The Impact of BPH and Management of Prostate Cancer (Obesity in Urology)

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Mount Sinai Health System
Population ≥65 Years for Developed and Developing Countries by Age

2000 to 2050

Developed Countries

In the US, the population aged ≥65 y is projected to increase from 35 million to 71 million between 2000-2030

Developing Countries

Worldwide, the population aged ≥65 y is projected to increase from 520 to 700 million between 2010 and 2020

News is Not Good for Everyone

- The mortality rate for white men and women ages 45-54 with less than a college education increased markedly between 1999 and 2013.
- Before then, death rates for that group dropped steadily, and at a faster pace.
Change in Age
Change in Age

- poisonings
- lung cancer
- suicides
- chronic liver disease
- diabetes

 deaths per 100,000

 year

Change in Age

![Graph showing change in age](image)
BPH = benign prostatic hyperplasia; LUTS = lower urinary tract symptoms.
4 OUT OF 3 PEOPLE STRUGGLE WITH MATH
GOOD DIET AND EXERCISE
Obesity
A Growing Epidemic
Obesity Trends* Among U.S. Adults
BRFSS, 1985
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1986
(*BMI ≥30, or ~30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1987

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1988
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults

BRFSS, 1989

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1990
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1991
(*BMI ≥30, or ~ 30 lbs. overweight for 5‘ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 1992
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1993
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1994
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1995
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1996
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults

BRFSS, 1997

(*BMI ≥30, or ~ 30 lbs. overweight for 5’4” person)

No Data          <10%           10%–14%           15%–19%           ≥20%

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1998
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 1999
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2000

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 2001

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 2002

(*BMI ≥30, or ~ 30 lbs. overweight for 5’4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2003
(*BMI $\geq 30$, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults

BRFSS, 2004

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)
Obesity Trends* Among U.S. Adults
BRFSS, 2005
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 2006
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 2007
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 2008
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults
BRFSS, 2009
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Trends* Among U.S. Adults

BRFSS, 2010

(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

White non-Hispanic

*BMI ≥ 30

- No sufficient sample**
- 25–29
- <20
- 30–34
- 20–24
- 35+

Black non-Hispanic

*BMI ≥ 30
- No sufficient sample
- <20
- 20–24
- 25–29
- 30–34
- 35+

Hispanic

(*BMI ≥ 30

- No sufficient sample**
- <20
- 25–29
- 30–34
- 20–24
- 35+
Obesity Trends* Among U.S. Adults
BRFSS, 1990, 2000, 2010
(*BMI ≥ 30, or about 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Prevalence* of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2013

*Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity

American Adults, by Weight Category
Weight category as determined by BMI

- % Normal weight (BMI 18.5 to <25)
- % Overweight (BMI 25 to <30)
- % Obese (BMI 30 or above)

Gallup-Healthways Well-Being Index
Obesity Affects Other Specialties As Well

Knee Replacements Almost Doubled in a Decade
The rate of total knee replacements among Americans 45 and older

Source: CDC National Center for Health Statistics
Obesity
A Growing Epidemic

Obesity worldwide
An estimated 641 million obese people in 2014, up from 105 million in 1975, according to a study published in the Lancet

Proportion of obese people

<table>
<thead>
<tr>
<th></th>
<th>1975</th>
<th>2014</th>
<th>Forecast 2025</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>6.4%</td>
<td>10.8</td>
<td>21</td>
</tr>
<tr>
<td>Men</td>
<td>3.2%</td>
<td>14.0</td>
<td>18</td>
</tr>
</tbody>
</table>

Analysis of global, regional and national trends in adult BMI between 1975 and 2014

Source: Lancet
Obesity
A Growing Epidemic

Obesity
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Obesity
A Growing Epidemic

The world’s population has become heavier by around **1.5kg (3.3lbs)** in each subsequent decade since 1975.

The research predicted if these global trends continue, by 2025 **18 per cent of the world’s men** and **21 per cent of women** will be obese.
Put in Words

- Lowest BMI of Developed Countries
  - Japan
- Highest BMI of Developed Countries
  - USA
- The country with the highest average BMI was American Samoa (average BMI of 35 kg/m² for women and 32 kg/m² for men), where the average individual is classed as obese.
- **Morbid obesity**, where a person’s weight interferes with basic physical functions such as breathing and walking, now affects around 1 per cent of men in the world, and 2 per cent of women. In total, **55 million adults are morbidly obese**.
“This epidemic of severe obesity is too extensive to be tackled with medications such as blood pressure lowering drugs or diabetes treatments alone, or with a few extra bike lanes. We need coordinated global initiatives - such as looking at the price of healthy food compared to unhealthy food, or taxing high sugar and highly processed foods”

Professor Majid Ezzati, study leader, Imperial College London
Obesity Challenges: Nutrition

"If you put a crouton on your sundae instead of a cherry, it counts as a salad."
“What fits your busy schedule better, exercising one hour a day or being dead 24 hours a day?”
Other Factors

- Sleep Apnea
- Stress

“Use of a Mouth Guard in Men with Sleep Bruxism in the Treatment of Concomitant Lower Urinary Tract Symptoms Secondary to Benign Prostatic Hyperplasia (BPH): A Pilot Study”
Prostate Biopsy After A Change in Nadir PSA of 0.4 ng/ml After Treatment With 5 – Alpha Reductase Inhibitors Markedly Enhances The Detection Rate of Prostate Cancer

Steven A. Kaplan, Richard K. Lee, Doreen E. Chung, Alexis E. Te, Douglas S. Scher, Ash Tewari and E. Darracott Vaughan

Weill Cornell Medical College
Cornell University
Background

- Patients with an elevated or fluctuating prostate specific antigen (PSA) with previous negative biopsy represent a diagnostic dilemma.
Background

- Can the magnitude of change in PSA after administration of 5 – alpha reductase inhibitors (5 – ARI) help in identifying men with prostate cancer?
- Elimination or reduction of PSA driven by “BPH background noise”
Objective

- Determine if changes in nadir PSA after a minimum of 6 months of 5 – ARI treatment in men with a previous negative biopsy could enhance prostate cancer detection
Methods

- 276 men with previous negative biopsy secondary to elevated PSA (n = 208) or a PSA velocity change of 0.75 ng / ml (n = 68) started on 5 - ARI
  - Finasteride (n = 154)
  - Dutasteride (n = 122)
Methods

- **Phase 1 (n = 97)**
  - PSA measured at 6 and 12 months
  - Repeat biopsy by protocol @ 1 year
  - Ascertain nadir PSA velocity

- **Phase 2 (n = 179)**
  - Biopsy triggered by a change in nadir PSA of > 0.4 ng/ml
  - Changes in prostate volume (PV), PSA and incidence of CaP assessed
Results

- Mean age was 60.5 +/- 7.6
- Baseline
  - Mean # previous negative biopsies: 2.3
  - PSA: 5.15 +/- 2.7 ng / ml
  - PV: 45.6 +/- 19.7 cc
Results

- **Phase 1**
  - Incidence of CaP: 27 (27.8%)
  - Minimum PSA velocity from nadir of 0.4 ng/ml (mean 0.56 ng / ml)
Results

Phase 1: 97 patients

27 (27.8%) with cancer  
70 (72.2%) without cancer

All patients underwent PSA testing at 6 and 12 months  
All patients underwent repeat biopsy at 12 months
Results

- **Phase 2**
  - Using 0.4 ng/ml as PSA nadir change, a total of 48 / 179 (26.8%) men underwent repeat biopsy at a mean of 14.6 months (9 – 28 months).
  - Of these 48 men, 26 (54.1%) were found to have CaP.
  - Of these 26 men, 20 (76.9%) were found to have Gleason Scores ≥ 7.
Results

Phase 2: 179 patients

Biopsy triggered by a change in nadir PSA of $\geq 0.4$ ng/ml

48 (26.8%) repeat biopsy

131 (73.2%) no repeat biopsy

26 (54.1%) cancer

22 (46.9%) no cancer

20 (76.9%) with Gleason $\geq 7$ tumor
# Prostate Cancer Detection

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Phase 1 (N = 97)</th>
<th>Phase 2 (N = 179)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number Biopsied</td>
<td>97 (100%)</td>
<td>48 (26.8%)</td>
</tr>
<tr>
<td>CaP detected</td>
<td>27 (27.8%)</td>
<td>26 (54.2%)</td>
</tr>
<tr>
<td>Change in PSA in men with cancer (ng/ml)</td>
<td>2.1 (-43.4%)</td>
<td>2.3 (-41.8%)</td>
</tr>
<tr>
<td>Change in PV in men with cancer (cc)</td>
<td>6.3 (-16.7%)</td>
<td>5.9 (-14.3%)</td>
</tr>
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**NO DIFFERENCE BETWEEN THE TWO GROUPS**
<table>
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<td>97 (100%)</td>
<td>48 (26.8%)</td>
<td></td>
</tr>
<tr>
<td>CaP detected</td>
<td>27 (27.8%)</td>
<td>26 (54.2%)</td>
<td>&lt; 0.003</td>
</tr>
<tr>
<td>Gleason 6</td>
<td>11 (40.7%)</td>
<td>6 (23.1%)</td>
<td>&lt; 0.02</td>
</tr>
<tr>
<td>Gleason ≥ 7</td>
<td>16 (59.3%)</td>
<td>20 (76.9%)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>
## Changes in PSA and PV @ 1 year or at Biopsy

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<th>Phase 2 (N = 179)</th>
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<tr>
<td>Change in PSA of BPH men (ng / ml)</td>
<td>2.8 (-51.2%)</td>
<td>2.9 (-50.2%)</td>
</tr>
<tr>
<td>Change in PSA in CaP men (ng / ml)</td>
<td>2.1 (-43.1%)</td>
<td>2.3 (-41.8%)</td>
</tr>
<tr>
<td>Change in PV in BPH men (cc)</td>
<td>8.6 (-19.1%)</td>
<td>9.1 (-18.7%)</td>
</tr>
<tr>
<td>Change in PV in CaP men (cc)</td>
<td>6.3 (-16.7%)</td>
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No difference between finasteride or dutasteride.
Prostate Cancer Detection

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<th>Parameter</th>
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<th>Phase 2</th>
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<tbody>
<tr>
<td>Gleason 6 PSA (ng/ml)</td>
<td>3.2</td>
<td>3.1</td>
</tr>
<tr>
<td>Gleason 6 PV (cc)</td>
<td>36.7</td>
<td>33.2</td>
</tr>
<tr>
<td>Gleason ≥7 PSA (ng/ml)</td>
<td>2.9</td>
<td>2.2</td>
</tr>
<tr>
<td>Gleason ≥7 PV (ml)</td>
<td>28.4</td>
<td>25.8</td>
</tr>
</tbody>
</table>

No difference between finasteride or dutasteride
Conclusions

- PSA velocity change of 0.4 ng/ml from nadir after a minimum of 6 months of a 5 – ARI markedly enhances the detection rate of prostate cancer in men with a previous negative biopsy.

- Most of the cancers were high grade
  - ? Easier to detect in smaller prostate volumes.
Conclusions

- PSA elevations and fluctuations in large part are secondary to “BPH background noise” which may be modulated by 5 - ARI
- 5 – ARI may be viewed as chemosuppressive
- Larger scale trials will continue to define the role of 5 – ARI in prostate cancer detection
Men’s Health

- Urologists have been playing small ball
- Need to expand
  - Advocacy
  - Preventive care
  - Holistic
- Expand beyond prostate and sexual function
Building A Men’s Health Center
Retrospective review of 82 prostate cancer patients treated at the Roudebush Veteran’s Administration, Indianapolis from 1998-2005 for biochemical relapse or radiographic evidence of distant metastasis

- Median age: 70yo
- 49% of men met ATPIII criteria for metabolic syndrome
- All treated with LHRH agonists

Primary endpoints: time to PSA progression and overall survival

Presence of the metabolic syndrome is associated with shorter time to castration-resistant prostate cancer

Presence of the metabolic syndrome is associated with shorter time to castration-resistant prostate cancer

<table>
<thead>
<tr>
<th>Variables</th>
<th>Comparison</th>
<th>Unadjusted HR (95% CI)</th>
<th>P value</th>
<th>Adjusted HR (95% CI)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic syndrome</td>
<td>Yes versus no</td>
<td>2.29 (1.30–4.06)</td>
<td>0.003</td>
<td>2.55 (1.37–4.77)</td>
<td>0.003</td>
</tr>
<tr>
<td>Fasting HDL &lt; 40 mg/dl</td>
<td>Yes versus no</td>
<td>1.67 (0.96–2.92)</td>
<td>0.07</td>
<td>2.22 (1.1–4.5)</td>
<td>0.026</td>
</tr>
<tr>
<td>TG &gt; 150 mg/dl</td>
<td>Yes versus no</td>
<td>1.31 (0.73–2.36)</td>
<td>0.36</td>
<td>1.31 (0.65–2.66)</td>
<td>0.449</td>
</tr>
<tr>
<td>BMI &gt; 30</td>
<td>Yes versus no</td>
<td>2.05 (1.18–3.56)</td>
<td>0.009</td>
<td>2.78 (1.4–5.51)</td>
<td>0.003</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Yes versus no</td>
<td>1.08 (0.48–2.44)</td>
<td>0.84</td>
<td>4.22 (1.27–14.06)</td>
<td>0.019</td>
</tr>
<tr>
<td>Fasting glucose &gt; 110 mg/dl</td>
<td>Yes versus no</td>
<td>2.83 (1.48–5.42)</td>
<td>0.001</td>
<td>2.8 (1.33–5.9)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

*Adjusted for age at Dx, race, presence of metastatic disease at Dx, PSA doubling time before ADT, PSA at diagnosis, PSA at time of ADT, time to PSA nadir on ADT, PSA nadir on ADT, prostatectomy treatment, and primary radiotherapy treatment.

- Cox proportional hazards model for time to progression show presence of the metabolic syndrome, low fasting HDL, BMI >30, HTN, and fasting glucose >110mg/dl significant.

Urology: Evolving Technology
But Are We Evolving?
Urology
Bottom Line

• Enormous opportunity
  • Carpe diem

• Technology
  • Build innovation, quality and TRUST