The Conundrum of Prostate Cancer Screening

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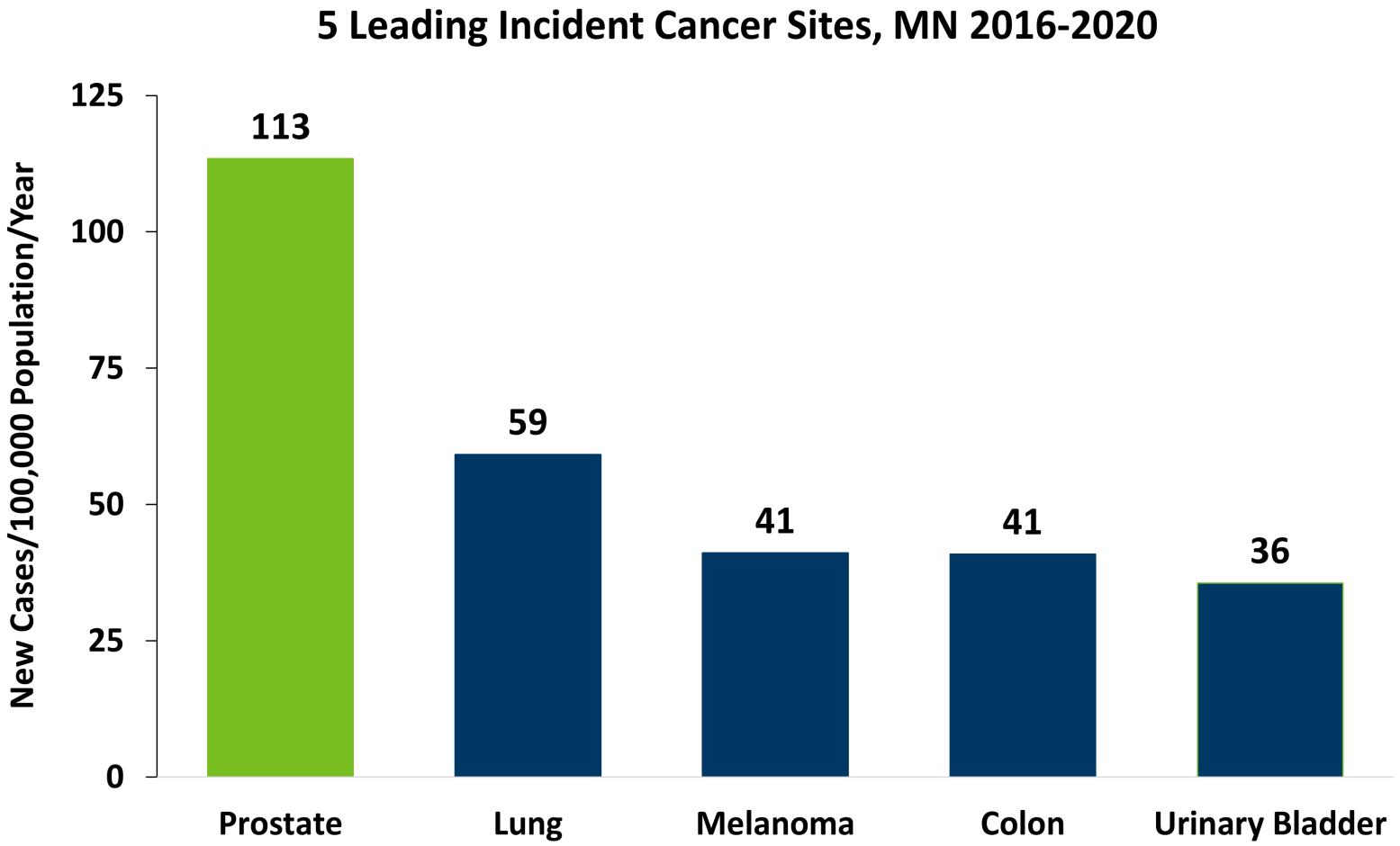
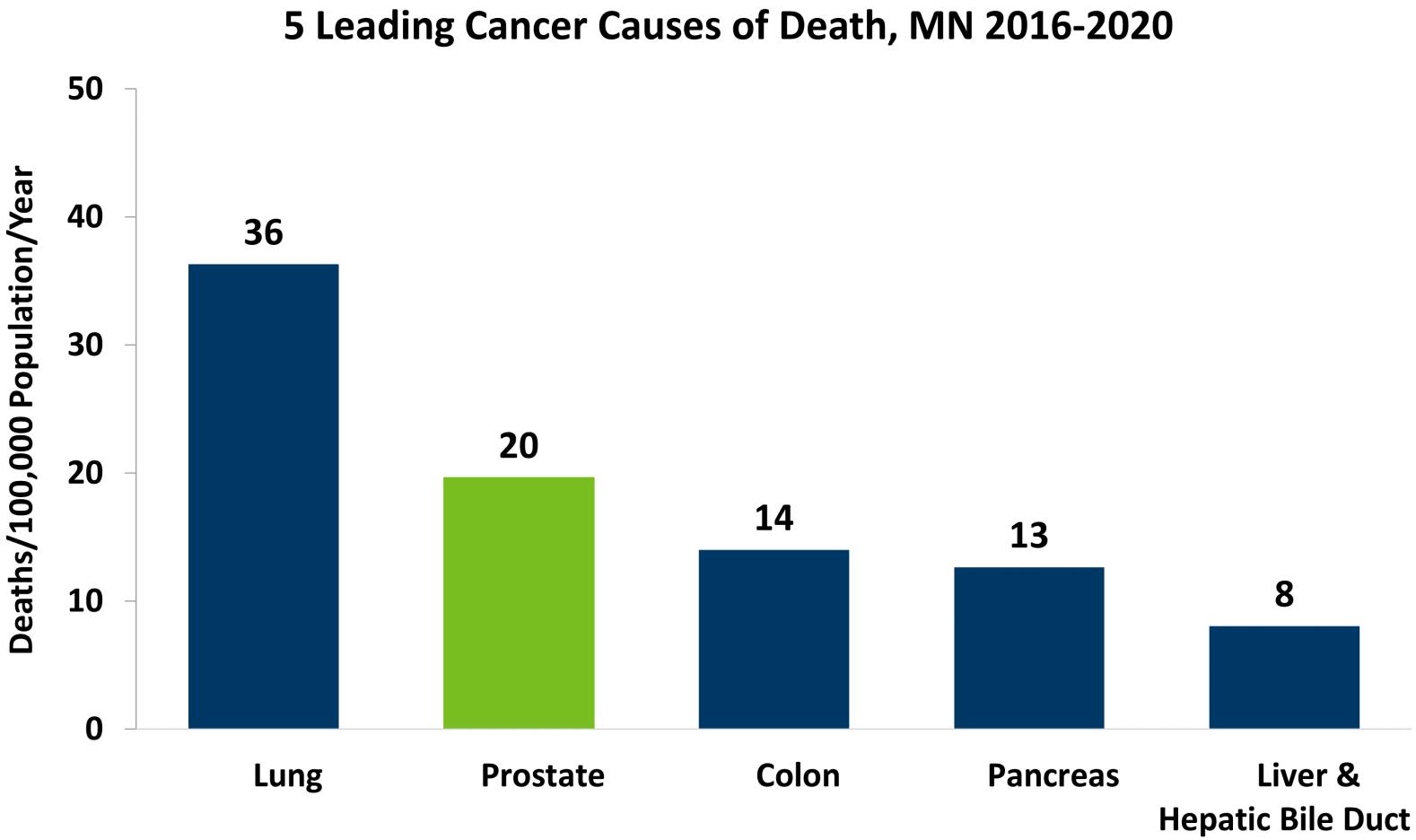
Why Is Prostate Cancer Important to Public Health? (1 of 2)

- Prostate cancer is the most commonly-diagnosed cancer in men (Minnesota, U.S.)
- It accounts for 1 in 4 new cancer cases in men (24%)



Why Is Prostate Cancer Important to Public Health? (2 of 2)

- Is second leading cause of cancer death in men (Minnesota, U.S.)
- Experts disagree on the effectiveness of mass screening in preventing prostate cancer death.



Prostate Cancer and the Prostate Specific Antigen (PSA) Test

- This is the “PSA era”. Most prostate cancer are diagnosed due to PSA testing.
- Prostate cancer is usually not symptomatic.
- The PSA test is not specific to prostate cancer. Many men with a positive test have benign hyperplasia.
- The PSA test cannot distinguish between tumors likely to grow rapidly and progress vs. slow growing less lethal tumors.
- Definitive diagnosis is based on biopsy results (Gleason score).

The Benefits of PSA Testing Appear Limited (1 of 3)

- The major randomized trials suggest that PSA testing followed by treatment leads to only a small reduction in mortality.
- Why is PSA screening problematic?
  - PSA test mainly detects local stage, indolent cancers – These are slow-growing, well-differentiated cancers that likely wouldn't have progressed even if left untreated.
  - PSA test is not very good at detecting, fast-growing, aggressive tumors.

The harms of prostate cancer treatment are common and debilitating

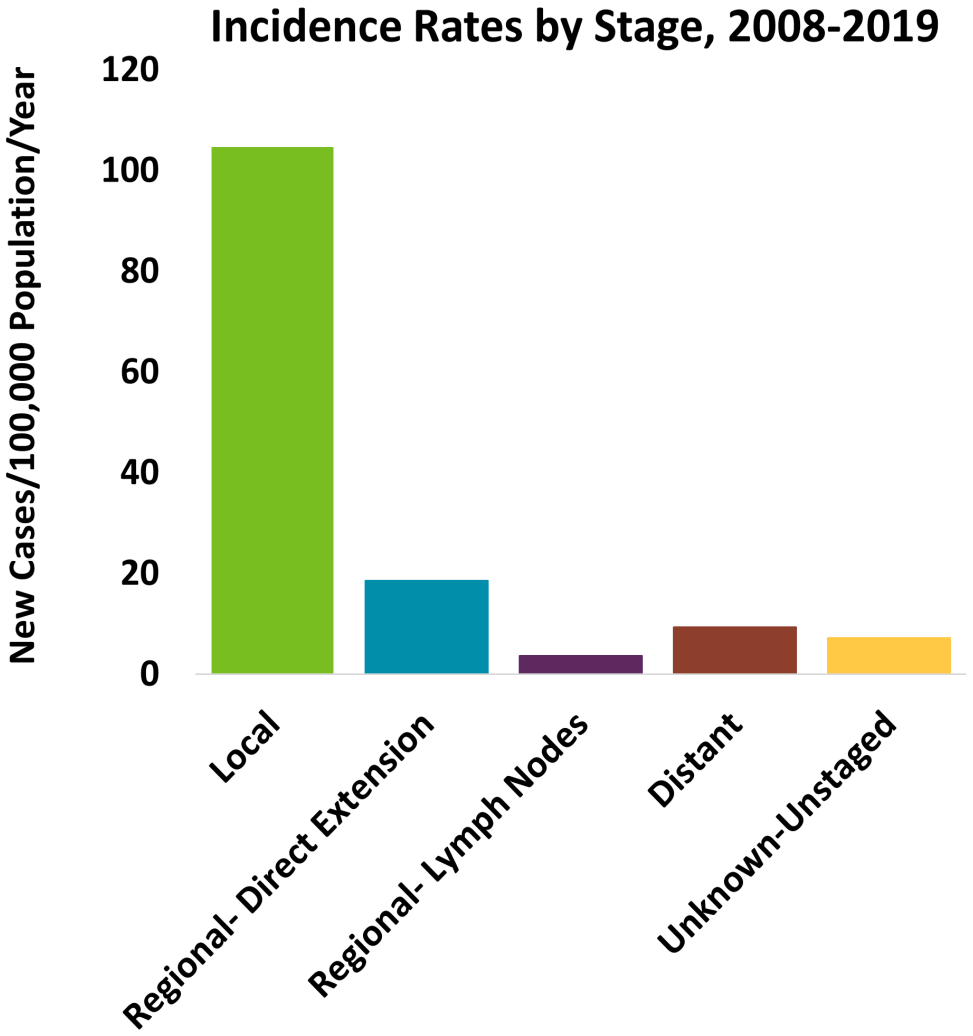
- Long term urinary incontinence - 1 in 5 men (prostatectomy)
- Fecal incontinence
- Long term erectile dysfunction – 2 in 3 men (prostatectomy)

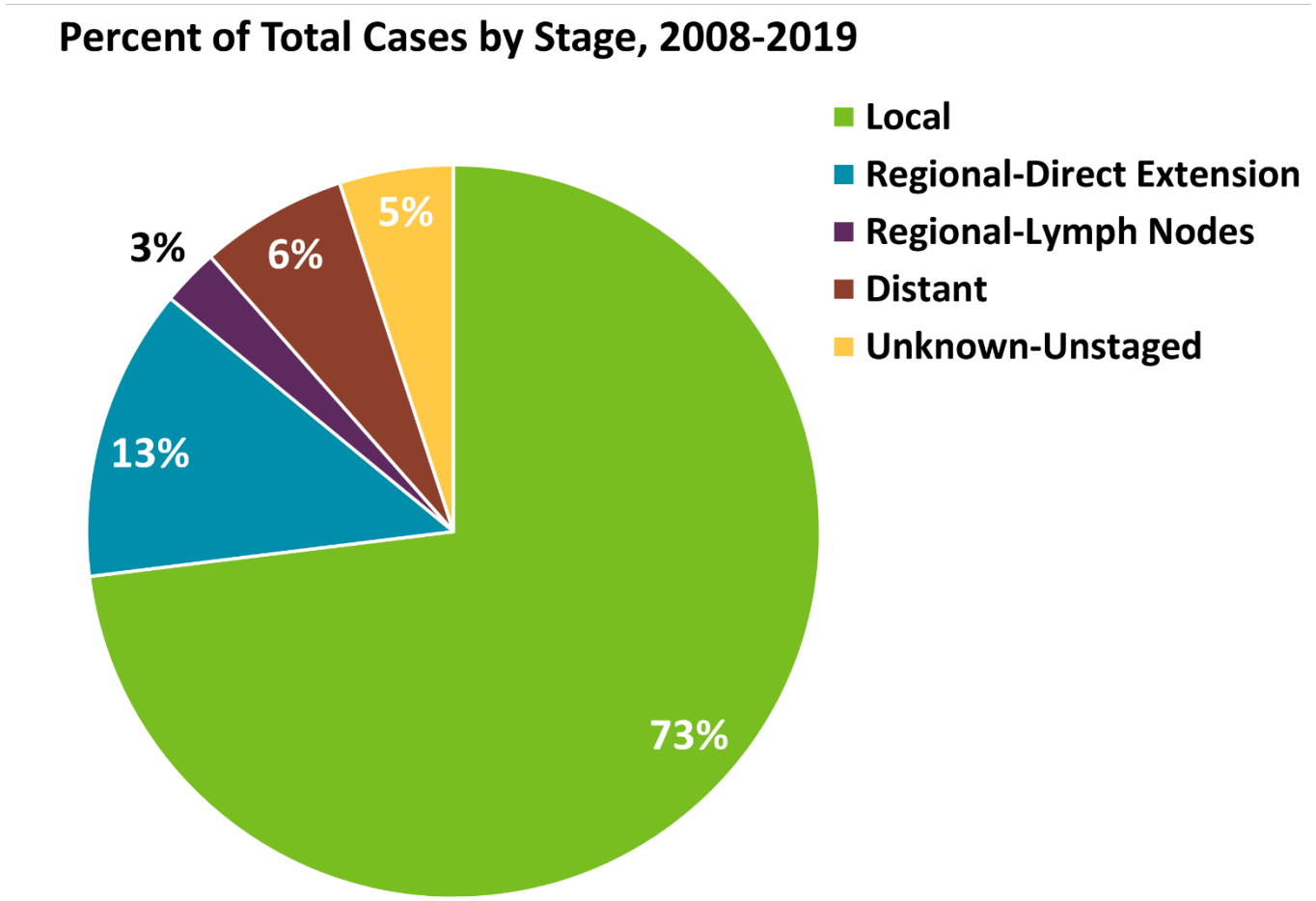
Men who are treated for prostate cancers that are unlikely to progress are exposed to the harms of treatment, but with little benefit.

Many older men harbor undiagnosed, very slow-growing prostate cancer

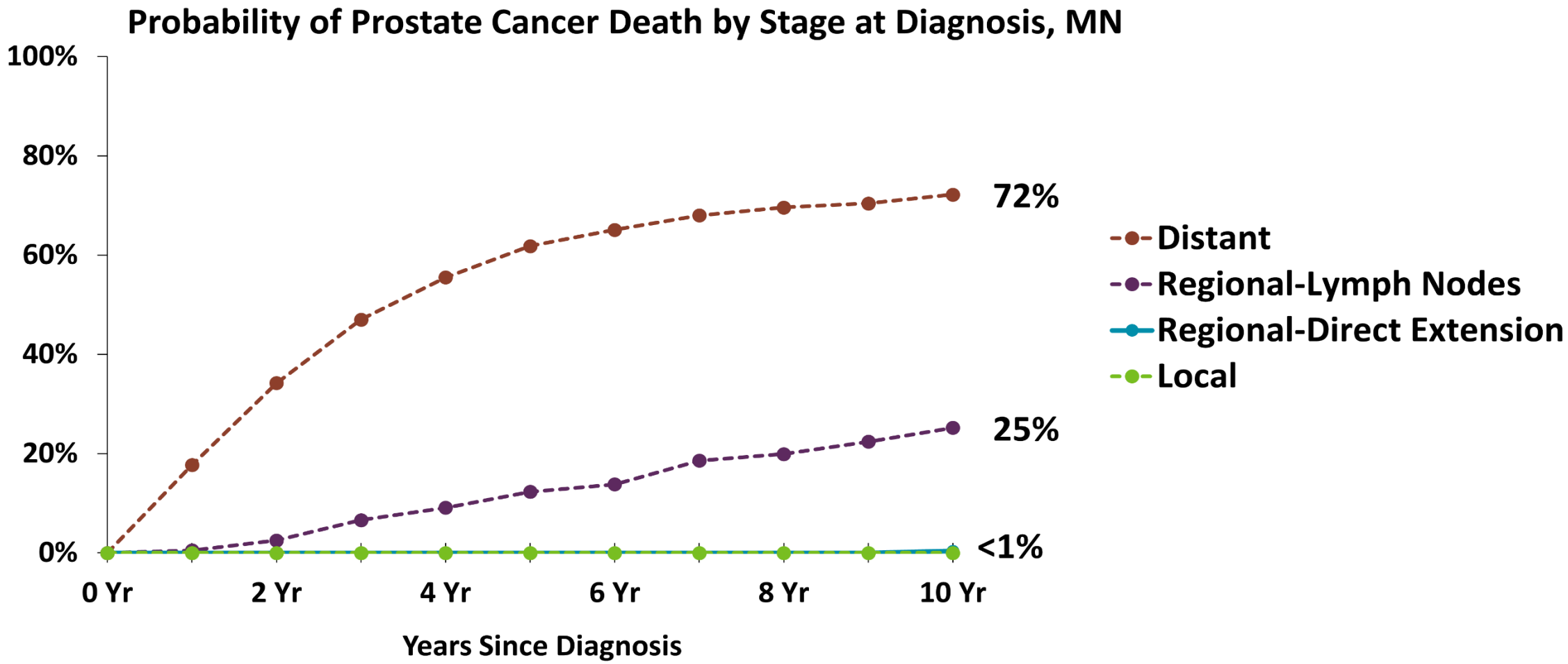
- 36% of White men and 51% percent of men Black men are estimated to harbor undiagnosed prostate cancer (based on autopsy studies).
  - The men in these studies appear to have lived out normal lives unaffected by- and unaware of their cancer, and died of causes other than prostate cancer.
- Detecting and treating these slow-growing, non-aggressive cancers doesn't save lives. These men would have lived normal lives whether or not their cancers were diagnosed and treated.

A High Percentage of Prostate Cancers are Diagnosed at Local Stage





10-Year Probability of Prostate Cancer Death



History of PSA Testing – Key Events

1986	• FDA approves PSA test for prostate cancer screening.
1988 to 1992	• PSA test becomes common; prostate cancer incidence skyrockets.
2008	• USPSTF: Men 75+ years of age should not be screened, based on "adequate evidence [for this age group] that benefits were small to none".
2012	• USPSTF: Men should not be screened, regardless of age, based on "convincing evidence that the number of men who avoid dying of prostate cancer because of screening … is at best, very small".
2018	• USPSTF: Men should make individual decision, consulting with doctor.

Caution in Interpreting Prostate Cancer Incidence

- We usually think of a cancer incidence rate as reflecting the prevalence of risk factors in a population.
- But prostate cancer incidence appears to be driven largely by the number of PSA tests being done and the number of positive PSA tests referred for biopsy.
- Because undetected, slow-growing prostate cancer is so common in older men, more PSA testing leads to more diagnoses, and more diagnoses lead to higher prostate cancer incidence.
- I will show how prostate cancer incidence appears to be driven by key events related to PSA testing.

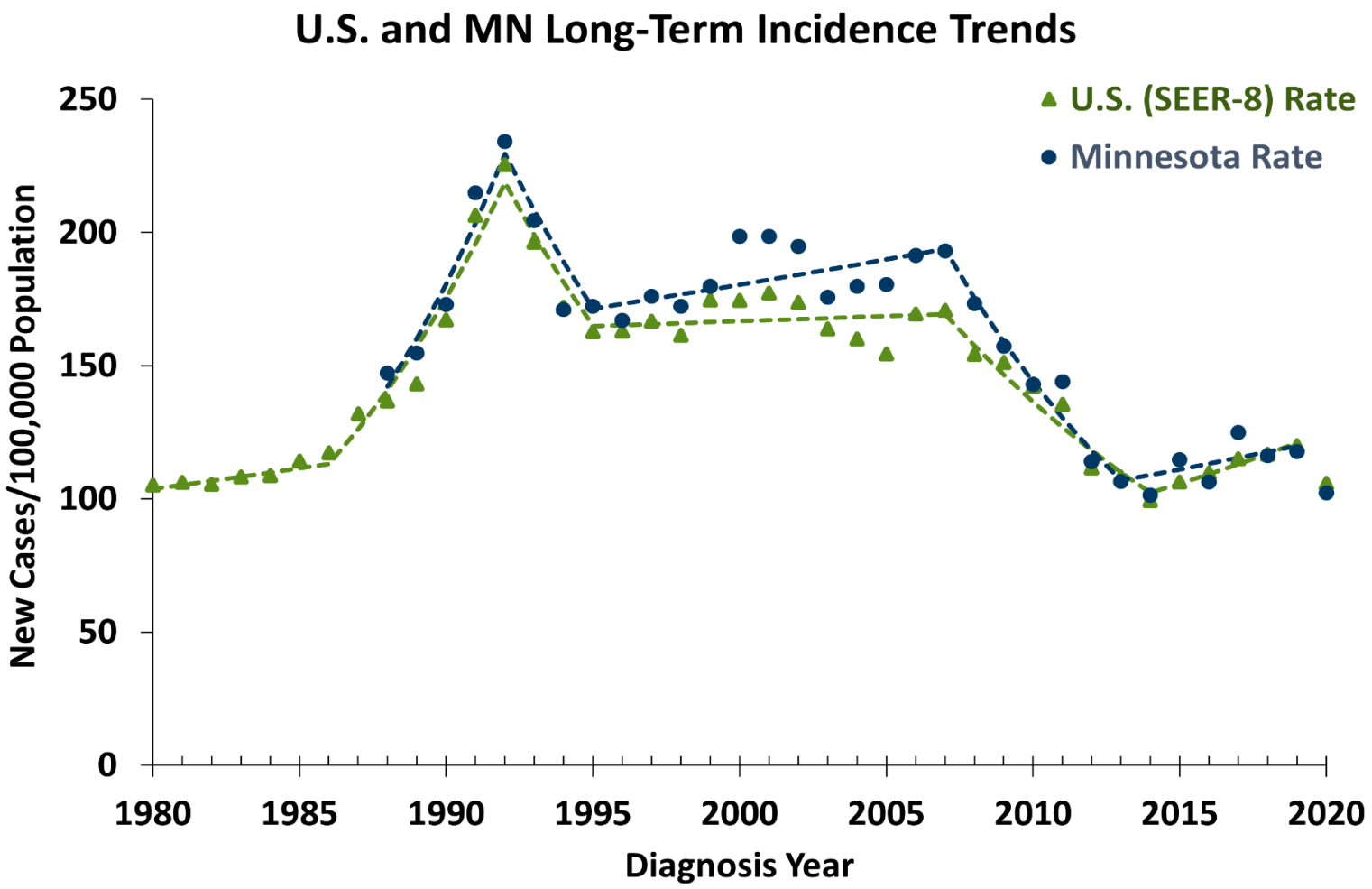
Results: Prostate Cancer Incidence and Mortality in Minnesota

Prostate Cancer Long-Term Incidence Trends in U.S. (SEER-8) and Minnesota (1 of 4)

U.S. (SEER-8) data reach back to 1975. Minnesota data reach back to 1988.

Figure layout

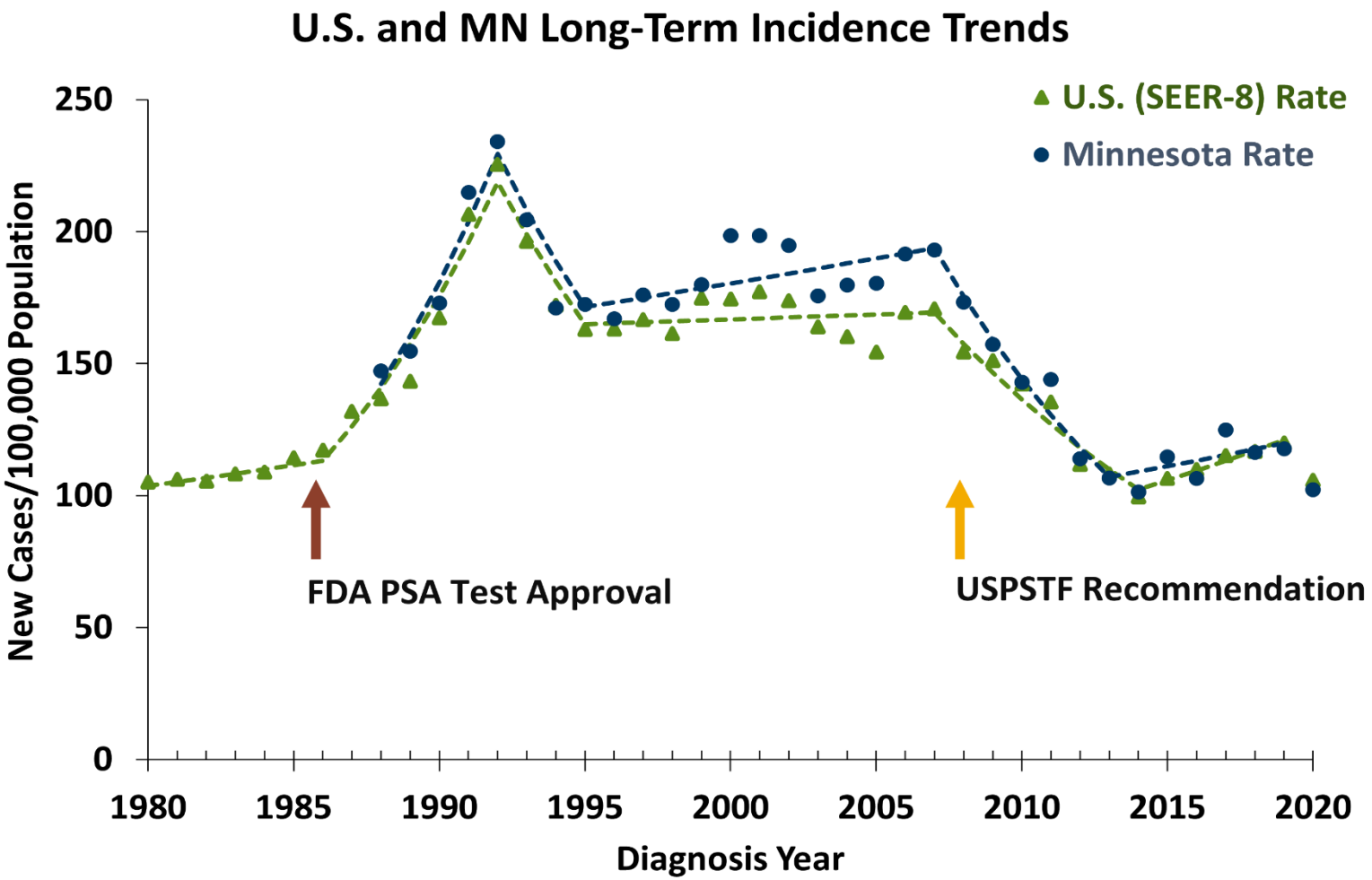
- Circles and triangles represent prostate cancer incidence rates.
- Dashed line segments indicate modeled incidence trends.
- APC is Annual Percent Change.



Key Events Influencing Prostate Cancer Incidence Trends in U.S. and Minnesota (2 of 4)

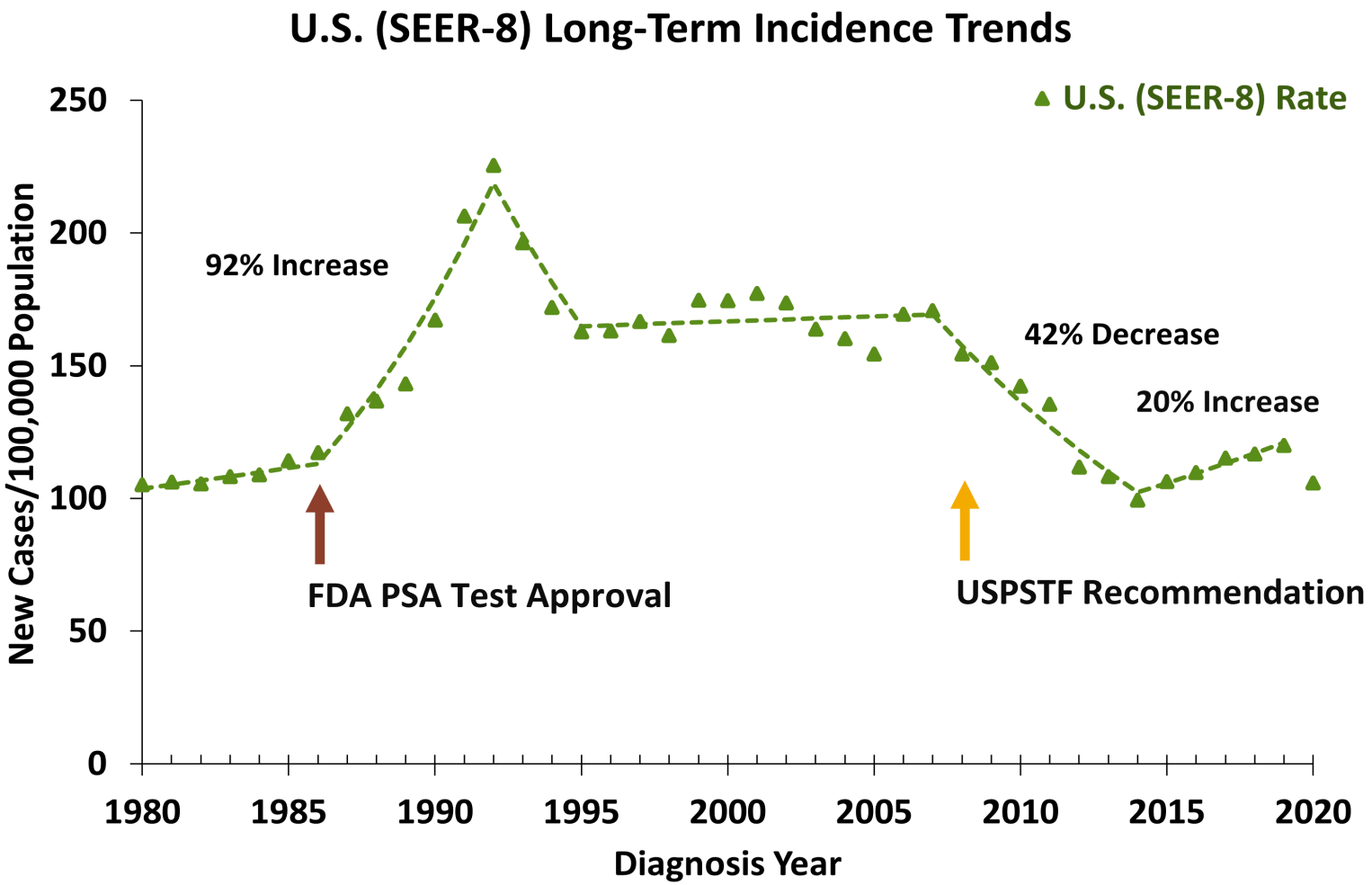
Two national events had large impacts on prostate cancer incidence rates.

1. In 1986 the FDA approved the PSA test for prostate cancer screening.
2. In 2008 the USPSTF recommended against screening men 75+ years of age.



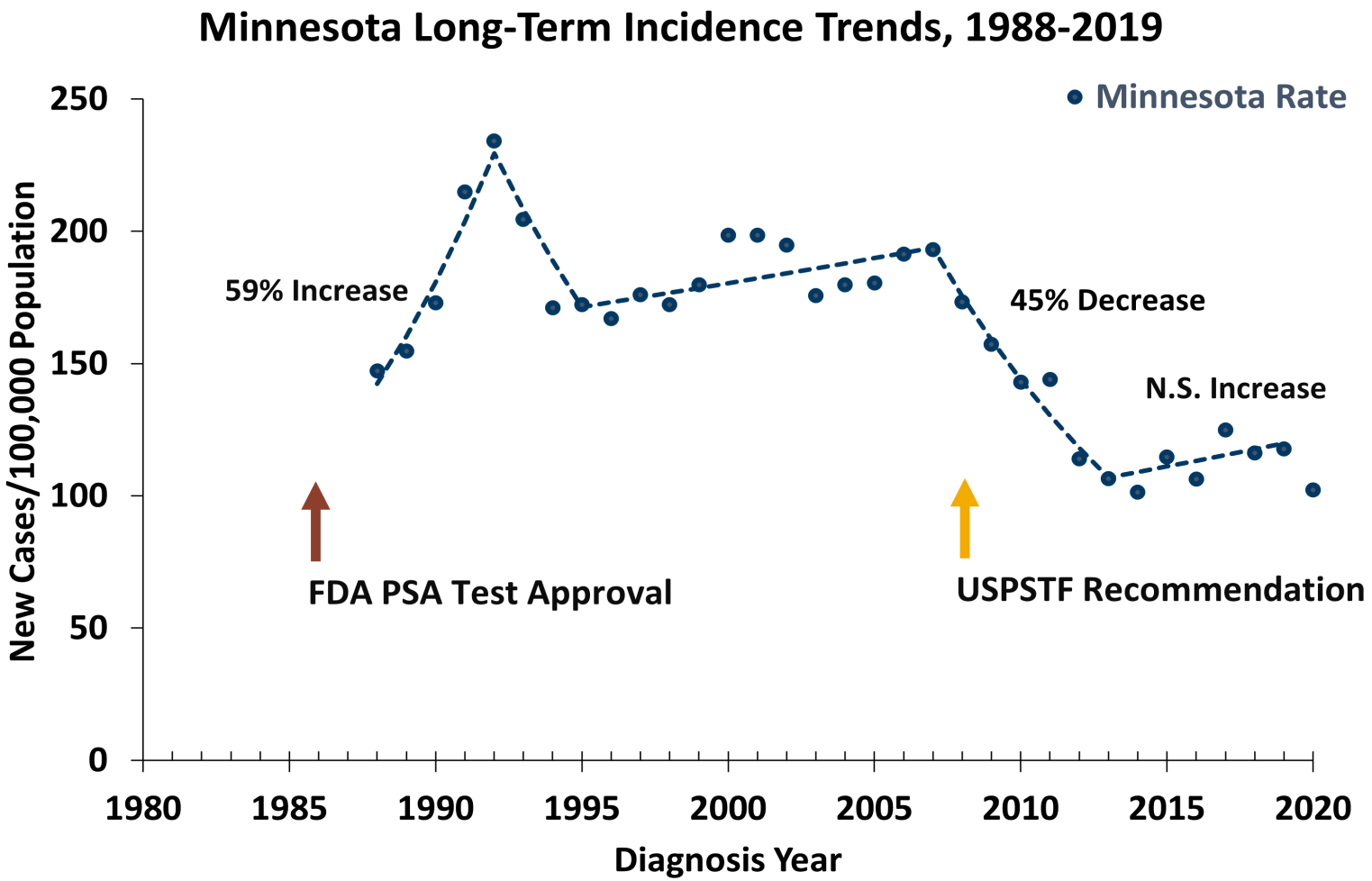
SEER-8 (U.S.) 40-Year Incidence Trends and Key PSA-Related Events (3 of 4)

- 1986-1992: U.S. incidence increased sharply after the FDA approved PSA testing in 1986.
- 2007-2014: U.S. incidence plummeted after 2008 USPSTF recommendation against screening older men.
- 2014-2019: U.S. incidence is currently increasing.



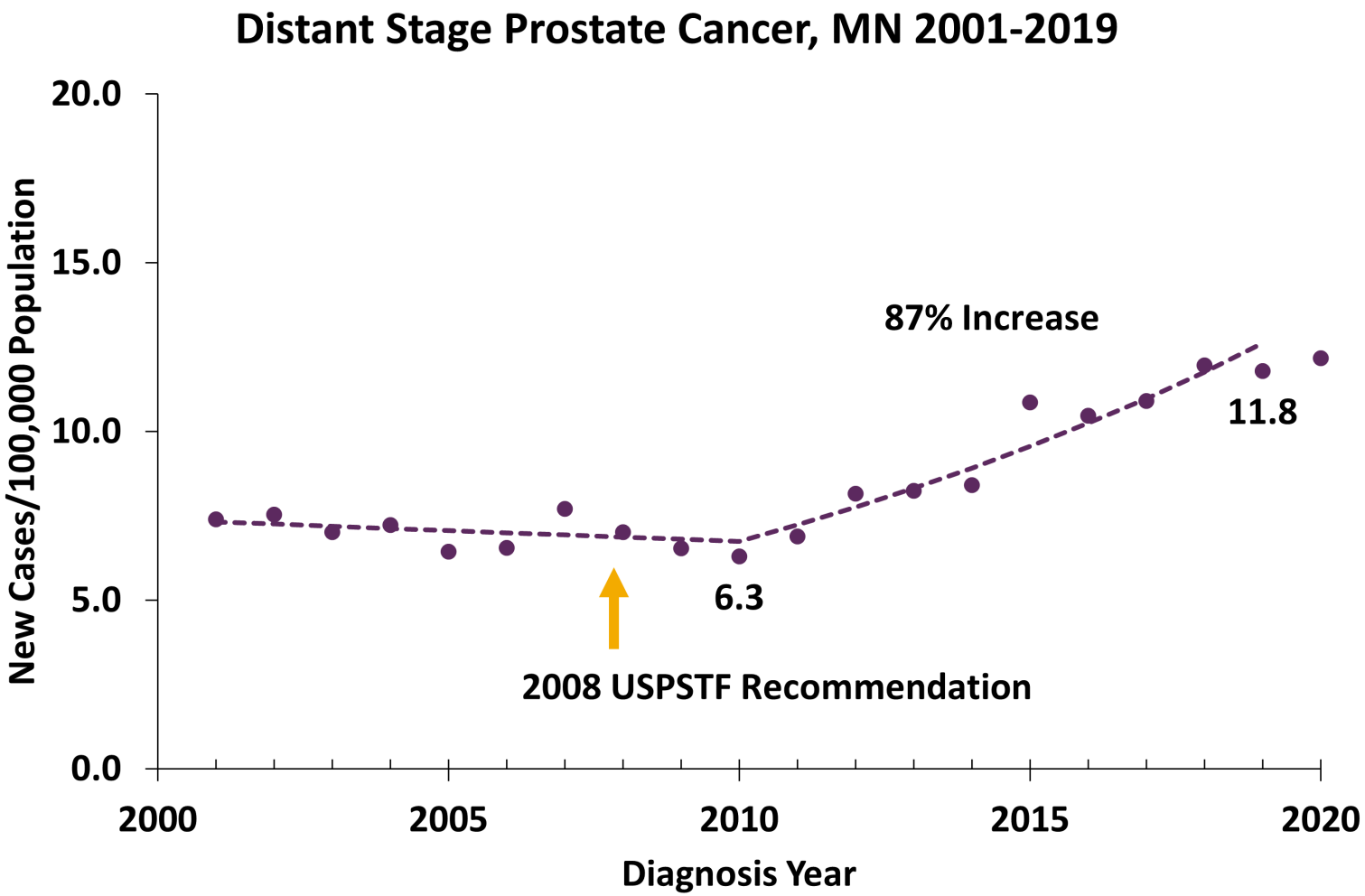
Minnesota 32-Year Incidence Trends and Key PSA-Related Events (4 of 4)

- 1988-1992: MN incidence increased sharply from 1st year of registry operation to 1992 peak.
- 2007-2013: MN incidence fell steeply following the 2008 USPSTF recommendation against screening older men.
- 2014-2019: MN incidence is currently stable (apparent increase is small and not stat. sig.).



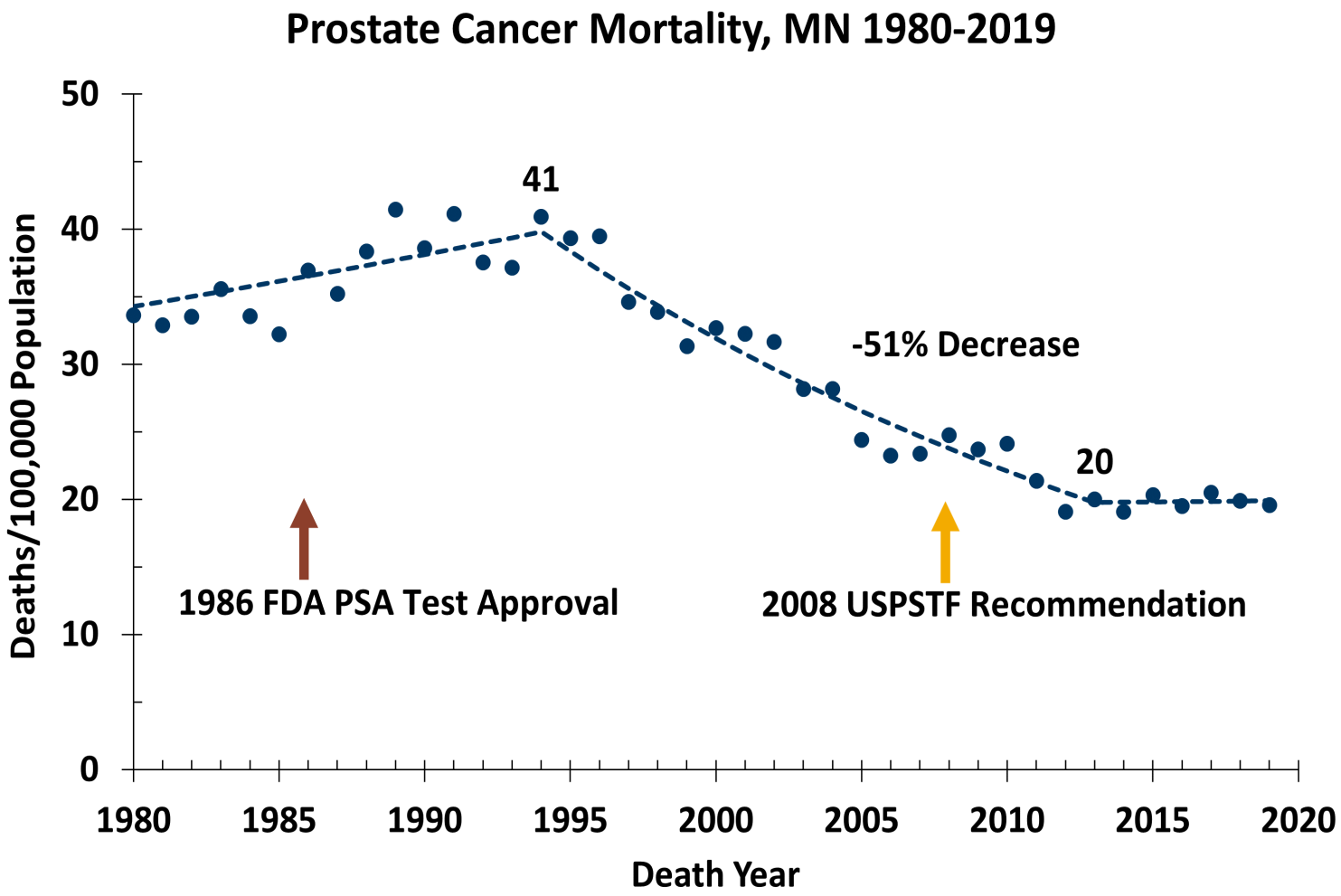
Minnesota Distant Stage Incidence Before and After the 2008 USPSTF Recommendation

- MN distant stage diagnoses began increasing in 2010, soon after the 2008 USPSTF recommendation against screening older men.
- The distant stage incidence rate has nearly doubled since 2010.



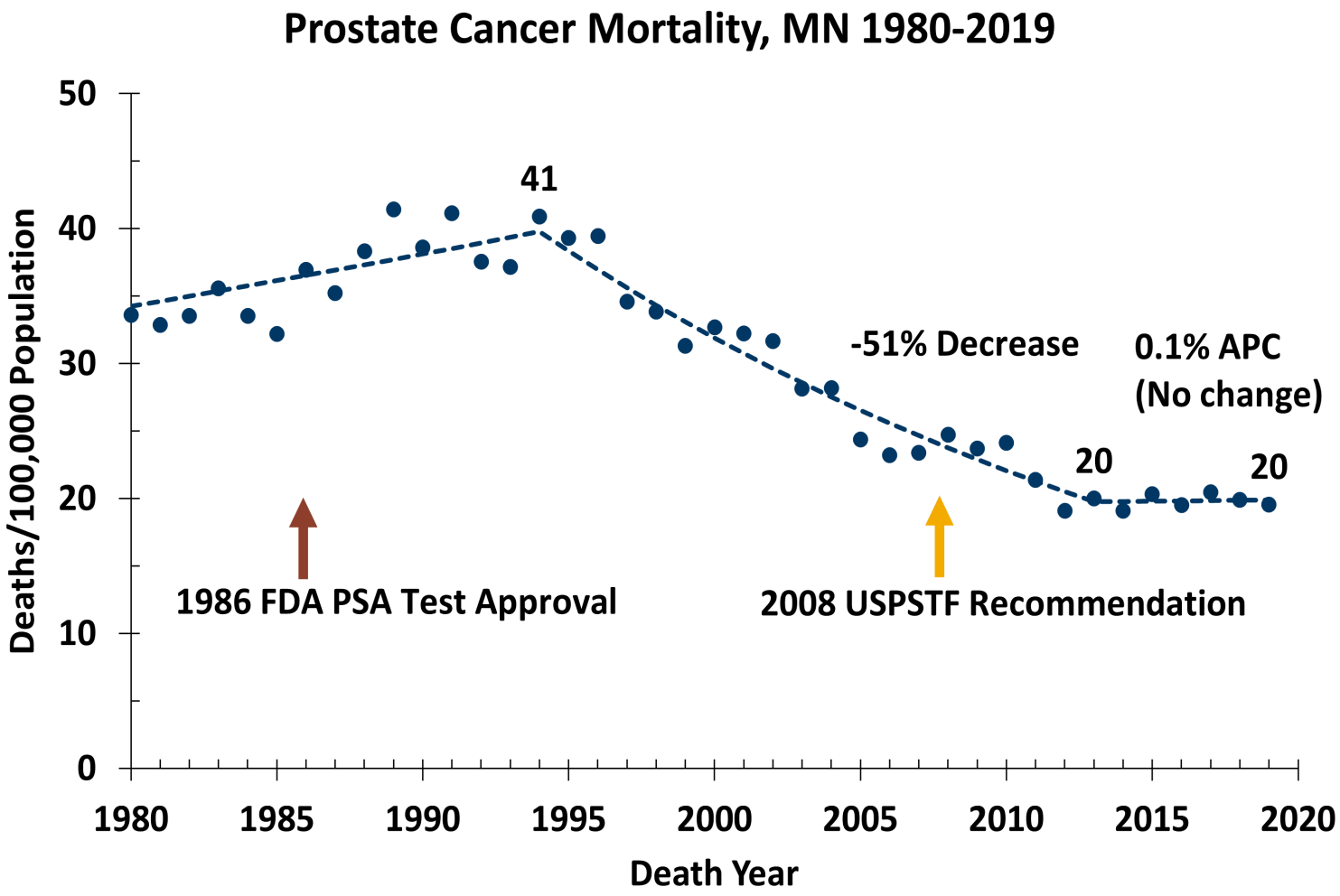
Minnesota Prostate Cancer Mortality Began to Decline 8 Years after FDA Approval of PSA Testing (1 of 2)

- Prostate cancer mortality in Minnesota gradually increased for several decades to peak in 1994, 8 years after the FDA approved the PSA test.
- The mortality rate then dropped by 51% between 1994 and 2013.
- Can uptake of PSA testing be **credited** for the mortality decline?



Prostate Cancer Mortality Stopped Falling 5 Years After 2008 USPSTF Recommendation Discouraging Screening (2 of 2)

- Prostate cancer mortality dropped by half from 1994 to 2013.
- But progress stalled in 2013, 5 years after the USPSTF recommendation discouraging screening.
- The rate is now flat.
- Did the recommendation against screening **cause** the mortality rate decline to end?



Currently (2018) the USPSTF recommends individual, informed decision-making, but not mass screening

For Men 55 to 69 Years of Age

- The decision to screen should be an individual one.
- Screening offers a small potential benefit of reducing prostate cancer death but also potential for numerous harms.
- Balance of benefits and harms may differ for different men.

For Men 70+ Years of Age

- USPSTF recommends against screening in this age group.
- Potential benefits do not outweigh the harms.

Arguments Both For and Against Mass Screening have Merit. The USPSTF Continues to Evaluate as Evidence Develops

- **Arguments against mass screening**
  - Most prostate cancer does not progress to cause problems.
  - At the population level PSA testing leads to only a small reduction in mortality (RCT evidence).
  - Mass testing exposes large numbers of men to the harms of treatment.
  - Treatment harms are common and debilitating.
- **Arguments for mass screening**
  - Widespread PSA testing deserves at least some credit for the 20-year decline in prostate cancer mortality (1994 to 2013).
  - Mortality is no longer decreasing.
  - Distant stage (aggressive) prostate cancer incidence is now increasing (2010 to 2019).
  - Medical practice has changed over time, mitigating the harms of screening.

Thank You

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Tribal-State Relations Acknowledgment Statement-Global

INSTRUCTIONS: This is a global statement that purposefully removes the agency specificity and can be used in a variety of spaces. It's best used both in-state and out of state.

The state of Minnesota is home to 11 federally recognized Indian tribes with elected Tribal government officials. The State of Minnesota acknowledges and supports the unique status of the Minnesota Tribal nations and their absolute right to existence, self-governance, and self-determination. The United States and the State of Minnesota have a unique relationship with federally recognized Indian tribes, formed by the Constitution of the United States, treaties, statutes, case law, and agreements. The State of Minnesota and the Minnesota Tribal governments significantly benefit from working together, learning from one another, and partnering where possible.

The Minnesota Department of Health (MDH) recognizes, values, and celebrates the vibrant and unique relationship between the 11 Tribal nations and the State of Minnesota. MDH believes that the partnerships formed, through a government-to-government relationship, with the 11 Tribal nations will effectively address health disparities and lead to better health outcomes for all of Minnesota.