A Decision Analysis to Assess the Value of Prostate Cancer Screening:

A Shift in Focus from Prostate Cancer Specific Mortality to Distant Metastasis Free Survival

Arie Pablo Dosoretz, Nataniel H. Lester-Coll, Shiyi Wang, and James B. Yu
Yale Department of Therapeutic Radiology, New Haven, CT
Prostate Cancer Screening

- Prostate Cancer is the 2nd leading cause of cancer deaths among men in the United States, with over 28,000 deaths estimated for 2012.

- The value of screening men for prostate cancer using prostate-specific antigen (PSA) testing has generated significant debate.

- Criticisms of screening include:
  - False-positive rates associated with PSA testing
  - Harms associated with work-up and prostate biopsies
  - Over-diagnosis and over-treatment

- Randomized-Control Trial Evidence includes:
  - *PCLO Study*: Included 76,685 men in the United States, aged 55-74, and found no statistically significant overall survival or prostate-cancer specific mortality differences from annual PSA testing.
  - *ERSPC study*: Included 162,388 European men, aged 55-69, and found a 20% reduction in prostate cancer mortality, but no overall mortality benefit from PSA testing every 4 years.

- In May of 2012, the United States Preventive Services Task Force (USPSTF) concluded “...that there is moderate certainty that the benefits of PSA-based screening for prostate cancer do not outweigh the harms.”
Purpose
To determine the quality-adjusted life expectancy (QALE) associated with screening men for prostate cancer with annual PSA testing

Methods
• A mathematical model (state transition Markov model) was constructed to compare QALE in men with and without annual PSA screening

• Men screened and found to be positive, after a confirmatory work-up, were assumed to have clinically localized, low-risk prostate cancer

• Unscreened men, who presented with prostate cancer, were also assumed to have low-risk prostate cancer, but could also present with metastatic disease

• All men with prostate cancer were assumed to undergo treatment with intensity-modulated radiation therapy (IMRT)

• Probabilities of transitioning between health states and quality of life values (utilities) for each state were entered into the model from a literature review

• Enhanced model constructed; included each risk group of prostate cancer and more detailed inclusion of possible toxicities from treatment
Results from Initial Model

- QALE benefit found for all ages
- Benefit diminished with increasing age
- Model sensitive to probability of developing metastatic disease without screening
- If 10-year probability was less than 4.9%, no-screening became the preferred strategy
Structure of Enhanced Model - Screening

- NED
  - PSA +
    - True positive
      - Low Risk CA IMRT
        - Int. Risk CA IMRT + STADT
        - High Risk CA IMRT + LTADT
    - False positive
      - NED after False Positive
- Work-Up
- Death from Other Cause
- NED after False Positive
- False positive
- NED w/o Adverse Effects
- DM
- Develop Toxicity
- DM
- DM
- Death from Other Cause
- PCSM
- DM
- PCSM
Results from Enhanced Model

- Other factors found to influence QALE and preferred strategy, including:
  - Incidence of prostate cancer
  - Proportion of men in the unscreened group presenting with distant metastatic disease
  - Probability of developing long-term adverse effects from treatment
Conclusions

• The decision to screen an individual or a population of men for prostate cancer is complex and nuanced

• Our model suggests that there may be a quality of life benefit associated with screening certain populations of men for prostate cancer with PSA testing

• Several factors were found to influence the quality of life effects of screening, including:
  – The proportion of unscreened men presenting with distant metastatic disease
  – The incidence of prostate cancer in the population
  – The probability of developing adverse effects from prostate cancer treatment

• Further research is needed in order to more thoroughly understand the impact of screening on quality of life and to optimize screening strategies