th>Relative weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ahmed et al 2011</td>
<td>0.335</td>
<td>0.262</td>
<td>0.427</td>
<td>-6.621</td>
<td>0.000</td>
<td>5.47</td>
<td></td>
</tr>
<tr>
<td>Arrus et al 2002</td>
<td>0.320</td>
<td>0.322</td>
<td>0.466</td>
<td>-6.365</td>
<td>0.000</td>
<td>5.06</td>
<td></td>
</tr>
<tr>
<td>Allen &amp; Desile 2017</td>
<td>0.382</td>
<td>0.317</td>
<td>0.481</td>
<td>-14.007</td>
<td>0.000</td>
<td>6.99</td>
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<tr>
<td>Apostolou et al 2009</td>
<td>0.236</td>
<td>0.207</td>
<td>0.307</td>
<td>-4.130</td>
<td>0.000</td>
<td>2.59</td>
<td></td>
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<tr>
<td>Bech et al 2008</td>
<td>0.532</td>
<td>0.374</td>
<td>0.740</td>
<td>-6.121</td>
<td>0.000</td>
<td>5.09</td>
<td></td>
</tr>
<tr>
<td>Cheng &amp; Ng 2007</td>
<td>0.960</td>
<td>0.892</td>
<td>1.033</td>
<td>-1.095</td>
<td>0.273</td>
<td>6.04</td>
<td></td>
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<tr>
<td>Etaa et al 2014</td>
<td>0.442</td>
<td>0.290</td>
<td>0.673</td>
<td>-3.803</td>
<td>0.000</td>
<td>4.53</td>
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<tr>
<td>Ghalyi et al 2010</td>
<td>0.490</td>
<td>0.373</td>
<td>0.644</td>
<td>-5.103</td>
<td>0.000</td>
<td>5.32</td>
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<tr>
<td>Janiszewski &amp; Kozieniewski 2009</td>
<td>0.724</td>
<td>0.580</td>
<td>0.901</td>
<td>-2.554</td>
<td>0.011</td>
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<tr>
<td>Kostrik et al 2009</td>
<td>0.844</td>
<td>0.630</td>
<td>1.120</td>
<td>-2.541</td>
<td>0.011</td>
<td>4.25</td>
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<tr>
<td>Me et al 2002</td>
<td>0.490</td>
<td>0.300</td>
<td>0.780</td>
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<td>5.10</td>
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<tr>
<td>Medallie et al 2015</td>
<td>0.520</td>
<td>0.396</td>
<td>0.674</td>
<td>-6.214</td>
<td>0.000</td>
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<td>Motera et al 2006</td>
<td>0.510</td>
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<td>-1.989</td>
<td>0.047</td>
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<td>Niccol et al 2003</td>
<td>0.421</td>
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<td>0.000</td>
<td>4.18</td>
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<tr>
<td>Oelade et al 2016</td>
<td>0.800</td>
<td>0.649</td>
<td>1.000</td>
<td>-0.816</td>
<td>0.414</td>
<td>3.91</td>
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<tr>
<td>Pina et al 2008</td>
<td>0.794</td>
<td>0.600</td>
<td>0.870</td>
<td>-3.657</td>
<td>0.000</td>
<td>5.81</td>
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<tr>
<td>Ramirez et al 2006</td>
<td>0.848</td>
<td>0.644</td>
<td>1.120</td>
<td>-2.530</td>
<td>0.011</td>
<td>4.23</td>
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<tr>
<td>Repic et al 2009</td>
<td>0.760</td>
<td>0.563</td>
<td>0.981</td>
<td>-3.591</td>
<td>0.000</td>
<td>5.84</td>
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<tr>
<td>Wang et al 2010</td>
<td>0.790</td>
<td>0.508</td>
<td>1.240</td>
<td>-1.540</td>
<td>0.124</td>
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<tr>
<td>Wu et al 2012</td>
<td>0.566</td>
<td>0.475</td>
<td>0.676</td>
<td>-6.325</td>
<td>0.000</td>
<td>5.84</td>
<td></td>
</tr>
</tbody>
</table>

Meta Analysis

40-50% decreased risk of ED
Similar moderate and high activity

Aerobic exercise of moderate to vigorous intensity 4 times per week for 40 minutes for 6 months contributes to a decrease of ED

CONCLUSION

Recommendations considering PA to decrease arterial ED should include supervised training consisting of aerobic exercise of moderate to vigorous intensity 4 times per week for 40 minutes. An overall weekly exercise dose of 160 minutes for 6 months contributes to a decrease of ED for men with arterial ED due to physical inactivity, obesity, HTN, MetS, and/or manifest CVD.
Physical activity and exercise for erectile dysfunction: a systematic review and meta-analysis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Experimental Mean</th>
<th>SD</th>
<th>Total</th>
<th>Control Mean</th>
<th>SD</th>
<th>Total</th>
<th>Weight</th>
<th>Mean Difference IV, Random, 95% CI</th>
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<tbody>
<tr>
<td>Dorey G (2004)</td>
<td>17.2</td>
<td>9.7</td>
<td>28</td>
<td>8.4</td>
<td>7.3</td>
<td>27</td>
<td>7.3%</td>
<td>8.80 [4.27, 13.33]</td>
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<tr>
<td>Kalka D (2013)</td>
<td>14.39</td>
<td>6.82</td>
<td>103</td>
<td>12.43</td>
<td>5.75</td>
<td>35</td>
<td>13.9%</td>
<td>1.96 [-0.36, 4.28]</td>
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<tr>
<td>Lamina S (2009)</td>
<td>15.14</td>
<td>4.92</td>
<td>22</td>
<td>8.95</td>
<td>3.9</td>
<td>21</td>
<td>12.7%</td>
<td>6.19 [3.54, 8.84]</td>
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<tr>
<td>Lin YH (2012)</td>
<td>8.14</td>
<td>4.86</td>
<td>35</td>
<td>5.96</td>
<td>0.98</td>
<td>27</td>
<td>16.5%</td>
<td>2.18 [0.53, 3.83]</td>
</tr>
<tr>
<td>Maio G (2010)</td>
<td>26.7</td>
<td>2.18</td>
<td>27</td>
<td>24.7</td>
<td>2.62</td>
<td>28</td>
<td>17.9%</td>
<td>2.00 [0.73, 3.27]</td>
</tr>
<tr>
<td>Maresca L (2013)</td>
<td>20.1</td>
<td>2.3</td>
<td>10</td>
<td>14.2</td>
<td>2.2</td>
<td>10</td>
<td>15.3%</td>
<td>5.90 [3.93, 7.87]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>280</strong></td>
<td></td>
<td><strong>203</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td></td>
<td></td>
<td><strong>3.88 [2.35, 5.41]</strong></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 2.97; Chi² = 23.99, df = 6 (P = 0.0005); I² = 75%
Test for overall effect: Z = 4.97 (P < 0.00001)

Summary box

- A systematic review and meta-analysis of seven randomised controlled trials of patients with erectile dysfunction.
- Different physical activity and exercise interventions increase short-term and long-term patient-reported erectile function in different patient population and treatment scenarios.
- The pooled evidence supports the need to review current recommendations for prescribing physical activity and exercise to patients with erectile dysfunction.

~4 points IIEF-EFD score!
End point IIEF-EFD score (200 mg vs placebo)

<table>
<thead>
<tr>
<th>Study name</th>
<th>Difference in means</th>
<th>Lower limit</th>
<th>Upper limit</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zhao et al., 2012</td>
<td>4.90</td>
<td>2.05</td>
<td>7.75</td>
<td>0.00</td>
</tr>
<tr>
<td>Goldstein et al., 2012</td>
<td>6.90</td>
<td>3.47</td>
<td>10.33</td>
<td>0.00</td>
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<tr>
<td>Goldstein et al., 2012*</td>
<td>4.10</td>
<td>2.07</td>
<td>6.13</td>
<td>0.00</td>
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<tr>
<td>Mulhall et al., 2013</td>
<td>5.00</td>
<td>1.23</td>
<td>8.77</td>
<td>0.00</td>
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<tr>
<td>Hellstrom et al., 2015</td>
<td>5.20</td>
<td>2.14</td>
<td></td>
<td>0.00</td>
</tr>
<tr>
<td>Overall</td>
<td>4.92</td>
<td>3.00</td>
<td></td>
<td>0.00</td>
</tr>
</tbody>
</table>

Physical activity improves 4 point IIEF-EFD (almost as avanafil)

~5 points IIEF-EFD score!
### Study name

<table>
<thead>
<tr>
<th>Statistics for each study</th>
<th>Difference in means and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Differences</td>
</tr>
<tr>
<td>Hirantrakul et al., 2010</td>
<td>0.79</td>
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<td>Arazi et al., 2012</td>
<td>5.00</td>
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<tr>
<td>Hayes et al., 2015</td>
<td>1.71</td>
</tr>
<tr>
<td>Armamento-Villareal et al., 2016</td>
<td>1.71</td>
</tr>
<tr>
<td>Kumagai et al., 2015</td>
<td>0.90</td>
</tr>
<tr>
<td>Kumagai et al., 2016</td>
<td>1.00</td>
</tr>
<tr>
<td>Hayes et al., 2017</td>
<td>1.40</td>
</tr>
<tr>
<td>Kumagai et al., 2018</td>
<td>1.50</td>
</tr>
<tr>
<td>Overall</td>
<td>1.61</td>
</tr>
</tbody>
</table>

**Physical exercise improves 1.6 nmoles/L TT**
## Diet

<table>
<thead>
<tr>
<th></th>
<th>Non-adjusted estimates</th>
<th>Age-adjusted estimates</th>
<th>Multivariable-adjusted estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>k OR (95% CI)</td>
<td>k OR (95% CI)</td>
<td>k OR (95% CI)</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>7 0.86 (0.77–0.96)</td>
<td>—</td>
<td>4 0.93 (0.81–1.06)</td>
</tr>
<tr>
<td>Fruit ± vegetable intake</td>
<td>3 0.90 (0.73–1.11)</td>
<td>—</td>
<td>2 0.57 (0.21–1.52)</td>
</tr>
<tr>
<td>Fat consumption</td>
<td>1 0.75 (0.61–0.92)</td>
<td>—</td>
<td>1 1.05 (0.95–1.16)</td>
</tr>
<tr>
<td>Mediterranean</td>
<td>1 0.73 (0.48–1.14)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>General population</td>
<td>4 0.87 (0.75–1.01)</td>
<td>—</td>
<td>2 1.00 (0.89–1.10)</td>
</tr>
<tr>
<td>Clinical population</td>
<td>3 0.72 (0.49–1.06)</td>
<td>—</td>
<td>2 0.57 (0.21–1.52)</td>
</tr>
</tbody>
</table>

**10% decreased risk of ED**

**Publication bias**

*Allen & Walter, J Sex Med. 2018;15:458-475*

- Mediterranean Diet and Activity improve erection and MS

*Pourmand et al. BJU Int. 2004;94:1310-1313*

*Kim SC. J Sex med 2010;7:s151-239*

*Esposito K. JAMA 2004;291:2978-84*
Secondary Hypogonadism is Related to Weight Change during follow-up (longitudinal results)

Change in Testosterone

T levels worsen with weight gain and improve with weight loss

Change in LH

LH levels are suppressed with weight gain and improve with weight loss

n = 2395, *p<0.05, **p<0.01

Weighted differences (with 95% confidence interval [CI]) of mean total testosterone before and after weight loss

**Effect of weight loss on T levels: meta-analysis**

**Diet improves 2.6 nmoles/L total T**
Corona J et al. 2019

**Bariatric surgery improves 9 nmoles/L of TT**
Rastrelli G et al. 2019

---

Corona et al., Eur J Endocrinol. 2013 May 2;168(6):829-43
Effects of Cocoa and Sugar on Flow Mediated Dilation

Adding 60 g/d of mixed raw nuts to a western-style diet for 14-wk improved the auto-reported orgasmic function and sexual desire parameters in a group of healthy reproductive-aged participants compared with an age-matched control group. No significant differences in changes between groups were shown in peripheral concentrations of no
Pay attention to relationship with the partner.
Proportion free of MACE (Kalplan-Meier curves) as a function of baseline reported partner’s hypoactive sexual desire in a consecutive series of 1687 ED subjects at the University of Florence, Florence, Italy

Having a partner who desires you is not only fun, …but it also protects from MACE (Cox regression HR=2.01 [1.34-3.02])
Lifestyle modification

- The effect of "lifestyle" adjustments and cardiovascular risks reduction on ED:
- Positive "lifestyle" changes (under pharmacotherapy) resulted in an improvement in IIEF-5 score.


- The T Trial has produced strong evidence that TTh improves multiple aspects of sexual function, to the extent that couples age 70 years engaged in sexual activity an average of 4 times per week.
- Walking distance was improved, and there were modest but statistically significant improvements in insulin resistance and lipid profiles.
- There were significant improvements in anemia and a 6.8% improvement in bone mineral density within 1 year.

Combined life style + TTh in obese men with low TT

• Prospective registry
• Inclusion: age>40, BMI>30, AC >102 cm, TT< 8.7nmol/l
• Interventions:
  Group 1: diet + exercise referral
  Group 2: TTh + life style advice
  Group 3: TTh + diet + exercise referral
<table>
<thead>
<tr>
<th></th>
<th>Group 1: referral</th>
<th>Group 2: TTh</th>
<th>Group 3: TTh + referral</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Followup m</strong></td>
<td>0  3  6  12</td>
<td>0  3  6  12</td>
<td>0  3  6  12</td>
</tr>
<tr>
<td><strong>N</strong></td>
<td>19  18  5  1</td>
<td>26  26  26  25</td>
<td>38  38  38  27</td>
</tr>
<tr>
<td><strong>Age yr</strong></td>
<td>61.2±4</td>
<td>60.9±6</td>
<td>61.1±3</td>
</tr>
<tr>
<td><strong>DM %</strong></td>
<td>10 53%</td>
<td>15 56%</td>
<td></td>
</tr>
<tr>
<td><strong>Weight kg</strong></td>
<td>110.8±12</td>
<td>108.9±10</td>
<td>109.6±9</td>
</tr>
<tr>
<td></td>
<td>110±10</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>34.4±4</td>
<td>33.7±4</td>
<td>33.9±3</td>
</tr>
<tr>
<td></td>
<td>33.9±3</td>
<td></td>
<td>34.1±2</td>
</tr>
<tr>
<td><strong>AC cm</strong></td>
<td>108±6</td>
<td>108±4</td>
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<tr>
<td><strong>TTh</strong></td>
<td>-</td>
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<tr>
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</table>

**Difficult to motivate the patients !!!**
- TTh + active intervention – better results
- TTh reduction possible

Bold= p<.05; IIEF under PDE5i use
The horsepower of Austrian physicians’ cars correlates with senior position and increased cardiovascular risk. However, no relationship found between sexual dysfunction or lack of sexual satisfaction and the horsepower of doctors’ cars.
Conclusion

• Men’s health require attention
• Lifestyle intervention are effective but
  – Combination
  – Patience
  – Motivation
• Sexual Medicine can improve quality of sexual life and may save life