# Trends in clinical and oncologic outcomes of Robotic Radical Prostatectomy before and after the 2012 US Preventive Services Task Force recommendation against PSA screening. A decade of experience.

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/BJU.15051

**Abstract**

**Objective:-**

To assess the influence of the 2012 USPSTF recommendation against PSA-based screening on oncological and functional outcomes following RALP.

**Materials and methods: -**

We retrospectively analyzed patients that underwent RALP between 2008-2018 with a minimum of 12 months follow up from a prospectively collected IRB approved database. The impact USPSTF statement against PSA screening on our surgical outcomes was assessed using a logistic regression model using two groups indicating patients treated before/after the USPSTF statement and time trends for each successive year.

**Results:-**

The mean preoperative PSA increased from 6.0 to 7.4 ng/ml after the USPSTF recommendations. We detected statistically significant time-trend changes after 2012 including an increase in the positive slope of Gleason ≥3+4 or ≥pT3. We detected a fall in bilateral FNS and increase in PNS. Total PSM rate after the USPSTF recommendation increased. However, PSM rates pertinent to each pathological stage did not change significantly after 2012. There was a significant negative trend change in the postoperative 12-month continence and potency indicating a breakpoint in functional outcomes after 2012. We detected a 1.7 fold increase in 12-month BCR rates. The 12-month BCR, potency and continence rates were maintained in young (<55 years) patients with SHIM>22 and low volume disease.

**Conclusion**: -

Since the USPSTF's recommendation in 2012, we have seen a significant increase in the incidence of the high-risk disease that has forced us to modify our approach to the procedure and the grade of NS leading to a wider resection to maintain the PSM has led to a decrease in postoperative functional recovery. Patients with good characteristics have performed well before and after the USPSTF's recommendation, implying that the quality of surgery did not change over time.

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Article type : Original Article

category: Urological Oncology

**Introduction:**

The advent of PSA screening in the early 1980s led to a significant increase in the overall diagnosis of prostate cancer (PCa) and subsequently a decrease in the rate of PCa mortality. (1) Over the last 2 decades, this has amounted to an earlier diagnosis of the disease and; therefore, to a reduction of approximately 25% in mortality for PCa in patients who were screened at least once in their lifetime(1). PCa is currently the most commonly diagnosed solid organ tumor in males and the second leading cause of cancer death with an estimated 31,620 deaths this year in the US. (2) Since the late 1980's PSA based screening for PCa has become routine and part of a normal men's yearly examination. (3) However, in 2012 the US preventive task force (USPSTF), the governmental body that advises and guides primary care physicians regarding basic screening, proposed a "D" recommendation for PCa screening. This recommendation basically recommended against all PSA based routine screening in all men of any age, ethnicity or family history. The rationale for this recommendation is that a significant number of patients were being over diagnosed and over treated for PCa, and the perceived lack of data supporting survival advantages from PSA screening(4). This decision was obviously controversial and is currently still debated.

The USPSTFs recommendation against PSA screening has had some profound effects as it led to the reduced utility of PSA by primary physicians and physicians in general. The PSA utility decreased 39% and PCa biopsy rate decreased by 30%(5,6) This has led to less diagnosis of intermediate and high-risk PCa, with diagnosis rates

falling from 17.5 per month to 10 males per month following this recommendation. (7) This has also led to the delay in the diagnosis of some men with PCa with significant disease. Ahlering et al recently reported a significant fall in Gleason Score (GS) 6 and increase in ≥ GS 4+4 by 24%, The 1-year Biochemical Recurrence (BCR) rate rose from 6.2 to 17.5%(8)

Our group recently published an article showing the changing trends in the PCa characteristics of our patients as a result of the USPSTF guided changes in PSA screening. Considering the changes in screening guidelines and referral patterns, we investigated the time trends in the patient's surgical and pathological characteristics before and after the recommendation (9,10). The analysis showed an increase in intermediate and high-risk PCa, with a demonstrable breakpoint following the USPSTF's recommendation (9). The current study assesses the impact of the changing landscape of PSA screening and PCa diagnosis on functional and oncological outcomes of patients that undergo surgical treatment with robot-assisted laparoscopic prostatectomy (RALP) in a single surgeon practice with a decade of experience.

**Materials and methods:**

We retrospectively analyzed all patients who underwent RALP between January 2008 to March 2018 from a prospectively collected IRB approved PCa database. After excluding patients who underwent salvage prostatectomy, 8,564 out of 10,409 patients with a minimum of 12 months follow up were available for analysis. The patients were then divided into two primary groups, from January 2008 to December 2012 (Group 1) and from January 2013 to March 2018 (Group 2). All patient referrals to us for up to 6 months after the USPSTF recommendations in 2012 were included in Group 1. The time frame for each group was decided upon the lag time for the screening recommendations to start changing clinical practice patterns in our referral community, and the delay from cancer diagnosis to scheduling surgery. These patients were then subjected to trend analysis for each year by comparing their oncological and functional outcomes at 12 months following surgery.

*Surgical technique:*

All patients underwent a 6-port transperitoneal RALP technique developed at our institution and all surgeries were performed by a single surgeon (11). Nerve-sparing (NS) was performed athermally with a modified, early retrograde release of the neurovascular bundle (NVB)(12). The quality of NVB preservation in each side was graded by the surgeon prospectively at the termination of RALP based on a 5-point NS grading system that was developed by our group(13). To perform descriptive and comparative analyses, the degree of NS was categorized into four groups based on the total score of both sides as described previously by our group(9) Bilateral standard pelvic lymph node dissection (PLND) was performed in patients classified as intermediate or high-risk, based on the D'Amico classification (14,15).

*Post-operative care and follow-up:*

Immediate post-operative complications were evaluated using the Clavien-Dindo grading system(16). The histopathological data of all patients were derived from the database and all specimens were processed by the same team of pathologists using the AJCC TNM staging system, GS, and the presence of positive surgical margins (PSM) (17). Follow-up data were prospectively collected at a regular interval (quarterly for the first year and then semiannually thereafter) using validated questionnaires like EPIC, SHIM and serum PSA levels to assess the BCR. All data were entered into the database and regularly updated by a dedicated research team by reviewing patients' follow-up charts and conducting regular phone calls.

*Definition of functional outcomes:*

Continence was defined as the usage of no pads. Potency was defined as the ability to penetrate and satisfactorily complete intercourse with or without PDE5 inhibitors in more than half of the attempts ( scores more than 3 in questions 2 and 5 in SHIM).BCR was defined as two consecutive PSA levels of > 0.2 ng/ml(18). Continence, potency, and BCR status at postoperative 12 months were included in the trifecta. Additionally, complications occurring either during or within 90 days of surgery, and the presence of a PSM were included in the postoperative pentafecta(16,19).

*Statistical analysis:*

Continuous variables were reported as median values (interquartile range-IQR) or as mean±standard deviation (SD) and were compared across independent groups by the Wilcoxon rank-sum test. Categorical variables were summarized as absolute and relative percent frequencies, and the chi-squared test was performed to compare their distribution across the two study groups. A subgroup analysis was performed by further categorizing the patients based on age, preoperative PCa risk class, and baseline sexual function, and their postoperative 12-month oncological and functional outcomes were compared between the pre- and post-USPSTF recommendation groups (Groups 1 and 2, respectively).

In order to detect the impact USPSTF statement against PSA screening on our functional and oncological outcomes, time-trend changes were investigated for these variables using a logistic regression model with two covariates and their interactions; the time numerical covariate designated for each successive year from 2008 to 2018, and a binary variable indicating patients treated before or after the USPSTF statement (ie. Groups 1 and 2, respectively). The likelihood-ratio (LR) test was used to test differences in the trend slopes and intercepts in Groups 1 and 2. A breakpoint was identified between the groups if the LR test showed a significant difference between the intercepts and/or slopes of the two linear trends. Statistical analyses were performed using SPSS 25 (IBM Corp, Chicago IL), Stata 15 (StataCorp 2017, College Station, TX), and R 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria) software. A p-value of less than 0.05 was considered statistically significant.

**Results:**

*Baseline patient characteristics:*

A total of 8,564 patients with at least 12 months follow up were analyzed (Table 1). Overall, 37.9%, 44.6%, and 18% of patients had D'Amico low-, intermediate-, and high-risk disease, respectively. The mean preoperative PSA increased from 6.0 to 7.4 ng/ml after the USPSTF recommendations. There was also a 19% increase in the incidence of intermediate- and high-risk disease. Baseline sexual function was not significantly different before and after the 2012 statement. (Table 1)

*Perioperative and pathological outcomes:*

Table 2 summarizes the perioperative and pathological characteristics before and after the 2012 USPSTF recommendations. We detected a 17% decrease in bilateral full (grade 1) NS and a 19% increase in partial (grades 2 and 3) NS after the USPSTF statement. Our non-organ confined disease (≥pT3) rates increased from 23.3% to 39%, a 1.7 fold increase and pathological GS ≥8 rates were doubled from 8.1% to 15.5%, a 1.9 fold increase ($p<0.001$, Table 2). There was a significant increase in the slope of the positive time-trend of GS>=3+4 or ≥pT3 disease rate after the end of 2012 (Figure 1a), indicating an association between the rise in the incidence of clinically significant disease and the USPSTF recommendation.

Overall, the positive surgical margins (PSM) rate was 16.7%. The total PSM rate increased from 14.1% to 18.9%, a 1.3 fold increase after the USPSTF recommendation ($p<0.001$). However, PSM rates pertinent to each pathological stage did not change significantly after the 2012 recommendation (Table 2). Our time-trend analyses also did not show any significant changes in the PSM time-trend after the 2012 USPSTF statement.

*Oncological outcomes:*

In the entire cohort, 4.3% of patients had PSA persistence and 10.8% had PSA recurrence at a median follow-up of 49 months (range: 12 to 137 months). We detected an increase in 12-month BCR rates from 2.4% to 4.2%, a 1.7 fold increase after the 2012 USPSTF recommendation ($p<0.001$). However, when subsets of patients based on age, PCa risk group, and baseline sexual function were examined, there were no differences between pre- and post-recommendation 12-month BCR across all patient groups (Table 3). Likewise, our logistic regression analyses did not demonstrate any significant changes in the time trends for 12-month BCR rates after the USPSTF recommendation (Figure 1 and Table 4).

*Functional outcomes:*

Overall, 90.6% of patients achieved full (pad free) continence. In Group 1, the continence rate was 94.3% and in group 2 it was 87.5 % ($p<0.001$). The median time to achieve continence was not different between the two groups (46 vs. 45 days). We detected a significant increase in the negative slope of postoperative 12-month continence and a significant difference between its intercepts after the USPSTF

recommendation (Table 4), indicating a breakpoint in continence recovery at the end of 2012 (Figure 1a).

The Overall potency rate at postoperative follow-up was 56.4%, irrespective of age, pre-operative SHIM score, and NS status. The Overall potency rate in group 1 was 65.6% as compared to 48.6% in group 2 ($p<0.001$), indicating a significant decline after the USPSTF statement. Our sub-group analysis revealed that 12-month potency and continence rates were maintained in young (<55 years) patients with good preoperative sexual function (SHIM>=22) and low volume disease. Following the recommendation, the subgroup with age < 55 yrs, SHIM >= 22 and D'Amico class 1 dropped from 60.1% to 39.9%. In this sub-group, pre- and post-recommendation potency rates were 93% vs. 88.7% in D'Amico class 1, and 88.9% vs.83% in D'Amico class 2 patients, respectively ($p>0.05$ for all comparisons, Table 3). In all other patient subsets, 12-month potency and continence rates showed a statistically significant decline after the USPSTF recommendation (Table 3). The worst outcomes were observed in patients >65 years with D'Amico high-risk cancer, in which the 12-month potency rate was 60% before vs. 36% after the USPSTF recommendation ($p=0.005$, Table 3). The outcomes were significantly correlated to disease status, the more advanced disease states resulted in poorer outcomes.

In line with continence and potency outcomes, there was a statistically significant decrease in our 12-month trifecta and pentafecta rates from 55.1% to 41.7%, and 49.1% to 36.6%, respectively, after the USPSTF statement ($p<0.001$ for both comparisons, Table 2). We also detected significant changes in the negative time-trends of postoperative 12-month trifecta and pentafecta after 2012 (Figure 1b, Table 4-), confirming an association between the decline in our trifecta/pentafecta outcomes and the USPSTF recommendation.

**Discussion:**

Historically, PSA has been a widely accepted screening tool for the detection of PCa (20,21). In 2012, the USPSTF recommended against the practice of using PSA for routine screening of PCa in all age groups. The rationale for this recommendation was that a significant number of patients were being over diagnosed and over treated for

PCa (4). However, the USPSTF's recommendation had widespread implications, resulting in a significant fall in the number of patients being referred with high PSA, and a significant decrease in the number of patients undergoing prostate biopsy in the subsequent years (7,22–24). Studies have further demonstrated that patients undergoing biopsy after 2012 had a higher GS and more positive cores. (5,25).These findings were also confirmed in our study. Specifically, there was a 1.3 fold increase in intermediate and a 1.7- fold increase in high-risk patients undergoing RALP after 2012. There was also a 1.7-fold increase in ≥pT3 disease following the recommendations ($p<0.001$).Although the GS>=3+4 or ≥pT3 were increasing prior to the recommendation due to factors like increased active surveillance of low-risk group and increased utilization of RALP,there was a significant time-trend change in high-risk disease following the recommendation ( Fig.1)(26,27)

Changes in PCa characteristics after the 2012 USPSTF recommendation have led to significant changes in RALP practice. In a recent study, our group reported data showing a rise in aggressive cancer features was associated with a significant decline in our bilateral full NS performance and a significant increase in our partial NS rates, to maintain our PSM rates (9). A breakpoint was detected in the time-trends of these NS grades at the end of 2012, suggesting an association between the changes in our NS performance and the USPSTF statement. In the present study, we have further analyzed the functional and oncological implications of these changes in our clinical practice.

We noted that our PSM rates pertinent to each pathological stage were maintained after the 2012 USPSTF recommendation as a result of increased performance of partial over bilateral full NS. Accordingly, our 12-month BCR rates showed a small but statistically significant increase from 2.4% to 4.2% a 1.7 fold change after the USPSTF recommendation. However, this significance was lost when short-term BCR rates were examined in patient subgroups based on age and PCa risk groups. Ahlering et al. recently compared 4-year pre- vs. post-USPSTF statement RALP outcomes in 19,602 patients from nine high-volume referral centers in the United States and reported a 2.8 fold increase in 1-year BCR rates from 6.2% to 17.5% after the recommendation (8). This difference between these authors and our BCR rates is

probably related to the multi-center nature of their study and differences in the RALP technique. Also, extensive experience of our group helped us to adapt our surgery to maintain stage-wise PSM rate which is probably the best one can offer surgically and the change in 12-month BCR is due to the inherent character of the disease itself due to deferred screening. Nevertheless, long-term data is needed to better elucidate the impact of 2012 USPSTF recommendations on trends oncological outcomes after RALP.

In our experience, the trade-off for compensating PSM and BCR rates with wider NVB dissection was a decrease in the functional recovery after RALP. In the entire cohort regardless of age, SHIM score or NS status, we found a significant decrease in full continence rates from 94% to 87.5%, and a significant decrease in potency rates from 66% to 49% after the USPSTF recommendation ($p<0.001$ for both comparisons). Our time-trend analysis demonstrated a significant breakpoint at the end of 2012, indicating an association between the decline in functional recovery and the task force's PSA screening recommendation. The decrease in continence and potency rates was associated with a significant decrease in our 12-month trifecta and pentafecta rates, as evidenced by the decline in the time-trends of these variables after 2012. To our knowledge, this is the first study to investigate the impact of 2012 USPSTF recommendations on functional recovery and trifecta and pentafecta rates after RALP.

In the present study, we performed a subgroup analysis to investigate the changes in functional and oncologic outcomes in different patient groups based on age and PCa risk class. Interestingly, the 12-month continence, potency, and BCR rates did not change significantly after the USPSTF recommendation in patients <55 years with D'Amico low- to intermediate-risk disease and a preoperative SHIM score>=22. Of note, the best postoperative outcomes were achieved in these patients. This suggests that our surgical technique was stable in the "ideal patient" with young age and low-volume disease, and the functional outcomes were less likely to be affected by changing cancer characteristics, leading to maintained high continence and potency recovery rates. In all other patient sub-groups, our functional recovery rates deteriorated after 2012, possibly due to the increasingly lower performance of high-quality NS in a growing population of patients with high-risk disease, or due to the higher age which may not compensate for the more aggressive technique as good as their younger counterparts.

Despite reporting novel information, the present study has some limitations that need to be addressed. First, our study has the inherent limitations of a retrospective analysis. However, our IRB approved, and prospectively maintained database ensures the quality of clinicopathological and follow-up data. Second, as a high-volume tertiary referral center treating increasingly more complex patients, our results may not be generalizable to other centers. Third, using a time-trend analysis may not account for all possible confounding factors and establish a direct cause/effect relationship. However, it can demonstrate a potential association between a factor and the outcome. Fourth, the length of our follow up, especially in the post-recommendation group, was not enough to draw final conclusions regarding the changes in long-term oncologic outcomes. Despite its limitations, this is the first study to analyze the effect of USPSTF's 2012 recommendations against PSA screening on both oncological and functional robotic prostatectomy outcomes.

**Conclusion:**

Comparing the characteristics of prostate cancer patients before and after the USPSTF's "D" recommendation for PSA screening in 2012, we have seen a significant increase in the incidence of the high-risk disease being treated in our practice. These changes have forced us to modify our approach to the procedure and the grade of NS. The wider resection and decreased amount of NS in order to maintain the PSM had led to a decrease in postoperative functional recovery. Patients with good characteristics have performed well before and after the USPSTF's recommendation, implying that the quality of surgery did not change over time. These results may suggest a benefit from earlier PSA screening in terms of maintaining high functional recovery rates in patients who are candidates for robotic prostatectomy. Further long-term studies are essential to investigate the pragmatic effect of this PSA recommendation throughout the community and PSA screening should be considered until an ideal screening tool is developed.

**Conflicts of interest**

None disclosed

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**Table 1 – Comparison of preoperative characteristics of the patient prior to and after the recommendations.**

| Parameters | Total | January 2008 to December 2012 | January 2013 to March 2018 | P-value |
|---|---|---|---|---|
| **Total** | 8564(%) | 3954(%) | 4610(%) | |
| **Age (mean±SD)** | 61.66(7.6) | 60.87(7.6) | 62.33(7.6) | < 0.001 |
| **Age (years)** | | | | |
| Less than 55 | 1854(21.6) | 885(19.2) | 969(24.5) | |
| 55 – 65 | 3756(43.9) | 1958(42.5) | 1797(45.4) | < 0.001 |
| More than 65 | 2954(34.5) | 1766(38.3) | 1188(30) | |
| **BMI (mean±SD)** | 28.32(4.2) | 28.15(4.1) | 28.46(4.3) | .001 |
| **BMI (kg/m$^2$)** | | | | .004 |
| Less than 30 | 6068(70.9) | 3206(69.5) | 2862(72.4) | |
| 30 and above | 2496(29.1) | 1092(27.6) | 1404(16.4) | |
| **D'Amico score** | | | | |
| Low risk | 3228(37.9) | 1895(48.1) | 1333(29) | |
| Intermediate risk | 3800(44.6) | 1532(38.9) | 2268(49.4) | < 0.001 |
| High Risk | 1536(18) | 511(13) | 1025(21.9) | |
| **PSA (mean±SD)** | 6.76(8.82) | 5.97(4.79) | 7.44(11.13) | < 0.001 |
| **Pre-op PSA (ng/dl)** | | | | |
| Less than 10 | 7466(87.2) | 3585(90.7) | 3881(84.2) | |
| 10-20 | 887(10.4) | 302(7.6) | 585(12.7) | < 0.001 |
| More than 20 | 211(2.5) | 67(1.7) | 144(3.1) | |
| **Preop SHIM (mean±SD)** | 18.03(7.6) | 18.36(7.5) | 17.75(7.74) | .062 |
| **Preop AUA (mean±SD)** | 8.95(7.2) | 8.44(6.8) | 9.28(7.4) | < 0.001 |

**Table 2 - Perioperative and postoperative outcomes after RALP.**

| Parameters | All patients N=8564 (%) | January 2008 to December 2012 N= 3954 (%) | January 2013 to March 2018 n= 4610 (%) | P Value |
|---|---|---|---|---|
| **Median (IQR) operative time (minutes)** | 122.5 (25.6) | 126.1 (26.5) | 117.9 (22.04) | <0.001 |
| **Median (IQR) console time (minutes)** | 76.9 (10.7) | 79.5 (10.9) | 76.2 (10.15) | <0.001 |
| **Median (IQR) estimated blood loss (ml)** | 118.2 (84.7) | 134.5 (97.96) | 100.0 (62.4) | <0.001 |
| **Nerve Sparing** | | | | <0.001 |
| Bilateral Full NS (Grade 1) | 3830(46) | 2046(55.1) | 1784(38.7) | |
| High-grade Partial NS (Grade 2) | 2810(33.8) | 993(26.7) | 1817(39.4) | |
| Low-grade Partial NS (Grade 3) | 1060(12.7) | 364(9.8) | 696(15.1) | |
| Poor NS (Grade 4) | 625(7.5) | 312(8.4) | 313(6.8) | |
| **Pathological stage** | | | | <0.001 |
| Organ confined (≤ pT2c) | 5842(68.2) | 3033(76.7) | 2809(61) | |
| Extra prostatic extension (pT3a) | 1929(22.5) | 651(16.5) | 1278(27.7) | |
| Seminal vesicle invasion (pT3b) | 676(7.9) | 236(6) | 440(9.5) | |
| Adjacent organ involved (pT4) | 117(1.4) | 34(0.9) | 83(1.8) | |
| **Pathological Node Positive** | 236 (2.7) | 43(1.08) | 193(4.1) | <0.001 |
| **Pathological Gleason score** | | | | <0.001 |
| 6 | 2158(25.5) | 1303(33.2) | 855(18.8) | |
| 7 | 5824(62.4) | 2305(58.7) | 2979(65.6) | |
| ≥ 8 | 1024(12.1) | 319 (8.1) | 705(15.5) | |
| **Positive Surgical Margin** | | | | |
| **Overall** | 1428(16.7) | 558(14.1) | 870(18.9) | <0.001 |
| In organ confined disease(pT2) | 524(9) | 264(8.8) | 260(9.3) | .469 |
| In Extra-prostatic extension (pT3a) | 499(25.9) | 169(26) | 330(25.8) | .948 |
| In seminal vesicle invasion (pT3b) | 291(43) | 93(39.4) | 198(45) | .162 |
| (pT4) | 114(97.4) | 32(94.1) | 82(98.8) | .446 |
| **Median-Follow up (months)** | 49(59) | 84(40) | 36 (29) | |
| **Continence** | 7762(90.6) | 3730(94.3) | 4032(87.5) | <0.001 |
| **Days to continence (Median(IQR))** | 46 (62) | 46 (59) | 45 (80) | |
| **Potency achieved (Irrespective of Age, Pre-op potency and NS)** | 4833(56.4) | 2593(65.6) | 2240(48.6) | <0.001 |
| **Days to potency (Median (IQR))** | 91 (224) | 82 (169) | 97 (240.5) | |
| **PSA persistence** | 370(4.3) | 134(3.4) | 236(5.1) | <0.001 |
| **BCR at 12 months** | 288(3.4) | 96(2.4) | 192(4.2) | <0.001 |
| **Trifecta achieved** | 4100(47.9) | 2179(55.1) | 1921(41.7) | <0.001 |
| **Pentafecta achieved** | 3583(41.8) | 1941(49.1) | 1642(36.6) | <0.001 |

**Table No 3: Comparison of outcomes before and after the recommendation sub stratified into preoperative factors**

| Patient groups | Continence | | | Potency | | | BCR | | |
|---|---|---|---|---|---|---|---|---|---|
| | January 2008 to December 2012 | January 2013 to March 2018 | P value | January 2008 to December 2012 | January 2013 to March 2018 | P value | January 2008 to December 2012 | January 2013 to March 2018 | P value |
| **Age less than 55, SHIM>= 22 and D Amico class 1** | 354(98.9) | 232(97.5) | .191 | 333(93) | 211(88.7) | .065 | 19(5.3) | 9 (3.8) | .669 |
| **Age less than 55, SHIM>= 22 and D Amico class 2** | 254(97.3) | 260(96.3) | .504 | 232(88.9) | 224(83) | .058 | 43(16.5) | 29(10.7) | .033 |
| **Age less than 55, SHIM>= 22 and D Amico class 3** | 54(96.4) | 60(84.5) | .028 | 47(83.9) | 45(63.4) | .010 | 14(25) | 15(21.1) | .535 |
| **Age between 55-65 years, SHIM>= 22 and D Amico class 1** | 409(95.6) | 289(95.1) | .754 | 375(87.6) | 231(76) | .000 | 24(5.6) | 10(3.3) | .332 |
| **Age between 55-65 years, SHIM>= 22 and D Amico class 2** | 341(96.6) | 454(93.6) | .053 | 292(82.7) | 339(69.9) | .000 | 53(15) | 52(10.7) | .110 |
| **Age between 55-65 years, SHIM>= 22 and D Amico class 3** | 102(93.6) | 137(85.6) | .042 | 70(64.2) | 69(43.1) | .001 | 28(25.7) | 35(21.9) | .562 |
| **Age > 65 years, SHIM>= 22 and D Amico class 1** | 143(92.3) | 82(82.8) | .021 | 100(64.5) | 55(55.6) | .153 | 0 | 1(1) | .210 |
| **Age > 65 years, SHIM>= 22 and D Amico class 2** | 132(92.3) | 192(80.7) | .002 | 97(67.8) | 96(40.3) | .000 | 3(2.1) | 11(4.6) | .439 |
| **Age > 65 years, SHIM>= 22 and D Amico class 3** | 43(95.6) | 107(78.7) | .009 | 27(60) | 49(36) | .005 | 5(11.1) | 13(9.6) | .786 |

**Table 4: - Time trends changes in outcomes following the 2012 USPSTF statement - the comparison between slopes and intercepts of various outcomes before and after the recommendation.**

| Parameter | Intercept | | | Slope | | |
|---|---|---|---|---|---|---|
| | **January 2008 to December 2012** | **January 2013 to March 2018** | **P-value** | **January 2008 to December 2012** | **January 2013 to March 2018** | **P-value** |
| GS>=3+4 or ≥pT3 | -269 (-368 to -170) | -423 (-527 to -318) | 0.040 | .13 (.09 to .18) | .21 (.16 to .26) | 0.036 |
| PSM | -36 (-172 to 100) | -182 (-277 to -87) | 0.189 | .02 (-.05 to .08) | .09 (.04 to .14) | 0.084 |
| Continence | 62 (-112 to 237) | 544 (438 to 650) | < 0.001 | -.03 (-.12 to .06) | -.27 (-.32 to -.22) | < 0.001 |
| Potency | 16 (-79 to 111) | 542 (462 to 622) | < 0.001 | -. 01 (-.05 to .04) | -.27 (-.31 to -.23) | < 0.001 |
| Biochemical Recurrence | -269 (-588 to 50) | -330 (-524 to -137) | 0.458 | .13 (-.03 to .29) | .16 (.07 to .26) | 0.748 |
| Trifecta | 33 (-62 to 128) | 587 (507 to 667) | < 0.001 | -.02 (-.06 to .03) | -.29 (-.33 to -.25) | < 0.001 |
| Pentafecta | 50 (-45 to 145) | 558 (478 to 638) | < 0.001 | -.02 (-.07 to .02) | -.28 (-.32 to -.24) | < 0.001 |

**Figure 1A - Trend change analysis in functional outcomes and oncological parameters (logit scale) following the 2012 USPSTF statement for patients undergoing surgery at 12 months.**

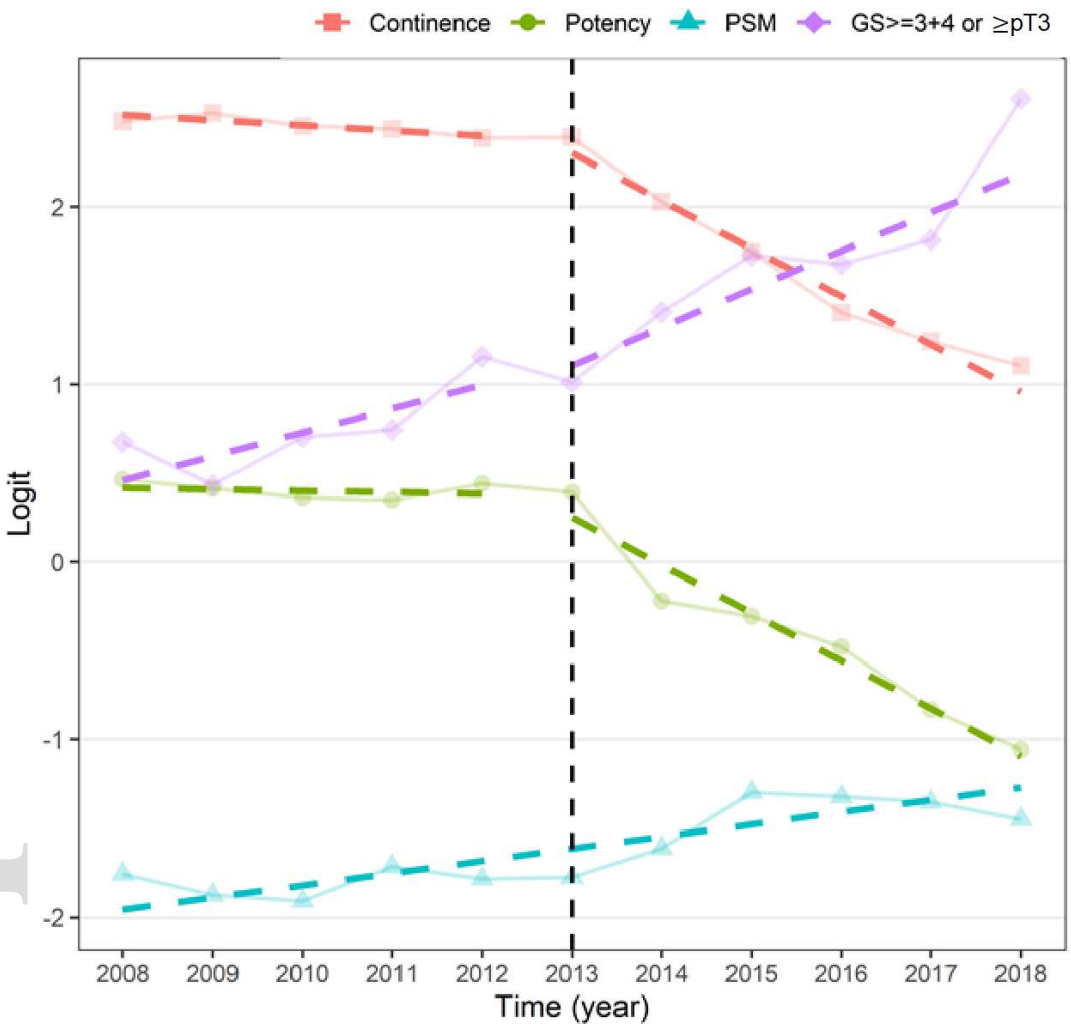

**Figure 1B - Trend change analysis in outcomes (logit scale) following the 2012 USPSTF statement for patients undergoing surgery at 12 months**