Long-term prostate cancer risk in the Prostate Cancer Prevention Trial

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The challenges of prostate cancer

• About 75% of men will have it during their lifetime
• We can detect many of these tumors
  – Significant risk of ‘overdetection’
  – Treatment has many toxicities
    • Erectile dysfunction, incontinence, GI toxicities, secondary malignancies
The challenges of prostate cancer

• Nonetheless, 3-6% of men, depending on race/ethnicity, will die from prostate cancer

• If diagnosed when symptomatic, most patients have metastases
  – Most with metastases will die from cancer
  – Treatments are morbid and expensive

• Screening with PSA detects disease early
  – Modest reduction in PCA mortality
What happens if we wait for symptoms? SWOG studies from 1980’s and 1990’s

Average survival – less than 4 years
Figure 2. Cumulative Hazard of Death from Prostate Cancer among Men 55 to 69 Years of Age.

Values are not included for centers in France because of the short follow-up period (median, 4.6 years). The Nelson–Aalen method was used to calculate the cumulative hazard of death from prostate cancer.

Options for Prostate Cancer Control

- Cure symptomatic disease
  - Death from cancer eventual outcome
- Screen for the disease
  - Risk of overtreatment, side effects, cost
- Prevention
Attractive features of prostate cancer prevention

Median age of death = 80. Average life years lost from prostate cancer = 9.

May not need to prevent it; delay will reduce mortality
Confluence of events in 1990


FDA Registration of finasteride
First 5AR inhibitor
Androgen Receptor

Testosterone

5-alpha reductase

Dihydrotestosterone*

*8-fold greater affinity for AR than testosterone
Development of 5ARI’s

Males with a SRD5A2 mutation don’t develop BPH or prostate cancer

For four decades, androgen deprivation therapy used for treatment of prostate cancer

Clinical studies of finasteride: well tolerated (later, approved for male-pattern baldness)
A confluence of events 1991

• Board of Scientific Counselors of Division of Cancer Prevention recommends study of finasteride for prostate cancer prevention

• SWOG leadership invited to NCI to design trial
Major design challenge

• Primary method of prostate cancer diagnosis – PSA
• Finasteride reduces PSA by about 50%
• *If study is simply finasteride vs placebo*
  – How would you adjust for PSA?
  – Does PSA drop the same in patients with CA?
• Only one answer – biopsy all men
Enrollment

Randomization

Placebo

Finasteride

Follow-up every 3 months for 7 years

For-cause cancers
PSA
DRE

End of Study Biopsy

End of Study Biopsy
PCPT Accrual
January 1994 - May 1997

Randomizations  N = 18,882
PCPT Randomizations

18,882 participants randomized at 219 Study Centers and Sites
Prostate Cancer Prevention Trial
Projected Biopsy Rate

Feb 2003: DSMC recommends study closure
- primary endpoint has been met
What was the impact on cancer risk?

Cancer Risk:
Placebo – 24%
Finasteride – 18%

Relative Risk Reduction - 24.8%
## Finasteride Reduces Risk of Cancer

<table>
<thead>
<tr>
<th></th>
<th>Finasteride</th>
<th>Placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of biopsies</td>
<td>4368</td>
<td>4692</td>
<td></td>
</tr>
<tr>
<td>Prostate cancer</td>
<td>803 (18%)</td>
<td>1147 (24%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Abnormal PSA or DRE</td>
<td>435 (10%)</td>
<td>571 (12%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Normal PSA/DRE (EOS)</td>
<td>368 (8%)</td>
<td>576 (12%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Number randomized</td>
<td>9423</td>
<td>9459</td>
<td></td>
</tr>
</tbody>
</table>

Relative Risk Reduction - 24.8%
Impact of Finasteride on Tumor grade: Gleason Scores

Effect: 345 fewer 35 fewer 319 fewer 6 more 37 more cancers

Number of Cancers

Gleason Score
February 2003

- DSMC releases data to SWOG.
- Recommends ending study due to futility
- Study leadership focus:
  - Stopping drug, ending end-of-study biopsies
  - Peer review publication of results for study participants and public

- Answering the paradox would have to wait
The Influence of Finasteride on the Development of Prostate Cancer

Contrary to the expectations of many experts, there was a substantial effect of finasteride on the rate of detection of cancer.

Should finasteride now be recommended to men in order to lower their risk of prostate cancer? Several disturbing findings in the report argue that it should not.

To understand the malignant potential of the large number of cancers detected in this trial, it will be important to document the type of treatment these men receive, their long-term survival, and which cancers progress.
Enrollment

Randomization

Placebo

Finasteride

Follow-up every 3 months for 7 years

End of Study Biopsy

End of Study Biopsy

For-cause cancers
PSA
DRE
Exposure and risk of cancer

Over time, risk curves **diverge.**

**Cumulative Rate of Endometrial Cancer in P-1**

- **Treatment Arm**
  - Placebo
  - Tamoxifen

- **# of Events**
  - Placebo: 15
  - Tamoxifen: 36

- **Rate/1,000**
  - Placebo: 5.4
  - Tamoxifen: 13.0

- **p < 0.003**

**Time to Endometrial Cancer (Months)**

- 0 6 12 18 24 30 36 42 48 54 60 66

**Cumulative Incidence Rate (per 1000)**

- 0 3 6 9 12

**BCPT – P1**

**Ann Int Med 2011;154:719-26.**
Risk of high grade disease in PCPT

Increase risk seen at year 1
No significant increase thereafter
To Determine if Prostate Cancer is present

Two things are necessary:

You must first suspect cancer.
(i.e., PSA or DRE must be Positive)

You must then pathologically diagnose cancer.
(i.e., your needle must strike the tumor.)
What we didn’t know about finasteride

Finasteride

- Increases sensitivity of PSA for cancer
- Increases sensitivity of DRE for cancer
- Improves sensitivity of prostate biopsy
Finasteride improves sensitivity of PSA
Finasteride Improves Sensitivity of DRE

Percent Sensitivity Of DRE

Prostate CA

Gleason 7-10

Gleason 8-10

p=0.015

p=0.25

p=0.86
Men with Gleason 7-10 at RP. What % were diagnosed at biopsy?

A 40% improvement in sensitivity for HG cancer on biopsy.

Finasteride: 70%
Placebo: 50%

p = 0.01
Overall Impact of Finasteride

Cancer
30% reduced risk (24-36%) p < .0001

Gleason ≤ 6
32% reduced risk (18-43%) p < .0001

Gleason ≥ 7
28% reduced risk (6-45%) p < .02

Redman M, et al.
Lingering Questions

While bias seemed to explain excess high-grade tumors, we were not certain

• How did survival differ between the arms?

• What happened when men stopped study drug….did the difference disappear?

• Most importantly, how did finasteride impact on prostate cancer mortality (understanding the study was underpowered for this endpoint)
Long-Term Survival of Participants in the Prostate Cancer Prevention Trial

Ian M. Thompson, Jr., M.D., Phyllis J. Goodman, M.S., Catherine M. Tangen, Dr.P.H., Howard L. Parnes, M.D., Lori M. Minasian, M.D., Paul A. Godley, M.D., Ph.D., M. Scott Lucia, M.D., and Leslie G. Ford, M.D.

ABSTRACT
Incorporating patients with prostate cancer diagnosed after the NEJM data freeze (until October 31, 2003). There may be operational biases.

Longer-term relative risk reduction = 30%
Figure 2. Kaplan–Meier Curves for Overall Survival.
Figure 3. Overall Survival of Men with Prostate Cancer, According to Cancer Grade.
Definition of Big Data

- Big data characterized as pertaining to the **Volume, Velocity, and Variety** of data (Laney, 2001; De Mauro, 2016)

Big Data Strategies in SWOG

- Emphasis on both **variety** and **volume**
- Using data from a large, NCI network group national clinical trials database, in combination with…
  - Registry (SEER)
  - Life-table
  - Census
  - Geospatial data
  - Publication
  - Citation
  - Medicare claims
“Geographic Distribution and Survival Outcomes for Rural Patients With Cancer Treated in Clinical Trials”*

- Combined SWOG treatment trial data with geospatial mapping data
- Examined 36,995 patients from 44 phase III treatment trials from all 50 states
- Rural patients had worse survival in only 1/17 cancer cohorts
- Best approach to improve outcomes for rural cancer patients may be to provide access to the kind of quality, guideline-based care available in trials

<table>
<thead>
<tr>
<th>Region</th>
<th>% of Total</th>
<th>% Rural</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SWOG</td>
<td>US</td>
</tr>
<tr>
<td>West</td>
<td>23%</td>
<td>23%</td>
</tr>
<tr>
<td>Midwest</td>
<td>39%</td>
<td>21%</td>
</tr>
<tr>
<td>South</td>
<td>24%</td>
<td>37%</td>
</tr>
<tr>
<td>Northeast</td>
<td>14%</td>
<td>18%</td>
</tr>
</tbody>
</table>

* Unger et al, JAMA Network Open, 2018
Prostate Cancer Prevention Trial: Lingering Questions

- Unclear if the trial duration was sufficient to determine the maximum benefit of finasteride
- Concern that the reduced risk of PC seen in subjects receiving finasteride might not be maintained after discontinuation
Limitations of Using Clinical Trial Data Alone

- Limited long term follow-up (7 years)
- No adverse events after treatment stops
- Limited utilization data (beyond protocol specified therapy)
Program Objectives

- Link PCPT trial records to Medicare claims
- Examine late effects, long term prostate cancer incidence, treatment utilization, and complications
The PCPT-Medicare Linked Database

- **Clinical trials**: baseline demographics; clinical risk factors; intervention duration; during-study prostate cancer diagnosis

- **Medicare claims data** (based on ICD-9, HCPCS, and CPT codes): long-term follow-up for other illnesses, new cancer diagnoses, and treatment utilization

- **Advantage of random assignment** for treatment comparisons (limits confounding)
What are the patterns of long-term prostate cancer diagnoses in the Prostate Cancer Prevention Trial?
Methods

- PCPT study records linked to Medicare claims to augment the detection of prostate cancer diagnoses

- Defined a (Medicare) claims-based prostate cancer diagnosis algorithm
  - Diagnosis and procedure codes

- All men were included in this analysis
  - Including those without a linkage to Medicare

- PCPT enrolled patients from 1993-1997; Medicare claims available from 1999-2011
Medicare Claims-Based Algorithm for Prostate Cancer Diagnosis

- Examined multiple claims-based algorithms
- Considered diagnosis of prostate cancer in PCPT as “gold standard”
- Compared PCPT to Medicare diagnoses among men with concurrent coverage in both databases
- This overlap region is especially useful for validating claims-based approaches to event identification
Medicare-Based Algorithm for PC Diagnosis

“Best” algorithm identified as…

- **Diagnosis** code 185 for PC
  - Any hospital claim, or
  - $ \geq 2$ physician or outpatient claims $>30$ days apart* but not more than 6 months apart

- **Procedure** code for radical prostatectomy
  - Based on ICD9 or HCPCS codes

- **Sensitivity**, 83.3%; **specificity**, 96.3%

*Smith et al., JCO, 2005*
Statistical Methods

- Cumulative incidence at 5, 10, and 15 yrs
- Cox regression to test intervention effect
- Due to required 7 year biopsy, examined intervention effect within intervals:
  - 0-6.5 years vs. 6.5-7.5 years vs. after 7.5 years
  - Change point analysis*

* Liang et al., Biometrics, 1990
Participant Characteristics

- N=14,176 participants (75.1%) had a Medicare linkage (placebo, 7107; finasteride, 7069)
- Subject characteristics by arm well balanced
- Median time from PCPT randomization = 16.0 years for each arm
  - Increase from 7 years using PCPT clinical records alone
# Prostate Cancer Diagnoses

<table>
<thead>
<tr>
<th>Diagnosed with prostate cancer by...</th>
<th>Overall</th>
<th>Placebo</th>
<th>Finasteride</th>
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</thead>
<tbody>
<tr>
<td>PCPT records alone</td>
<td>895</td>
<td>528</td>
<td>367</td>
</tr>
<tr>
<td>Medicare alone</td>
<td>959</td>
<td>455</td>
<td>504</td>
</tr>
<tr>
<td>PCPT and Medicare</td>
<td>1390</td>
<td>822</td>
<td>568</td>
</tr>
<tr>
<td>Total</td>
<td>3244</td>
<td>1805</td>
<td>1439</td>
</tr>
</tbody>
</table>
Cumulative Incidence of Prostate Cancer

Panel A

- Placebo
- Finasteride

Cumulative incidence from SWOG clinical records alone

7-year biopsy window, +/- 6 months

<table>
<thead>
<tr>
<th>Year after Randomization</th>
<th>Placebo</th>
<th>Finasteride</th>
</tr>
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<tbody>
<tr>
<td>6.5</td>
<td>0.25</td>
<td>0.25</td>
</tr>
<tr>
<td>7.5</td>
<td>0.25</td>
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<td>8.5</td>
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<td>9.5</td>
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<tr>
<td>10</td>
<td>0.25</td>
<td>0.25</td>
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<td>11</td>
<td>0.25</td>
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<tr>
<td>12</td>
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<td>13</td>
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<td>0.25</td>
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<tr>
<td>14</td>
<td>0.25</td>
<td>0.25</td>
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<tr>
<td>15</td>
<td>0.25</td>
<td>0.25</td>
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<td>16</td>
<td>0.25</td>
<td>0.25</td>
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<tr>
<td>17</td>
<td>0.25</td>
<td>0.25</td>
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<td>18</td>
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<td>0.25</td>
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<tr>
<td>20</td>
<td>0.25</td>
<td>0.25</td>
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</table>

No. at Risk

<table>
<thead>
<tr>
<th>Year</th>
<th>Placebo</th>
<th>Finasteride</th>
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<tbody>
<tr>
<td>0</td>
<td>9457</td>
<td>9522</td>
</tr>
<tr>
<td>1</td>
<td>9522</td>
<td>9510</td>
</tr>
<tr>
<td>2</td>
<td>9510</td>
<td>9895</td>
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<td>9895</td>
<td>8654</td>
</tr>
<tr>
<td>4</td>
<td>8654</td>
<td>8933</td>
</tr>
<tr>
<td>5</td>
<td>8933</td>
<td>8691</td>
</tr>
<tr>
<td>6</td>
<td>8691</td>
<td>6591</td>
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<td>20</td>
<td>6591</td>
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</tr>
</tbody>
</table>
Cumulative Incidence of Prostate Cancer

Panel B

Cumulative incidence using extended follow-up from PCPT-Medicare linkage

7-year biopsy window, +/- 6 months

Year after Randomization

<table>
<thead>
<tr>
<th>Intervention Arm</th>
<th>5-year</th>
<th>10-year</th>
<th>15-year</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finasteride</td>
<td>3.0%</td>
<td>14.5%</td>
<td>17.3%</td>
<td>18.1%</td>
</tr>
<tr>
<td>Placebo</td>
<td>3.8%</td>
<td>18.0%</td>
<td>21.3%</td>
<td>22.3%</td>
</tr>
</tbody>
</table>
Long-term PC diagnoses using Medicare claims

Forest plot of HR of time to prostate cancer (finasteride vs placebo)

<table>
<thead>
<tr>
<th>Period</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 7.5 years</td>
<td>0.71</td>
<td>0.66 - 0.77</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>After 7.5 years</td>
<td>1.10</td>
<td>0.96 - 1.26</td>
<td>.18</td>
</tr>
<tr>
<td>Overall</td>
<td>0.79</td>
<td>0.74 - 0.84</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Line of equal hazard (HR=1.0)

Test for heterogeneity of effects: p<.001

Lower hazard

Higher hazard
Bias Assessment

- No differences in utilization patterns for finasteride vs. placebo:

<table>
<thead>
<tr>
<th>Utilization type</th>
<th>Finasteride</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate cancer screening claims</td>
<td>13,228</td>
<td>12,457</td>
</tr>
<tr>
<td>Hospital inpatient or physician outpatient visits</td>
<td>3204</td>
<td>3277</td>
</tr>
<tr>
<td>Overall claims</td>
<td>302,183</td>
<td>308,279</td>
</tr>
</tbody>
</table>

- No evidence of bias in diagnosis dates
- No evidence of differences in baseline demographic and clinical risk factors
Summary

- No evidence that 7 years of finasteride continued to prevent new PC diagnoses after finasteride was discontinued
- Also, no evidence that finasteride had more PCs after completing finasteride use
- Finasteride provides a substantial reduction (21%) in risk of PC through a median of 16 years of follow-up
Using Secondary Data for Clinical Trial Follow Up

- Cancer prevention trials involve following a large number of participants for many years.
- Costs of conducting such studies are very high.
- Use of secondary data sources augments detection of long term outcomes at much reduced cost.
CONCLUSION

- Big data strategies can be used to both **extend and enrich** valuable NCTN and NCORP clinical trial data either...
  - Extending follow-up or data collection for individual trials
  - Through their inclusion in secondary data analyses

- Approach is especially advantageous in disease settings with rare or long term events including prevention or adjuvant treatment (i.e. early stage breast or prostate)
Prostate cancer mortality

• If high-grade disease is more common (and not an artifact), risk of a higher prostate cancer death rate.
• Given high prevalence and low mortality, prostate cancer mortality is the most important outcome.
Brief Methods

• Using linkage analyses including SSN, PCPT participants were matched with the U.S. National Death Index.

• Studied for outcomes:
  – Death
  – Death due to prostate cancer
  – Assessment made based on death certificate
<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Finasteride</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total eligible randomized</td>
<td>9457</td>
<td>9423</td>
</tr>
<tr>
<td>Deaths (total)</td>
<td>2979</td>
<td>3048</td>
</tr>
<tr>
<td>Prostate cancer death</td>
<td>56</td>
<td>42</td>
</tr>
<tr>
<td>PCA diagnosis on PCPT</td>
<td>40</td>
<td>27</td>
</tr>
<tr>
<td>Later PCA diagnosis</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>Follow-up for patients still alive (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (IQ range)</td>
<td>18.4</td>
<td>18.4</td>
</tr>
<tr>
<td>Inter-Quartile range</td>
<td>17.4, 18.7</td>
<td>17.3, 18.7</td>
</tr>
<tr>
<td>Total person-years of follow-up</td>
<td>148,895</td>
<td>147,947</td>
</tr>
</tbody>
</table>

PCA = prostate cancer; IQ=Inter-quartile range
<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Finasteride</th>
<th>p-value $^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PCA/Not PCA death $^1$</td>
<td>PCA death</td>
<td>PCA/Not PCA death $^1$</td>
</tr>
<tr>
<td>Total</td>
<td>1372</td>
<td>56</td>
<td>962</td>
</tr>
<tr>
<td><strong>Gleason Score</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\leq 6$</td>
<td>1021 (98.5%)</td>
<td>16 (1.5%)</td>
<td>582 (98.8%)</td>
</tr>
<tr>
<td>7</td>
<td>213 (96.0%)</td>
<td>9 (4.1%)</td>
<td>228 (97.9%)</td>
</tr>
<tr>
<td>8 - 10</td>
<td>55 (83.3%)</td>
<td>11 (16.7%)</td>
<td>88 (87.1%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>83</td>
<td>20</td>
<td>64</td>
</tr>
<tr>
<td><strong>Age at diagnosis (years)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>55 - 64</td>
<td>300 (97.7%)</td>
<td>7 (2.3%)</td>
<td>190 (96.0%)</td>
</tr>
<tr>
<td>65 - 69</td>
<td>392 (97.5%)</td>
<td>10 (2.5%)</td>
<td>291 (97.0%)</td>
</tr>
<tr>
<td>70 - 74</td>
<td>410 (97.4%)</td>
<td>11 (2.6%)</td>
<td>285 (99.0%)</td>
</tr>
<tr>
<td>$\geq 75$</td>
<td>270 (95.7%)</td>
<td>12 (4.3%)</td>
<td>196 (96.6%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td><strong>PSA at diagnosis $^3$</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.3 – 2.0</td>
<td>633 (97.8%)</td>
<td>14 (2.2%)</td>
<td>441 (98.4%)</td>
</tr>
<tr>
<td>2.1 – 4.0</td>
<td>423 (96.6%)</td>
<td>15 (3.4%)</td>
<td>270 (97.5%)</td>
</tr>
<tr>
<td>4.1 – 6.0</td>
<td>243 (97.6%)</td>
<td>6 (2.4%)</td>
<td>157 (98.1%)</td>
</tr>
<tr>
<td>$&gt; 6.0$</td>
<td>72 (93.5%)</td>
<td>5 (6.5%)</td>
<td>94 (90.4%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td><strong>DRE at diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1175 (97.4%)</td>
<td>31 (3.6%)</td>
<td>818 (97.5%)</td>
</tr>
<tr>
<td>Suspicious</td>
<td>197 (95.6%)</td>
<td>9 (4.4%)</td>
<td>144 (96.0%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PCPT Biopsy prompt</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other $^4$</td>
<td>550 (95.7%)</td>
<td>25 (4.4%)</td>
<td>419 (95.4%)</td>
</tr>
<tr>
<td>EOS</td>
<td>822 (96.4%)</td>
<td>31 (3.6%)</td>
<td>543 (96.1%)</td>
</tr>
</tbody>
</table>
HR=0.75, 95% CI (0.50, 1.12), p=0.16 (finasteride vs placebo)

<table>
<thead>
<tr>
<th></th>
<th>10 years</th>
<th>15 years</th>
<th>18 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number at risk</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>8229</td>
<td>7094</td>
<td>4060</td>
</tr>
<tr>
<td>Finasteride</td>
<td>8198</td>
<td>7026</td>
<td>4012</td>
</tr>
<tr>
<td><strong>Incidence (95%CI)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>0.14% (0.07, 0.23)</td>
<td>0.35% (0.02, 0.49)</td>
<td>0.60% (0.45, 0.78)</td>
</tr>
<tr>
<td>Finasteride</td>
<td>0.12% (0.06, 0.21)</td>
<td>0.31% (0.21, 0.44)</td>
<td>0.43% (0.31, 0.59)</td>
</tr>
</tbody>
</table>
Cost of finasteride in 2018

- Good Rx (CVS) - $8.65
- Walmart (with free discount) - $4.00
- Kroger (with free coupon) - $8.57
- Costco (free coupon) - $8.78
- Albertsons (free coupon) - $9.23
- Health Warehouse (online) - $7.50

- About 25¢ a day
Chemoprevention of Prostate Cancer with Finasteride

- After 20 years, 7 years of finasteride treatment reduces risk of prostate PCA by 25-30%
- This risk reduction is in the face of improved prostate cancer detection
- Reduction in risk is durable
- Most tumors prevented are Gleason 3+3
- Risk of prostate cancer death is 25% less with finasteride (not statistically significant)
Pros/cons of chemoprevention

Pros:

- 25-30% reduction in risk of diagnosis
  Likely translates into less surgery, radiation, treatment complications
- No excess risk of prostate cancer death (25% reduction in risk of prostate cancer death [not statistically significant])
- Significant improvement in current urinary symptoms and reduced complications from BPH (retention, TURP)
- Inexpensive (compared to other interventions)
Pros/cons of chemoprevention

Cons:

• Small but increased risk of sexual side effects
• Gynecomastia: placebo-2.8%. Finasteride-4.5%
Commentary

Some will posit that tumors prevented are inconsequential

Response:
- Diagnosis of low-grade cancer is an adverse event
  - 30-50% risk of eventual treatment (with side effects)
- Repeated MD visits, PSA anxiety
- Repeated biopsies (expensive, sepsis)
- Cost of surveillance is as expensive as surgery
- 38% of prostate cancer deaths in PCPT were due to Gleason 3+3 tumors.
- Almost 50% of prostate cancer deaths were in patients with normal PSA/DRE
The final chapter awaits

- Dr Unger and colleagues will examine the impact of finasteride chemoprevention on risk of other outcomes.

- If you aren’t diagnosed with prostate cancer, you won’t be treated for prostate cancer and you therefore cannot suffer side effects of treatment.
Initial analysis plans (*precis*)

**Diagnoses**
- Radiation proctitis
- Radiation cystitis
- Urinary incontinence
- Sexual Dysfunction
- Urinary retention
- Urosepsis
- Prostatitis

**Procedures**
- Placement of AUS
- Placement of IPP
- Incision of stricture
Who deserves the credit for this body of work?

• Far too many people for us to acknowledge at this time.

• Hundreds of investigators at >200 sites

• Even more research associates
Most of all, thanks to 18,882 remarkable men