**Supplemental Table 1. Cancer Mortality-** Effect of weight loss medication on PCa, CRC and HRC mortality among men 65+ years old in SEER-Medicare 2007-2015a

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **PCa Mortality**  **(adjusted for stage and grade at diagnosis)†** | | | **CRC Mortality**  **(adjusted for stage and grade at diagnosis)†** | | | **HRC Mortality**  **(adjusted for stage and grade at diagnosis)†** | | |
|  | **Events/n** | **HR** | **95% CI** | **Events/n** | **HR** | **95% CI** | **Events/n** | **HR** | **95% CI** |
| **Weight loss**  **medication**  **(Yes *vs* No)** | 357/  5218 | 1.15 | 0.96, 1.39 | 534/  2074 | 1.00 | 0.85, 1.17 | 895/  7354 | 1.11 | 0.99, 1.26 |

†Multivariable analysis adjusted for age, race/ethnicity, hypogonadism, hypertension, diabetes, use of insulin, muscular wasting, malaise and fatigue, osteoporosis, erectile dysfunction, depression, anterior pituitary disorder, education (percentage of persons older than 25 years with less than 12 years education), percentage of adults below poverty line at census tract level, patients’ primary care (PCP), prostate-specific antigen (PSA), breast cancer screening, and colorectal cancer screening, and mutual adjustment for TTh and metformin.

aCancer incidence [events/n] in this study are extrapolated to the whole SEER-Medicare program

SEER-Medicare guideline presentation has been followed and all counts less than 11 have been suppressed. No male breast cancer mortality data was included due to limited power sample size.

**Supplemental Table 2. Positive use of TTh among men-** effect of weight loss medication, and years of use, on incident PCa, and high-grade at diagnosis among men 65+ years old in SEER-Medicare 2007-2015a

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Incidence†** | | | **High Grade†** | | |
|  | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** |
| **Weight loss**  **medication**  **(Yes *vs* No)** | 264/  16380 | **0.62** | **0.52, 0.74** | 98/  16214 | **0.55** | **0.43, 0.71** |
|  | | | |  |  |  |
| No use | 1138/  45227 | 1 |  | 471/  44560 | 1 |  |
| <1 year | 187/  10107 | **0.74** | **0.60, 0.90** | 70/  9990 | **0.65** | **0.48, 0.87** |
| 1-3 years | 43/  4048 | **0.42** | **0.30, 0.60** | 17/  4022 | **0.41** | **0.25, 0.69** |
| >3 years | 34/  2225 | **0.50** | **0.33, 0.77** | 11/  2202 | **0.39** | **0.20, 0.77** |
| *P for trend* | <.0001 | | | <.0001 | | |

†Multivariable analysis adjusted for age, race/ethnicity, hypogonadism, hypertension, diabetes, use of insulin, muscular wasting, malaise and fatigue, osteoporosis, erectile dysfunction, depression, anterior pituitary disorder, education (percentage of persons older than 25 years with less than 12 years education), percentage of adults below poverty line at census tract level, patients’ primary care (PCP), prostate-specific antigen (PSA), breast cancer screening, and colorectal cancer screening, and mutual adjustment for TTh and metformin.

aCancer incidence [events/n] in this study are extrapolated to the whole SEER-Medicare program

SEER-Medicare guideline presentation has been followed and all counts less than 11 have been suppressed. No advanced stage at diagnosis of PCa was included due to limited power sample size.

**Supplemental Table 3. Negative use of TTh among men-** effect of weight loss medication, and years of use, on incident PCa, grade and stage at diagnosis among men 65+ years old in SEER-Medicare 2007-2015a

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Incidence†** | | | **High Grade†** | | | **Advanced Stage†** | | |
|  | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** |
| **Weight loss**  **medication**  **(Yes *vs* No)** | 4954/  262314 | **0.58** | **0.55, 0.61** | 2247/  259607 | **0.62** | **0.59, 0.66** | 768/  258128 | **0.64** | **0.58, 0.71** |
|  | | | |  |  |  |  |  |  |
| No use | 9115/  268327 | 1 |  | 3912/  263124 | 1 |  | 1419/  260631 | 1 |  |
| <1 year | 1239/  77635 | **0.53** | **0.49, 0.57** | 547/  76943 | **0.54** | **0.49, 0.61** | 212/  76608 | **0.64** | **0.55, 0.75** |
| 1-3 years | 1140/  83076 | **0.42** | **0.39, 0.46** | 509/  82445 | **0.45** | **0.40, 0.50** | 204/  82160 | **0.54** | **0.46, 0.63** |
| >3 years | 2575/  101603 | **0.74** | **0.70, 0.79** | 1191/  100219 | **0.81** | **0.75, 0.88** | 352/  99380 | **0.73** | **0.64, 0.83** |
| *P for trend* | <.0001 | | | <.0001 | | | <.0001 | | |

†Multivariable analysis adjusted for age, race/ethnicity, hypogonadism, hypertension, diabetes, use of insulin, muscular wasting, malaise and fatigue, osteoporosis, erectile dysfunction, depression, anterior pituitary disorder, education (percentage of persons older than 25 years with less than 12 years education), percentage of adults below poverty line at census tract level, patients’ primary care (PCP), prostate-specific antigen (PSA), breast cancer screening, and colorectal cancer screening, and mutual adjustment for TTh and metformin.

aCancer incidence [events/n] in this study are extrapolated to the whole SEER-Medicare program

SEER-Medicare guideline presentation has been followed and all counts less than 11 have been suppressed.

**Supplemental Table 4. Positive use of TTh among men-** effect of weight loss medication, and years of use, on incident CRC, and high-grade at diagnosis among men 65+ years old in SEER-Medicare 2007-2015a

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Incidence†** | | | **High Grade†** | | |
|  | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** |
| **Weight loss**  **medication**  **(Yes *vs* No)** | 69/  16380 | 0.74 | 0.55, 1.01 | 14/  16325 | 1.11 | 0.57, 2.17 |
|  | | | |  |  |  |
| No use | 255/  45227 | 1 |  | 40/  45012 | 1 |  |
| <1 year | 37/  10107 | 0.67 | 0.45, 0.98 | <11/  10077 | 0.85 | 0.36, 1.98 |
| 1-3 years | 22/  4048 | 0.89 | 0.54, 1.49 | <11/  4032 | 2.12 | 0.83, 5.37 |
| >3 years | <11/  2225 | 0.84 | 0.42, 1.67 | <11/  2216 | 0.62 | 0.08, 4.78 |
| *P for trend* | 0.2203 | | | 0.3646 | | |

†Multivariable analysis adjusted for age, race/ethnicity, hypogonadism, hypertension, diabetes, use of insulin, muscular wasting, malaise and fatigue, osteoporosis, erectile dysfunction, depression, anterior pituitary disorder, education (percentage of persons older than 25 years with less than 12 years education), percentage of adults below poverty line at census tract level, patients’ primary care (PCP), prostate-specific antigen (PSA), breast cancer screening, and colorectal cancer screening, and mutual adjustment for TTh and metformin.

aCancer incidence [events/n] in this study are extrapolated to the whole SEER-Medicare program

SEER-Medicare guideline presentation has been followed and all counts less than 11 have been suppressed. No advanced stage at diagnosis of CRC was included due to limited power sample size.

**Supplemental Table 5. Negative use of TTh among men-** effect of weight loss medication, and years of use, on incident CRC, and high-grade at diagnosis among men 65+ years old in SEER-Medicare 2007-2015a

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Incidence†** | | | **High Grade†** | | | **Advanced Stage†** | | |
|  | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** |
| **Weight loss**  **medication**  **(Yes *vs* No)** | 2005/  262314 | **0.86** | **0.80, 0.92** | 303/  260612 | 0.97 | 0.81, 1.15 | 826/  261135 | 0.96 | 0.86, 1.07 |
|  | | | |  |  |  |  |  |  |
| No use | 2507/  268327 | 1 |  | 359/  266179 | 1 |  | 959/  266779 | 1 |  |
| <1 year | 580/  77635 | **0.87** | **0.78, 0.97** | 97/  77152 | 1.09 | 0.86, 1.38 | 247/  77302 | 1.03 | 0.88, 1.21 |
| 1-3 years | 585/  83076 | **0.79** | **0.71, 0.87** | 94/  82585 | 0.94 | 0.74, 1.20 | 269/  82760 | 0.98 | 0.85, 1.14 |
| >3 years | 840/  101603 | **0.90** | **0.82, 0.99** | 112/  100875 | 0.90 | 0.71, 1.14 | 310/  101073 | 0.89 | 0.77, 1.03 |
| *P for trend* | <.0001 | | | 0.6135 | | | 0.3592 | | |

†Multivariable analysis adjusted for age, race/ethnicity, hypogonadism, hypertension, diabetes, use of insulin, muscular wasting, malaise and fatigue, osteoporosis, erectile dysfunction, depression, anterior pituitary disorder, education (percentage of persons older than 25 years with less than 12 years education), percentage of adults below poverty line at census tract level, patients’ primary care (PCP), prostate-specific antigen (PSA), breast cancer screening, and colorectal cancer screening, and mutual adjustment for TTh and metformin.

aCancer incidence [events/n] in this study are extrapolated to the whole SEER-Medicare program

SEER-Medicare guideline presentation has been followed and all counts less than 11 have been suppressed.

**Supplemental Table 6. Positive use of TTh among men-** effect of weight loss medication, and years of use, on incident male breast cancer, and high-grade at diagnosis among men 65+ years old in SEER-Medicare 2007-2015a

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | **Incidence†** | | | **High Grade†** | | |
|  | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** |
| **Weight loss**  **medication**  **(Yes *vs* No)** | 21/  16380 | 1.60 | 0.62, 4.15 | 11/  16375 | 0.47 | 0.06, 4.05 |
|  | | | |  |  |  |
| No use | 14/  45227 | 1.22 | 0.34, 4.35 | <11/  45222 | 1 |  |
| <1 year | <11/  10107 | 3.20 | 0.99, 10.37 | <11/  10105 | 0.74 | 0.10, 5.76 |
| 1-3 years | <11/  4048 | NDb | ND | <11/  4045 | ND | ND |
| >3 years | <11/  2225 | ND | ND | <11/  2225 | ND | ND |
| *P for trend* | <.0001 | | | <.0001 | | |

†Multivariable analysis adjusted for age, race/ethnicity, hypogonadism, hypertension, diabetes, use of insulin, muscular wasting, malaise and fatigue, osteoporosis, erectile dysfunction, depression, anterior pituitary disorder, education (percentage of persons older than 25 years with less than 12 years education), percentage of adults below poverty line at census tract level, patients’ primary care (PCP), prostate-specific antigen (PSA), breast cancer screening, and colorectal cancer screening, and mutual adjustment for TTh and metformin.

aCancer incidence [events/n] in this study are extrapolated to the whole SEER-Medicare program

SEER-Medicare guideline presentation has been followed and all counts less than 11 have been suppressed. No advanced stage at diagnosis of male breast cancer was included due to limited power sample size.

bNot determined

**Supplemental Table 7. Negative use of TTh among men-** effect of weight loss medication, and years of use, on incident male breast cancer, and high-grade at diagnosis among men 65+ years old in SEER-Medicare 2007-2015a

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Incidence†** | | | **High Grade†** | | | **Advanced Stage†** | | |
|  | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** |
| **Weight loss**  **medication**  **(Yes *vs* No)** | 120/  262314 | 0.87 | 0.57, 1.32 | 34/  262275 | 0.79 | 0.35, 1.80 | 26/  262273 | 1.43 | 0.66, 3.13 |
|  | | | |  |  |  |  |  |  |
| No use | 65/  268327 | 1 |  | 18/  268280 | 1 |  | 12/  268274 | 1 |  |
| <1 year | 16/  77635 | 0.91 | 0.50, 1.65 | <11/  77626 | 1.28 | 0.46, 3.57 | <11/  77622 | 0.97 | 0.27, 3.48 |
| 1-3 years | 11/  83076 | 0.61 | 0.31, 1.20 | <11/  83066 | 0.20 | 0.03, 1.52 | <11/  83068 | 0.95 | 0.26, 3.43 |
| >3 years | 28/  101603 | 1.05 | 0.63, 1.74 | <11/  101583 | 0.90 | 0.32, 2.53 | <11/  101583 | 2.23 | 0.88, 5.65 |
| *P for trend* | 0.4832 | | | 0.3906 | | | 0.3304 | | |

†Multivariable analysis adjusted for age, race/ethnicity, hypogonadism, hypertension, diabetes, use of insulin, muscular wasting, malaise and fatigue, osteoporosis, erectile dysfunction, depression, anterior pituitary disorder, education (percentage of persons older than 25 years with less than 12 years education), percentage of adults below poverty line at census tract level, patients’ primary care (PCP), prostate-specific antigen (PSA), breast cancer screening, and colorectal cancer screening, and mutual adjustment for TTh and metformin.

aCancer incidence [events/n] in this study are extrapolated to the whole SEER-Medicare program

SEER-Medicare guideline presentation has been followed and all counts less than 11 have been suppressed.

**Supplemental Table 8.** Effect of osteoporosis medication on incident hormone-related cancers (HRCs) among men 65+ years old in SEER-Medicare 2007-2015a

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Incidence HRCs†** | | |
|  | **Events/n** | **OR** | **95% CI** |
| **osteoporosis medication**  **(Yes *vs* No)** | 45941/  219836 | **1.03** | **0.95, 1.13** |

†Multivariable analysis adjusted for age, race/ethnicity, hypogonadism, obesity, hypertension, diabetes, use of insulin, muscular wasting, malaise and fatigue, erectile dysfunction, depression, anterior pituitary disorder, education (percentage of persons older than 25 years with less than 12 years education), percentage of adults below poverty line at census tract level, patients’ primary care (PCP), prostate-specific antigen (PSA), breast cancer screening, and colorectal cancer screening, and mutual adjustment for TTh  and metformin.

aCancer incidence [events/n] in this study are extrapolated to the whole SEER-Medicare program

SEER-Medicare guideline presentation has been followed and all counts less than 11 have been suppressed.

**Supplemental Table 9. Propensity score matching results (Table 5-1. Only HRCs)-** Effect of weight loss medication, and years of use, on incident HRCs, grade and stage at diagnosis among men 65+ years old in SEER-Medicare 2007-2015a

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **Incidence†** | | | **High Grade†** | | | **Advanced Stage†** | | |
|  | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** | **Events/n** | **OR** | **95% CI** |
| **Weight loss**  **medication**  **(Yes *vs* No)** | 3595/  11410 | **0.68** | **0.65, 0.72** | 1323/  9138 | **0.69** | **0.65, 0.73** | 818/  8633 | **0.80** | **0.75, 0.86** |
|  | | | |  |  |  |  |  |  |
| No use | 3451/  8563 | 1 |  | 1262/  6375 | 1 |  | 666/  5778 | 1 |  |
| <1 year | 971/  3387 | **0.64** | **0.59, 0.68** | 342/  2758 | **0.62** | **0.57, 0.67** | 239/  2655 | **0.80** | **0.73, 0.88** |
| 1-3 years | 902/  3385 | **0.55** | **0.51, 0.59** | 315/  2798 | **0.52** | **0.48, 0.57** | 251/  2734 | **0.78** | **0.71, 0.86** |
| >3 years | 1721/  4637 | **0.82** | **0.78, 0.87** | 665/  3582 | **0.88** | **0.82, 0.94** | 327/  3244 | **0.82** | **0.75, 0.90** |
| *P for trend* | <.0001 | | | <.0001 | | | <.0001 | | |

†Multivariable analysis adjusted for age, race/ethnicity, hypogonadism, obesity, hypertension, diabetes, use of insulin, muscular wasting, malaise and fatigue, osteoporosis, erectile dysfunction, depression, anterior pituitary disorder, education (percentage of persons older than 25 years with less than 12 years education), percentage of adults below poverty line at census tract level, patients’ primary care (PCP), prostate-specific antigen (PSA), breast cancer screening, and colorectal cancer screening, and mutual adjustment for TTh and metformin.

aCancer incidence [events/n] in this study are extrapolated to the whole SEER-Medicare program

SEER-Medicare guideline presentation has been followed and all counts less than 11 have been suppressed.