# Behavior within a Clinical Trial and Implications for Mammography Guidelines

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# U.S. Preventive Services Task Force (USPSTF) 2016 Guidelines for Women in 40's:

*"The decision to start screening mammography in women prior to age 50 years should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin biennial screening between the ages of 40 and 49 years"*

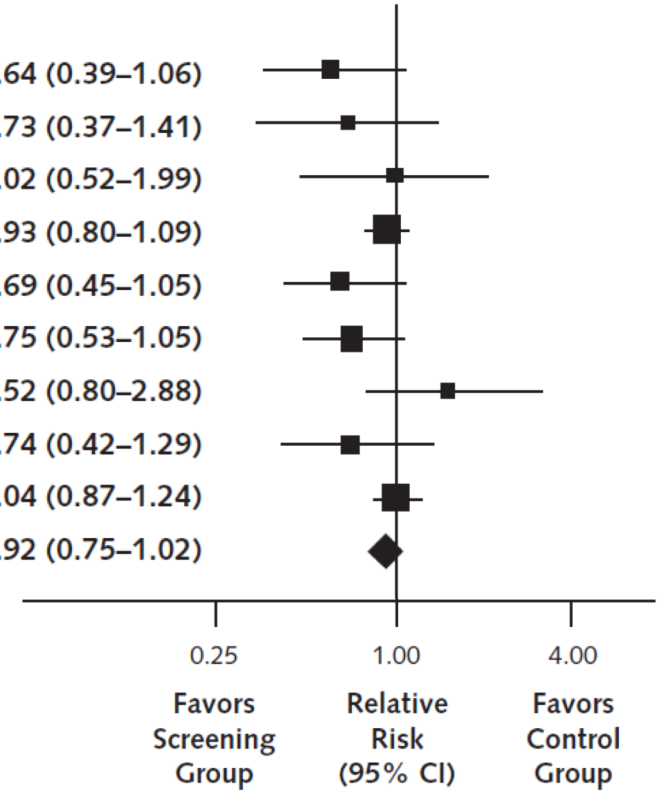
# USPSTF 2016 Guidelines Based on RCT's

**Annals of Internal Medicine** REVIEW

## Effectiveness of Breast Cancer Screening: Systematic Review and Meta-analysis to Update the 2009 U.S. Preventive Services Task Force Recommendation

Heidi D. Nelson, MD, MPH; Rochelle Fu, PhD; Amy Cantor, MD, MPH; Miranda Pappas, MA; Monica Daeges, BA; and Linda Humphrey, MD, MPH

| Author, Year (Reference) | Trial Name | Mean Follow-up, *y* | Relative Risk (95% CI) |
|---|---|---|---|
| Women aged 39–49 y | | | |
| Nyström et al, 2002 (30)* | MMST II | 11.2 | 0.64 (0.39–1.06) |
| Tabár et al, 1995 (26) | Kopparberg | 12.5 | 0.73 (0.37–1.41) |
| Tabár et al, 1995 (26) | Östergötland | 12.5 | 1.02 (0.52–1.99) |
| Moss et al, 2015 (27) | Age | 17.5 | 0.93 (0.80–1.09) |
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| Habbema et al, 1986 (29) | HIP | 14.0 | 0.75 (0.53–1.05) |
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| Miller et al, 2014 (15) | CNBSS-1 | 21.9 | 1.04 (0.87–1.24) |
| Overall ($I^2$ = 25%; $P$ = 0.230) | | | 0.92 (0.75–1.02) |



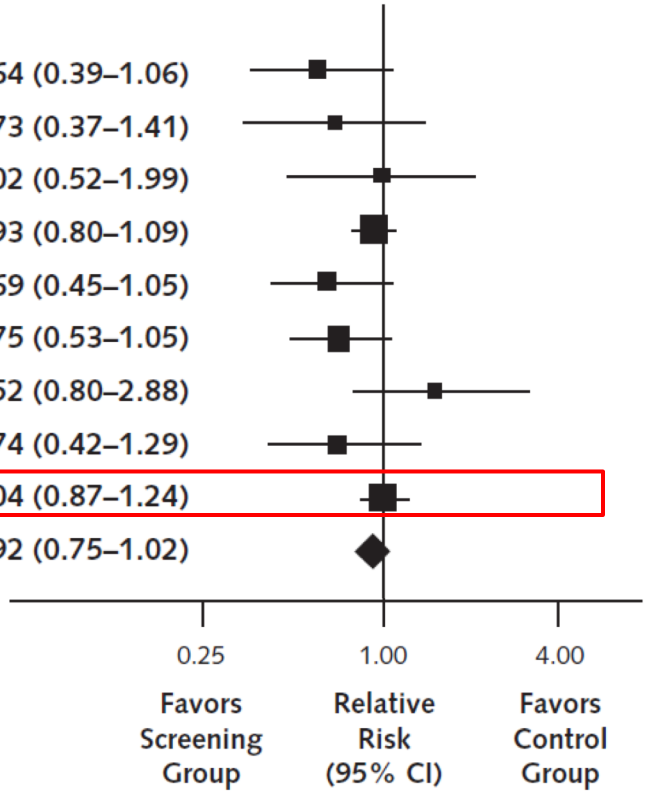
# CNBSS Consistent with Meta-analysis of RCT's

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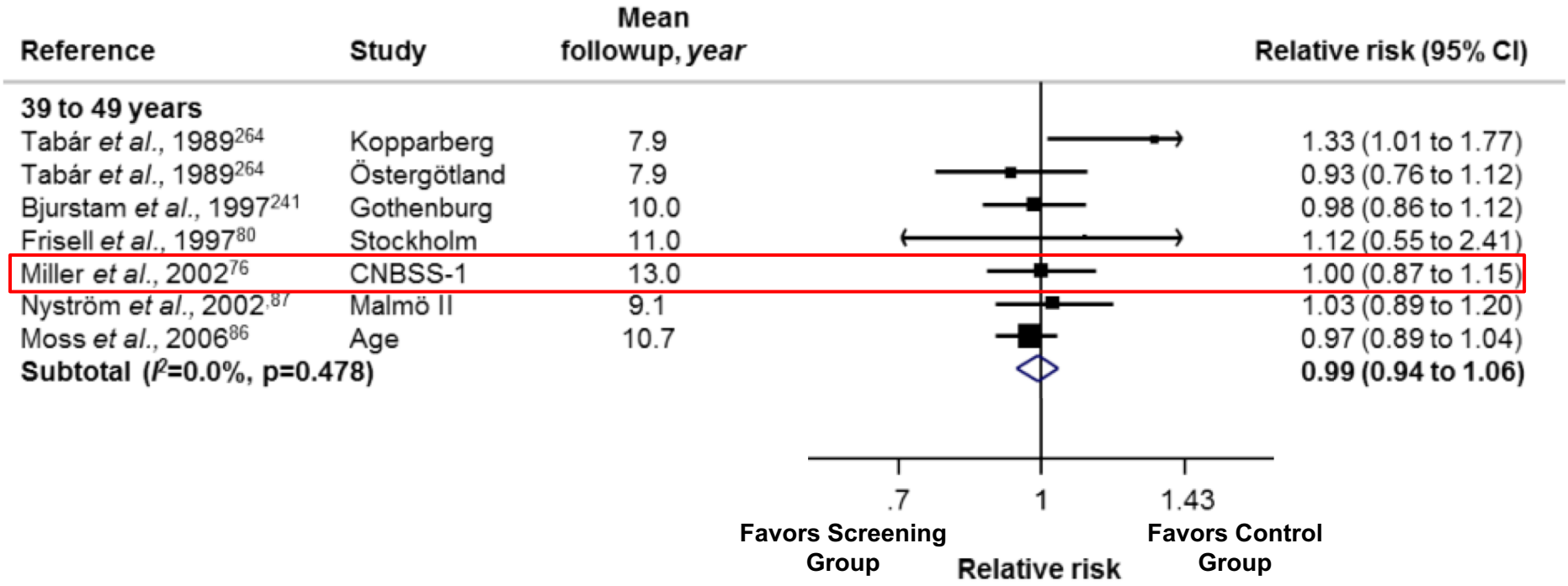
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# Meta-analysis for All Cause Mortality

***Evidence Synthesis***
**Number 124**

**Screening for Breast Cancer: A Systematic Review to Update the 2009 U.S. Preventive Services Task Force Recommendation**



# I Examine Micro Data from the CNBSS

- Canadian National Breast Screening Study
  - 89,835 patients enrolled
  - Patients received mammograms for 4 to 5 years during active study period
  - Recorded mammogram receipt, even in control group
  - Followed patient outcomes from 1980 to 2005 through cancer registry and death records (no attrition)
  - Collected risk factors and demographic data

# I Examine Behavior within a Clinical Trial

- Medical literature examines clinical trials
  - See Nelson (2016)
- Economics literature examines mammogram takeup
  - Strumpf, Chai, and Kadiyala (2010)
  - Kadiyala and Strumpf (2011, 2016)
  - Zanella and Banerjee (2016)
  - Buchmueller and Goldzahl (2018)
  - Kim and Lee (2017)

# I Examine Behavior within a Clinical Trial

- I build on LATE and MTE literatures from economics
  - Bjorklund and Moffitt (1987)
  - Imbens and Angrist (1994)
  - Heckman and Vytlacil (1999, 2005, 2007)
  - Vytlacil (2002)
  - Brinch, Mogstad, Wiswall (2015)

# I Examine Behavior within a Clinical Trial

"Doing More When You're Running LATE: Applying Marginal Treatment Effect Methods to Examine Treatment Effect Heterogeneity in Experiments." *NBER WP 22363.*

"Extrapolation Using Selection and Moral Hazard Heterogeneity from Within the Oregon Health Insurance Experiment." *NBER WP 24647.*

"How to Examine External Validity Within an Experiment." *NBER WP 24834.*

"Behavior within a Clinical Trial and Implications for Mammography Guidelines." *NBER WP 25049.*

"A Model of a Randomized Experiment with an Application to the PROWESS Clinical Trial." *NBER WP 25670.*

"Counting Defiers." *NBER WP 25671.*

# Behavior within a Clinical Trial and Implications for Mammography Guidelines

- **Model**
  - **First Stage: Mammography**
  - Second Stage: Mortality
- Results
  1. Selection Heterogeneity
     - *Women more likely to receive mammograms are healthier*
  2. Treatment Effect Heterogeneity
     - *Women more likely to receive mammograms are more likely to be harmed by them*
- Robustness
- Conclusions

**First Stage:**

$$V = V_U + (V_T - V_U)D$$
$$V_T - V_U = \mu_D(Z) - \nu_D$$

**First Stage:**

$$V = V_U + (V_T - V_U)D$$
$$V_T - V_U = \mu_D(Z) - \nu_D$$

**Assumptions:**

**A.1.** (Continuity) $F(\cdot)$: absolutely continuous with respect to the Lebesgue measure

**First Stage:**

$$V = V_U + (V_T - V_U)D$$
$$V_T - V_U = \mu_D(Z) - \nu_D \qquad U_D = F(\nu_D),\ U_D \sim U[0,1]$$

**Assumptions:**

**A.1.** (Continuity) $F(\cdot)$: absolutely continuous with respect to the Lebesgue measure

**Proof:** $\boldsymbol{U_D \sim U[0,1]}$

$$\begin{aligned} F_{U_D}(u) &= P(U_D \le u) \\ &= P(F(\nu_D) \le u) \\ &= P(\nu_D \le F^{-1}(u)) \qquad (F(\cdot) \text{ absolutely continuous by A.1}) \\ &= F(F^{-1}(u)) = u \end{aligned}$$

**First Stage:**

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$$V_T - V_U = \mu_D(Z) - \nu_D \qquad U_D = F(\nu_D),\ U_D \sim U[0,1]$$

**Assumptions:**

**A.1.** (Continuity) $F(\cdot)$: absolutely continuous with respect to the Lebesgue measure

**A.2.** (Independence) $(U_D, \gamma_T)$ and $(U_D, \gamma_U) \perp Z$

**First Stage:**

$$
\begin{aligned}
V &= V_U + (V_T - V_U)D \\
V_T - V_U &= \mu_D(Z) - \nu_D \qquad\qquad U_D = F(\nu_D),\ U_D \sim U[0,1] \\
D &= 1\{0 \le V_T - V_U\} \\
\Rightarrow D &= 1\{U_D \le P(D = 1 \mid Z = z)\}
\end{aligned}
$$

**Assumptions:**

**A.1.** (Continuity) $F(\cdot)$: absolutely continuous with respect to the Lebesgue measure

**A.2.** (Independence) $(U_D, \gamma_T)$ and $(U_D, \gamma_U) \perp Z$

**Proof:** $\boldsymbol{D = 1\{U_D \le \mathrm{P}(D = 1 \mid Z = z)\}}$

$$
\begin{aligned}
D &= 1\{0 \le V_T - V_U\} \\
&= 1\{0 \le \mu_D(Z) - \nu_D\} \\
&= 1\{\nu_D \le \mu_D(Z)\} \\
&= 1\{F(\nu_D) \le F(\mu_D(Z))\} && \text{(definition of } F(\cdot) \text{ from A.1)} \\
&= 1\{U_D \le F(\mu_D(Z))\} && (U_D = F(\nu_D) \text{ by definition}) \\
&= 1\{U_D \le \mathrm{P}(D = 1 \mid Z = z)\},
\end{aligned}
$$

where the last equality follows from

$$
\begin{aligned}
F(\mu_D(Z)) &= \mathrm{P}(\nu_D \le \mu_D(Z)) \\
&= \mathrm{P}(\nu_D \le \mu_D(z) \mid Z = z) && (\nu_D \perp Z \text{ by A.2}) \\
&= \mathrm{P}(0 \le \mu_D(Z) - \nu_D \mid Z = z) \\
&= \mathrm{P}(0 \le V_T - V_U \mid Z = z) \\
&= \mathrm{P}(D = 1 \mid Z = z).
\end{aligned}
$$

**First Stage:**

$$
\begin{aligned}
V &= V_U + (V_T - V_U)D \\
V_T - V_U &= \mu_D(Z) - \nu_D \qquad\qquad U_D = F(\nu_D),\ U_D \sim U[0,1] \\
D &= 1\{0 \leq V_T - V_U\} \\
\Rightarrow D &= 1\{U_D \leq P(D = 1 \,|\, Z = z)\}
\end{aligned}
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**Assumptions:**

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**A.3.** (Instrument Relevance) $\mu_D(Z)$: nondegenerate random variable

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& D = 1\{0 \le V_T - V_U\} \\
\Rightarrow & D = 1\{U_D \le P(D = 1 \mid Z = z)\} \\
& Z = 0: \quad D = 1\{U_D \le p_C\}, \quad p_C = P(D = 1 \mid Z = 0) \\
& Z = 1: \quad D = 1\{U_D \le p_I\}, \quad p_I = P(D = 1 \mid Z = 1)
\end{aligned}
$$

**Assumptions:**

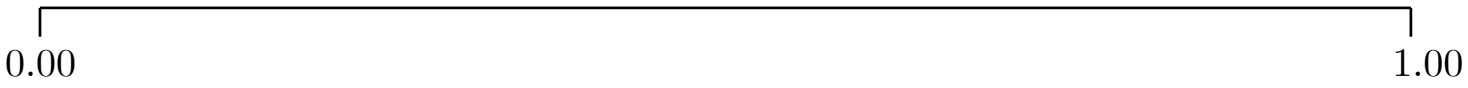
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$U_D$: unobserved net cost of treatment

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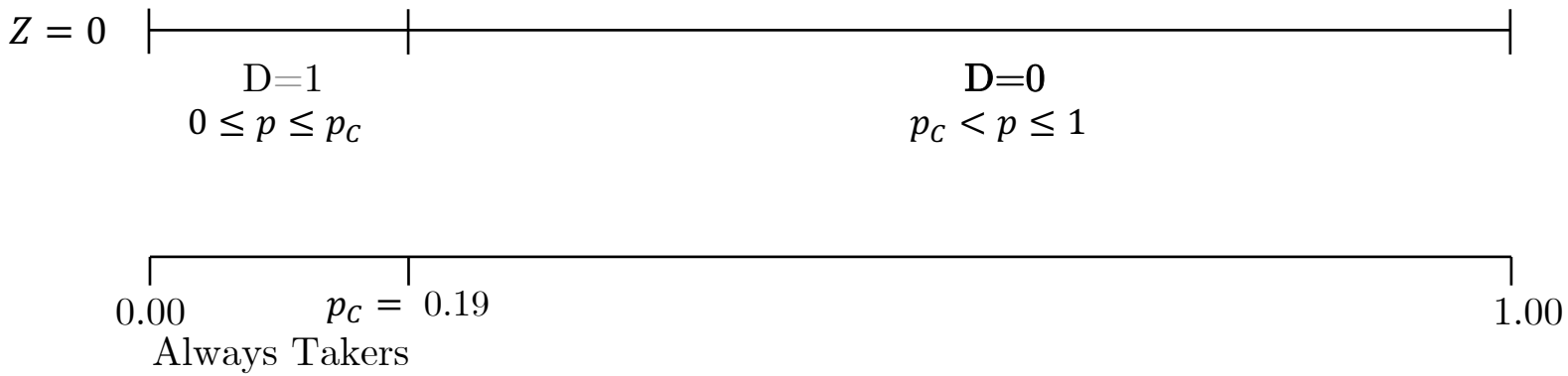
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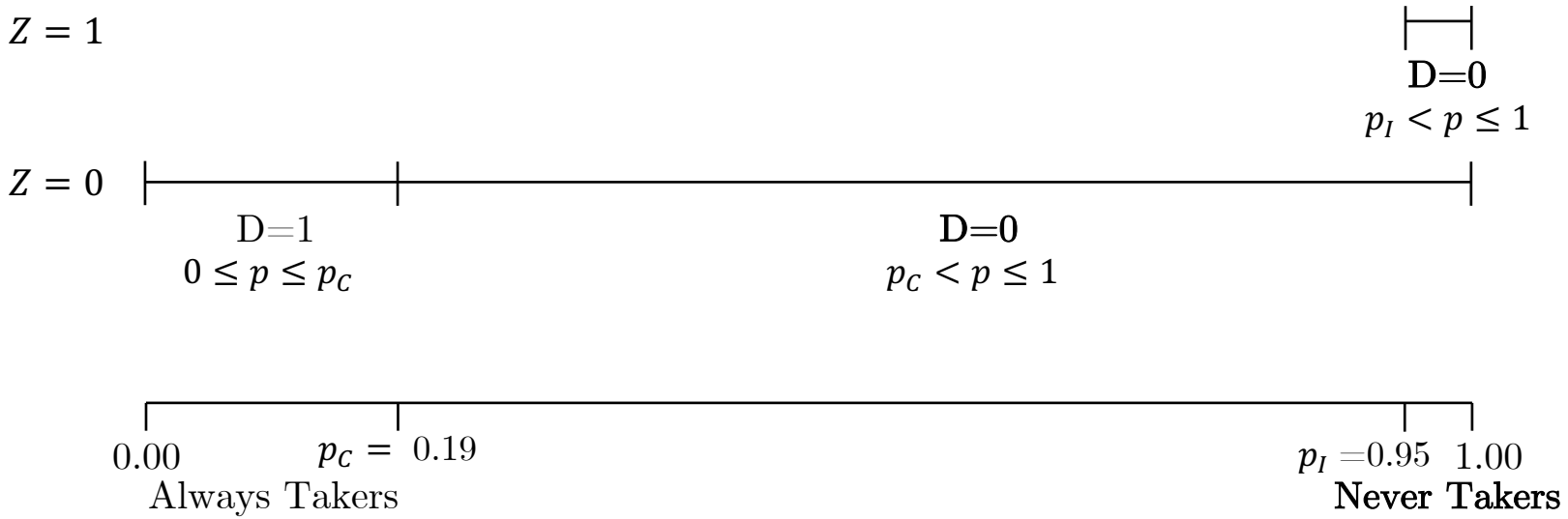
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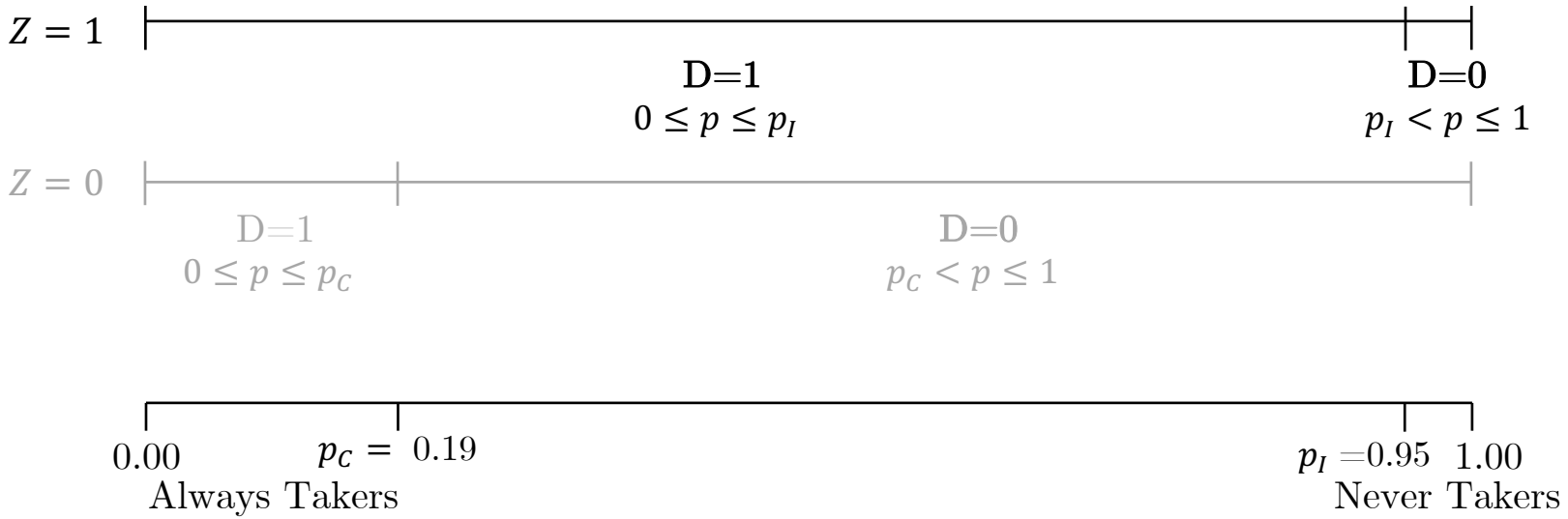
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$U_D$: unobserved net cost of treatment

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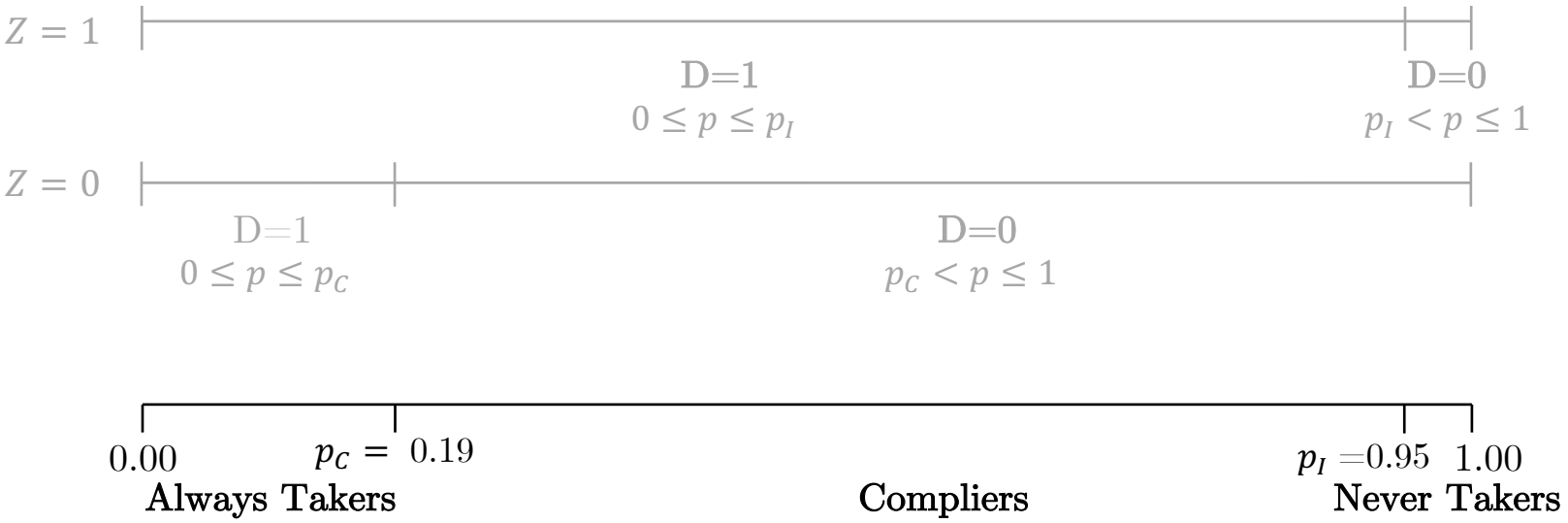
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$U_D$: unobserved net cost of treatment

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\end{aligned}
$$

**Second Stage:**

$$
\begin{aligned}
& Y = Y_U + (Y_T - Y_U)D \\
& Y_T = g_T(U_D, \gamma_T) \\
& Y_U = g_U(U_D, \gamma_U) \qquad\qquad Z \perp (\gamma_T, \gamma_U) \text{ by A.2.}
\end{aligned}
$$

**Assumptions (Second Stage):**

**A.4.** (Treated and Untreated) $0 < \mathrm{P}(D = 1) < 1$

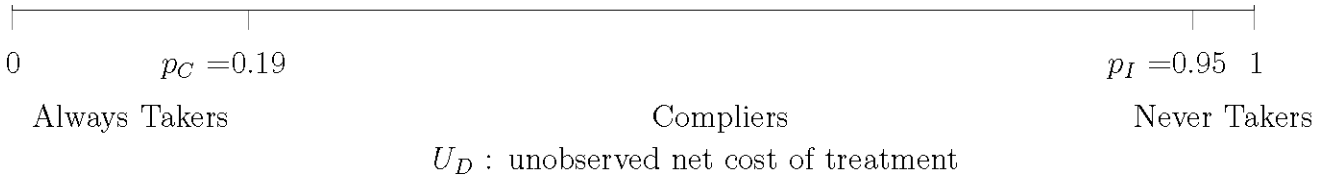
**A.5.** (Finite Average Outcomes) $E[Y_T], E[Y_U]$ are finite

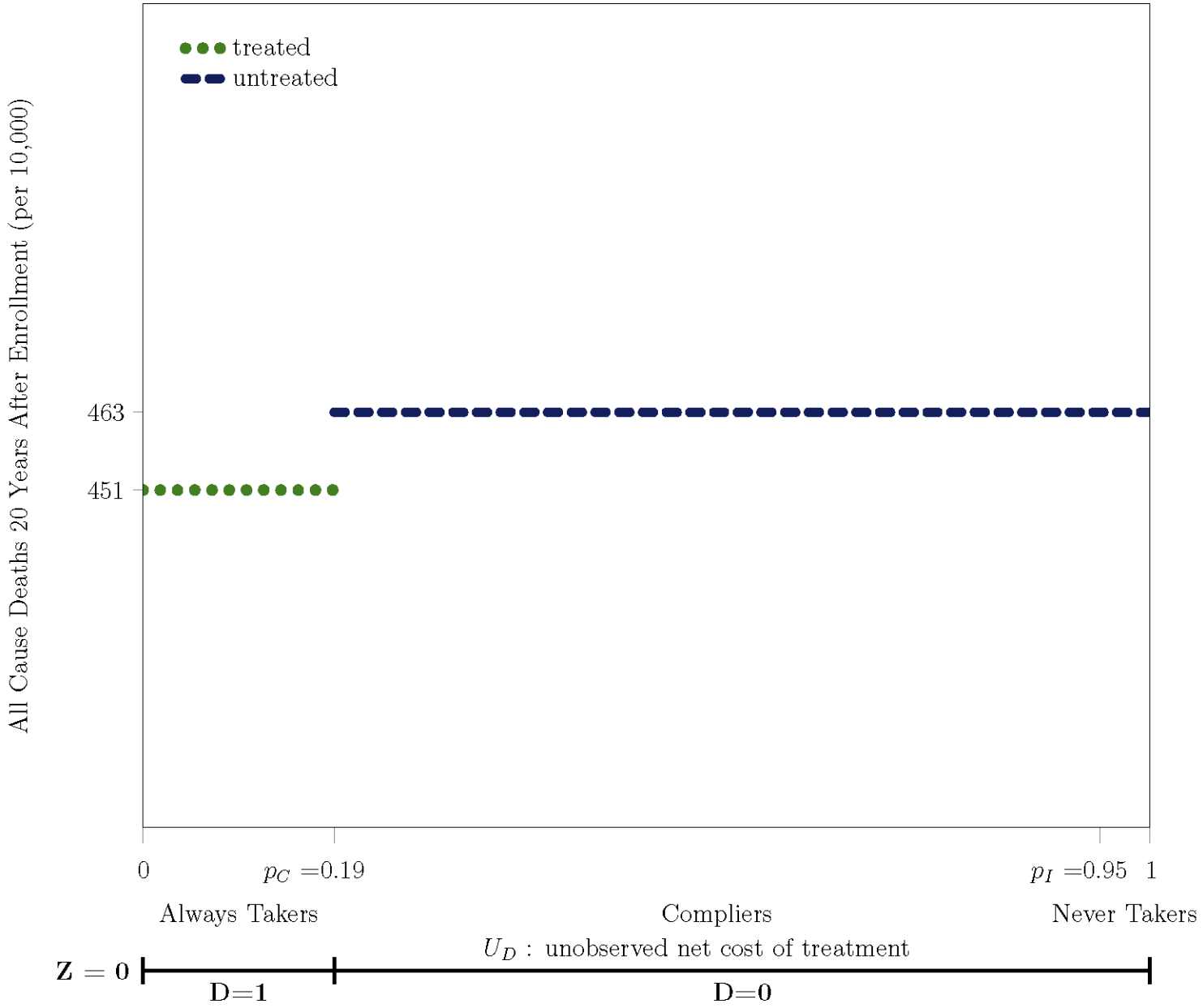
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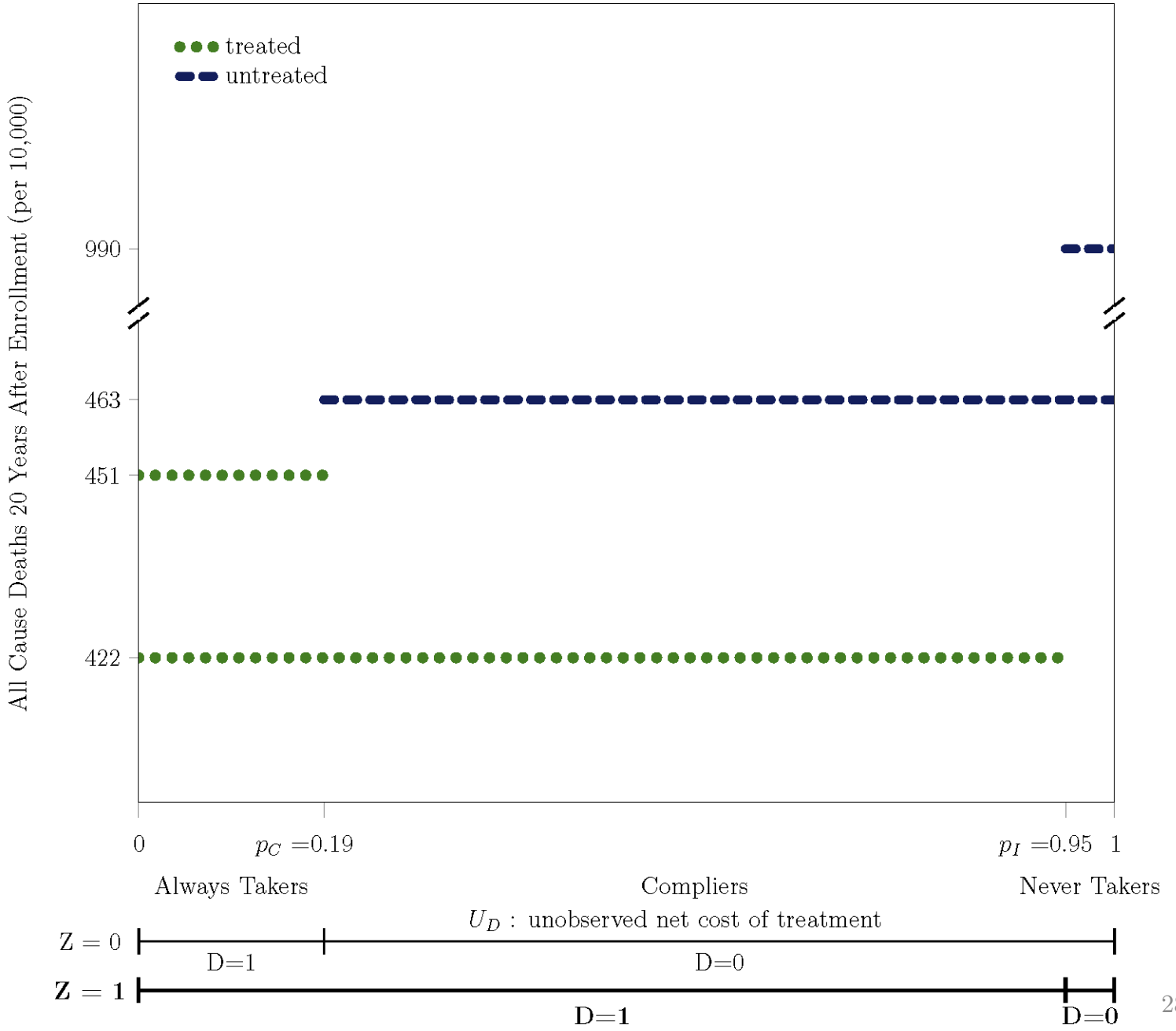
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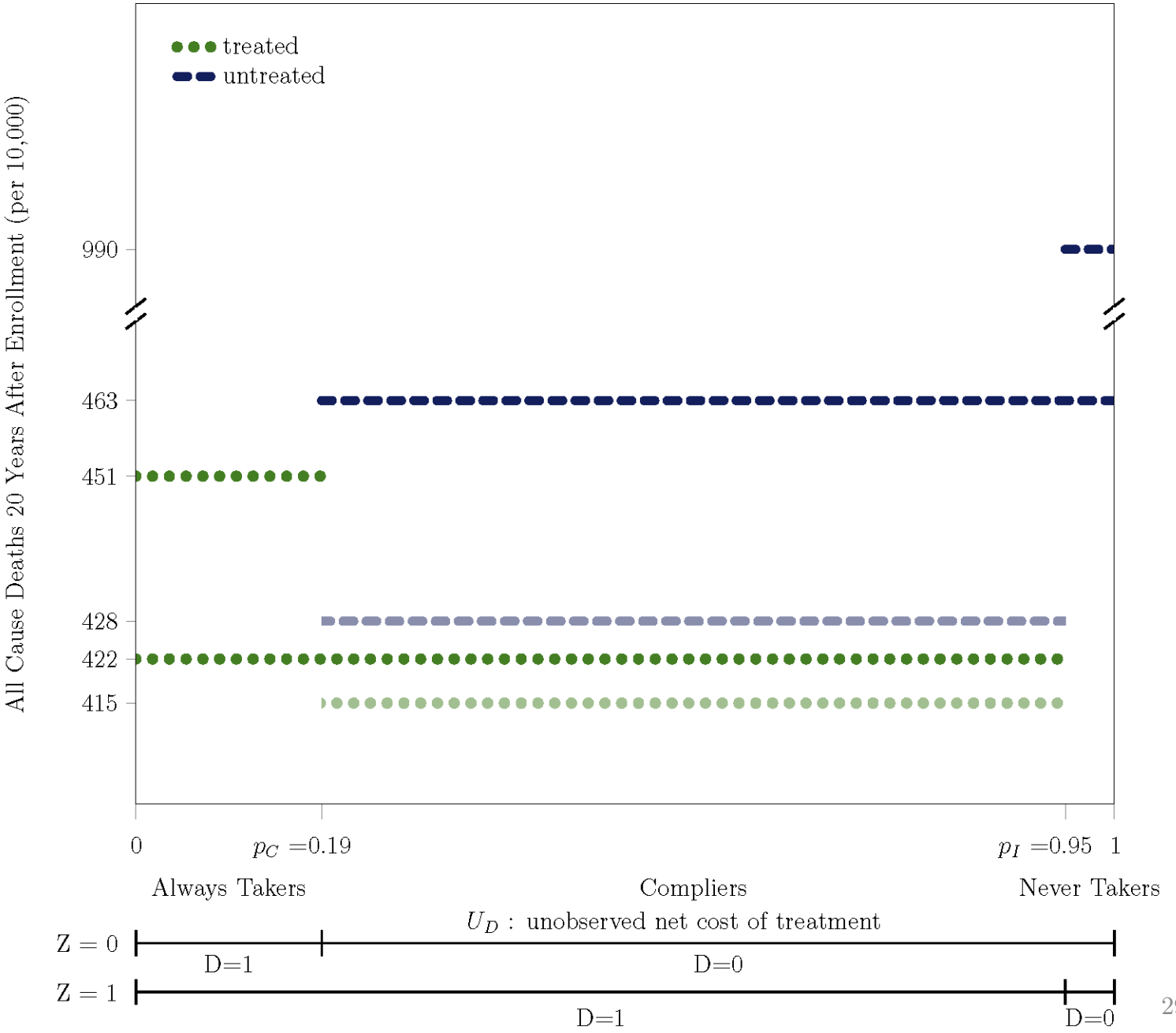
**Second Stage:**

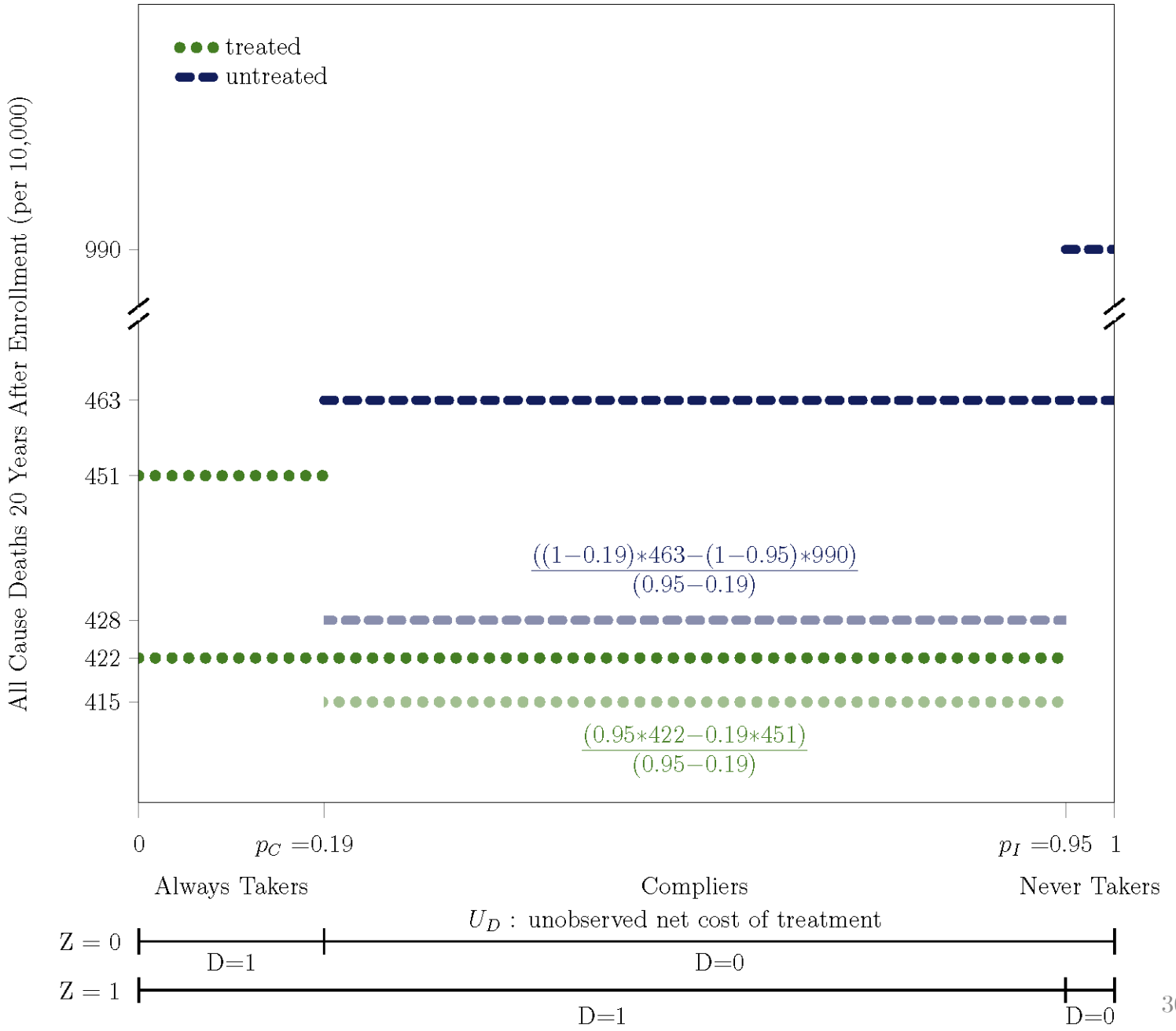
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&Y_T = g_T(U_D, \gamma_T) \\
&Y_U = g_U(U_D, \gamma_U) \qquad\qquad Z \perp (\gamma_T, \gamma_U) \text{ by A.2.}
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$$

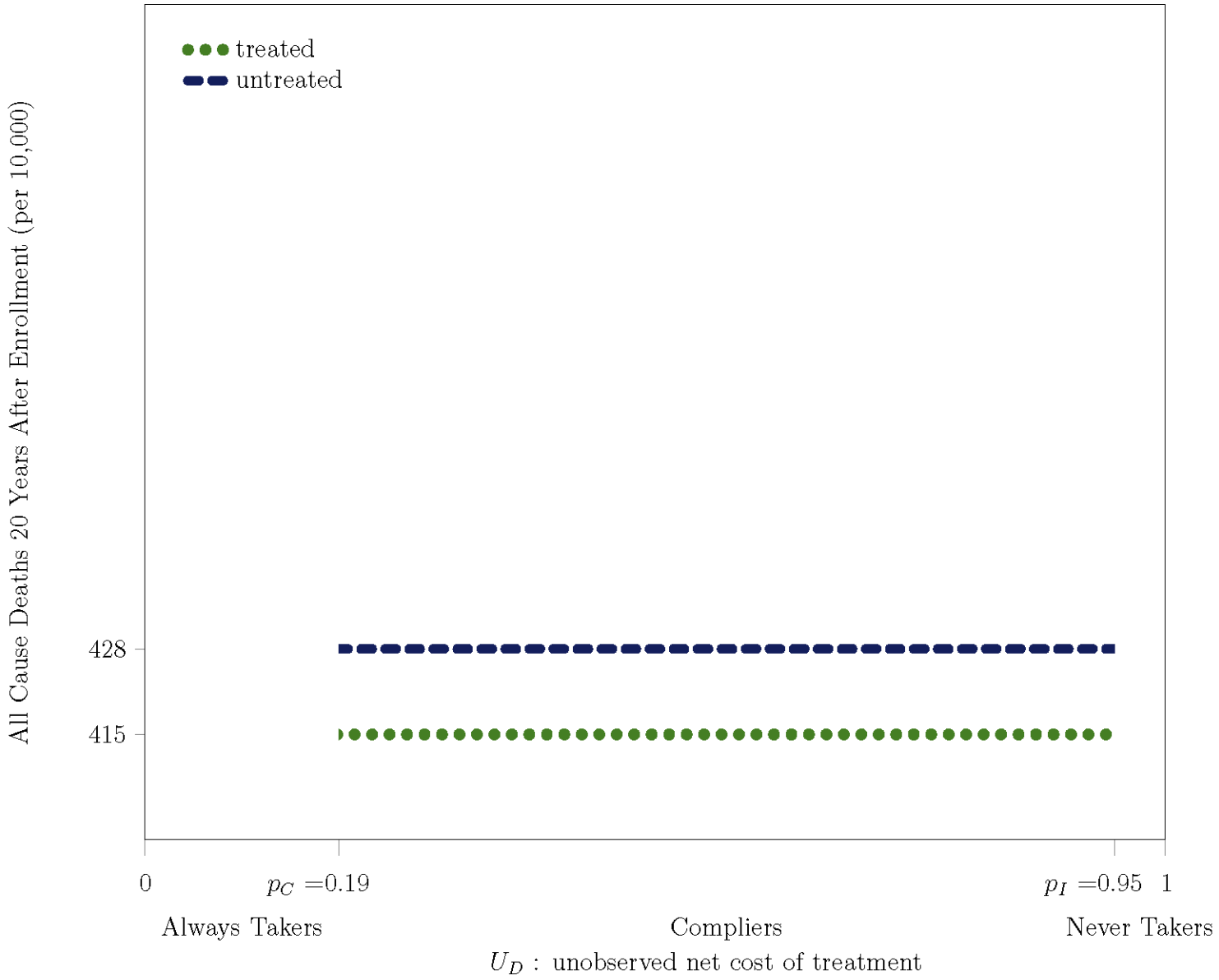


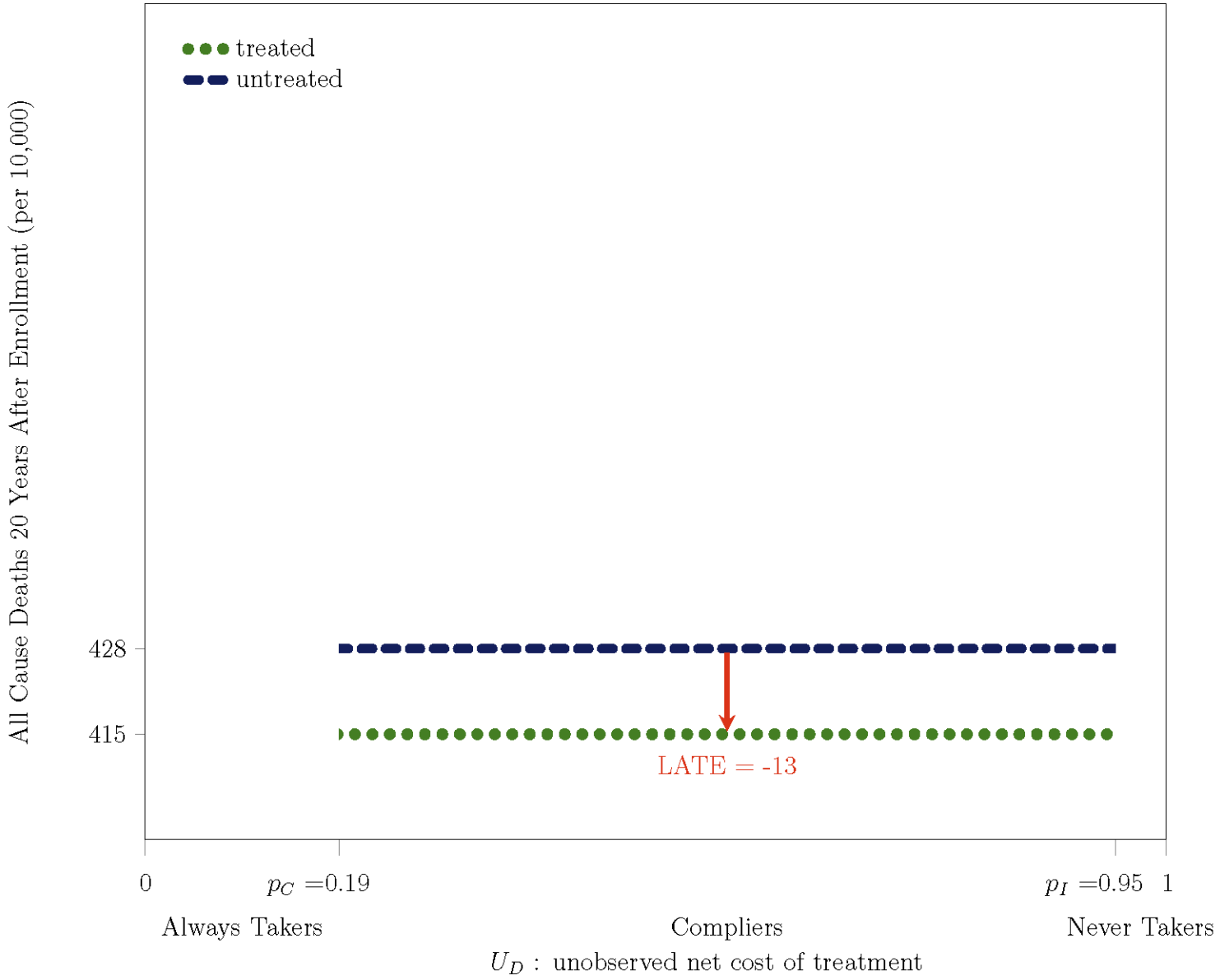

treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
463
451
0
$p_C$ =0.19
$p_I$ =0.95
1
Always Takers
Compliers
Never Takers
$U_D$ : unobserved net cost of treatment
Z = 0
D=1
D=0

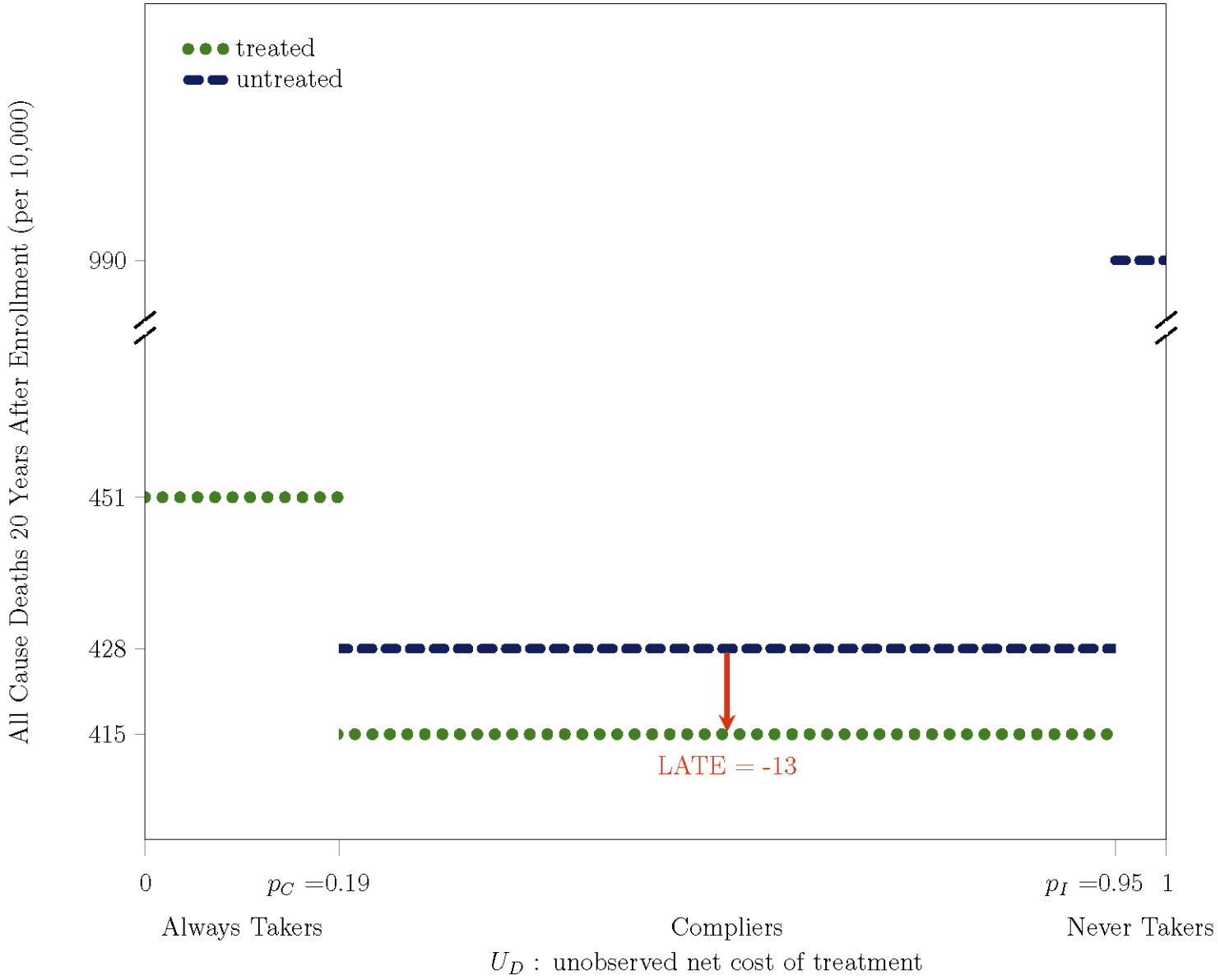

treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
990
463
451
422
0
$p_C$ =0.19
$p_I$ =0.95
1
Always Takers
Compliers
Never Takers
$U_D$ : unobserved net cost of treatment
Z = 0
D=1
D=0
Z = 1
D=1
D=0


treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
990
463
451
428
422
415
0
$p_C$ =0.19
$p_I$ =0.95
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Always Takers
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Z = 0
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D=0
Z = 1
D=1
D=0


treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
990
463
451
428
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415
((1−0.19)∗463−(1−0.95)∗990)
(0.95−0.19)
(0.95∗422−0.19∗451)
(0.95−0.19)
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$p_C$ =0.19
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D=0
Z = 1
D=1
D=0


treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
428
415
0
$p_C$ =0.19
$p_I$ =0.95
1
Always Takers
Compliers
Never Takers
$U_D$ : unobserved net cost of treatment


treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
428
415
LATE = -13
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treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
990
451
428
415
LATE = -13
0
$p_C$ =0.19
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1
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Compliers
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# Behavior within a Clinical Trial and Implications for Mammography Guidelines

- Model
  - First Stage: Mammography
  - Second Stage: Mortality
- **Results**
  1. **Selection Heterogeneity**
     - ***Women more likely to receive mammograms are healthier***
  2. Treatment Effect Heterogeneity
     - *Women more likely to receive mammograms are more likely to be harmed by them*
- Robustness
- Conclusions

**First Stage:**

$$
\begin{aligned}
V &= V_U + (V_T - V_U)D \\
V_T - V_U &= \mu_D(Z) - \nu_D \qquad\qquad U_D = F(\nu_D),\ U_D \sim U[0,1] \\
D &= 1\{0 \leq V_T - V_U\} \\
\Rightarrow D &= 1\{U_D \leq P(D=1 \mid Z=z)\}
\end{aligned}
$$

**Second Stage:**

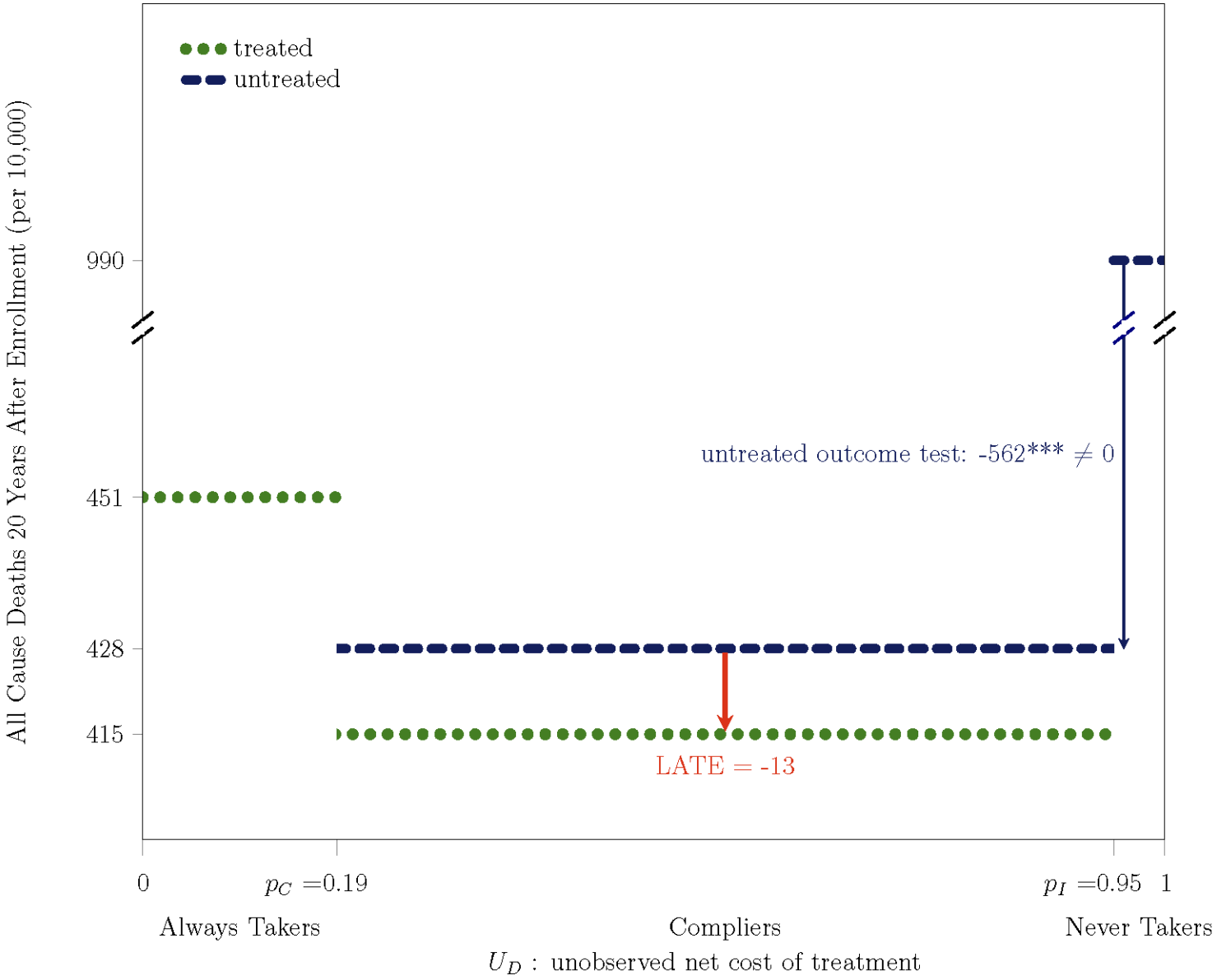
$$
\begin{aligned}
Y &= Y_U + (Y_T - Y_U)D \\
Y_T &= g_T(U_D, \gamma_T) \\
Y_U &= g_U(U_D, \gamma_U) \qquad\qquad Z \perp (\gamma_T, \gamma_U) \text{ by A.2.}
\end{aligned}
$$

**Untreated Outcome Test:**

$$
\mathrm{E}[Y_U \mid p_C < U_D \leq p_I] - \mathrm{E}[Y_U \mid p_I < U_D \leq 1] = \int_0^1 (\omega(p, p_C, p_I) - \omega(p, p_I, 1))\,\mathrm{MUO}(p)\,\mathrm{d}p
$$

where $\omega(p, p_L, p_H) = 1\{p_L \leq p < p_H\}/(p_H - p_L)$

(Bertanha and Imbens (2014); Guo, Cheng, Lorch, and Small (2014); Black, Joo, LaLonde, Smith, and Taylor (2015); Mogstad, Santos, and Torgovitsky (2018).)


treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
990
451
428
415
untreated outcome test: -562*** ≠ 0
LATE = -13
0
$p_C$ =0.19
$p_I$ =0.95
1
Always Takers
Compliers
Never Takers
$U_D$ : unobserved net cost of treatment

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V &= V_U + (V_T - V_U)D \\
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D &= 1\{0 \leq V_T - V_U\} \\
\Rightarrow D &= 1\{U_D \leq P(D = 1 \,|\, Z = z)\}
\end{aligned}
$$

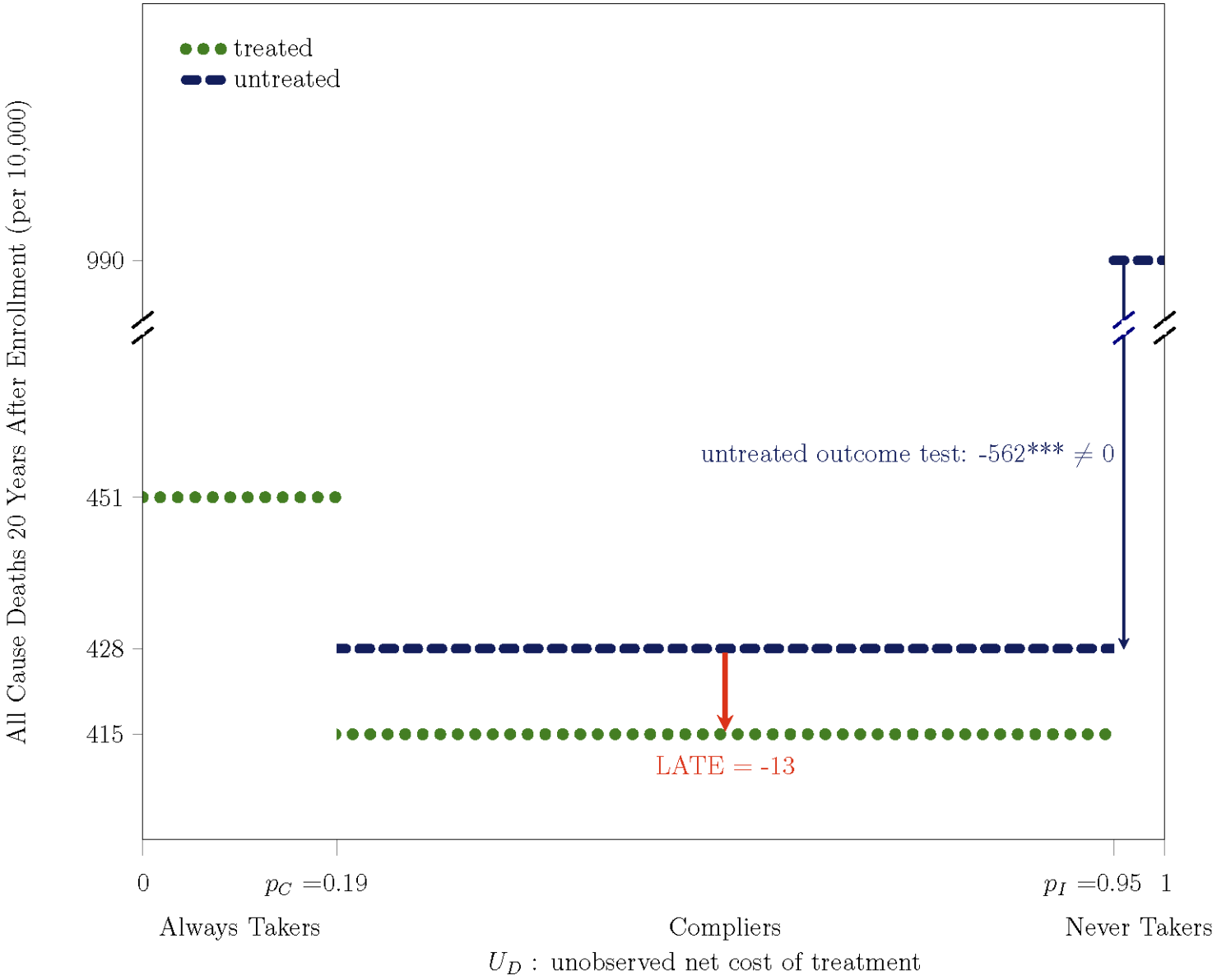
**Second Stage:**

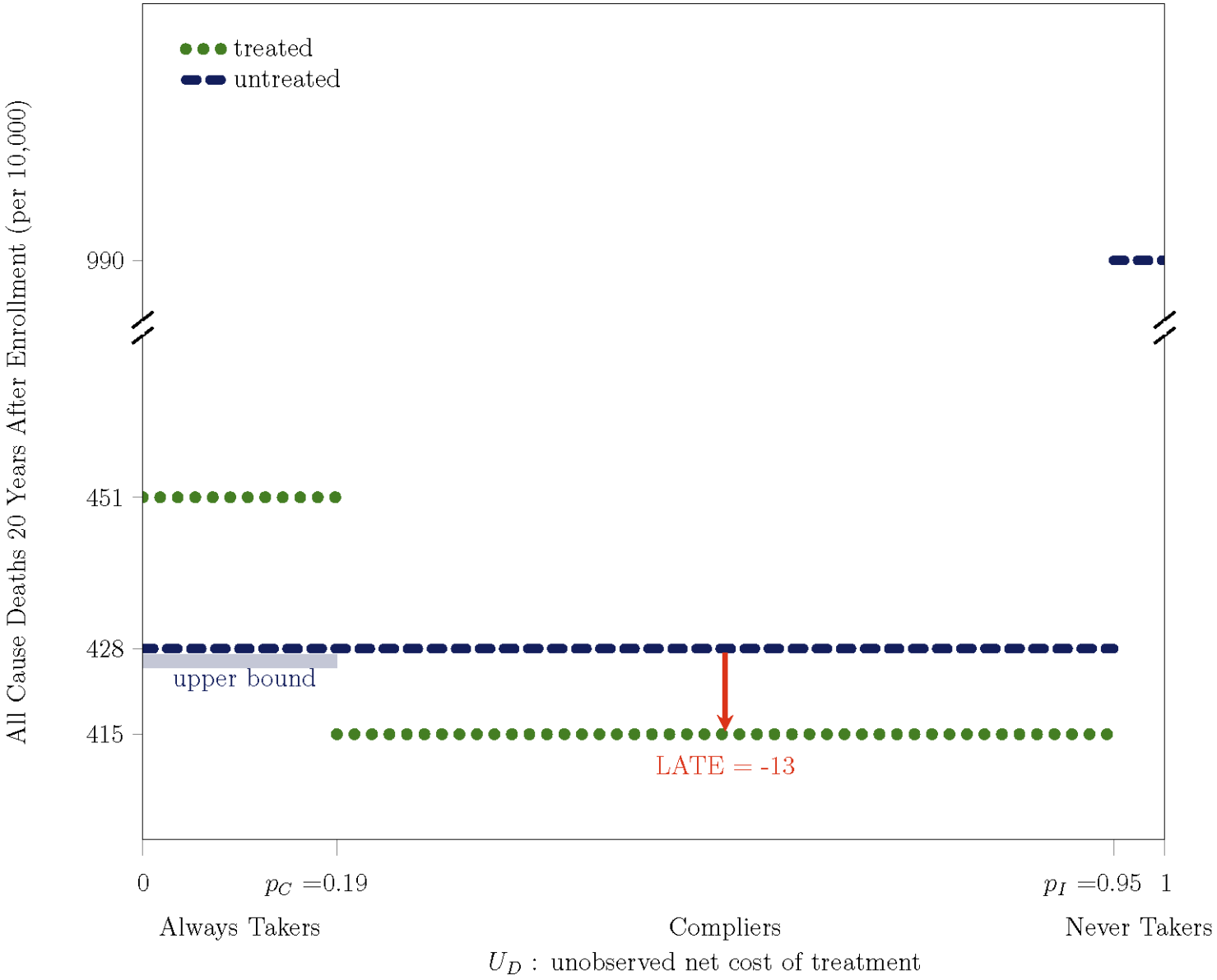
$$
\begin{aligned}
Y &= Y_U + (Y_T - Y_U)D \\
Y_T &= g_T(U_D, \gamma_T) \\
Y_U &= g_U(U_D, \gamma_U) \qquad\qquad Z \perp (\gamma_T, \gamma_U) \text{ by A.2.}
\end{aligned}
$$

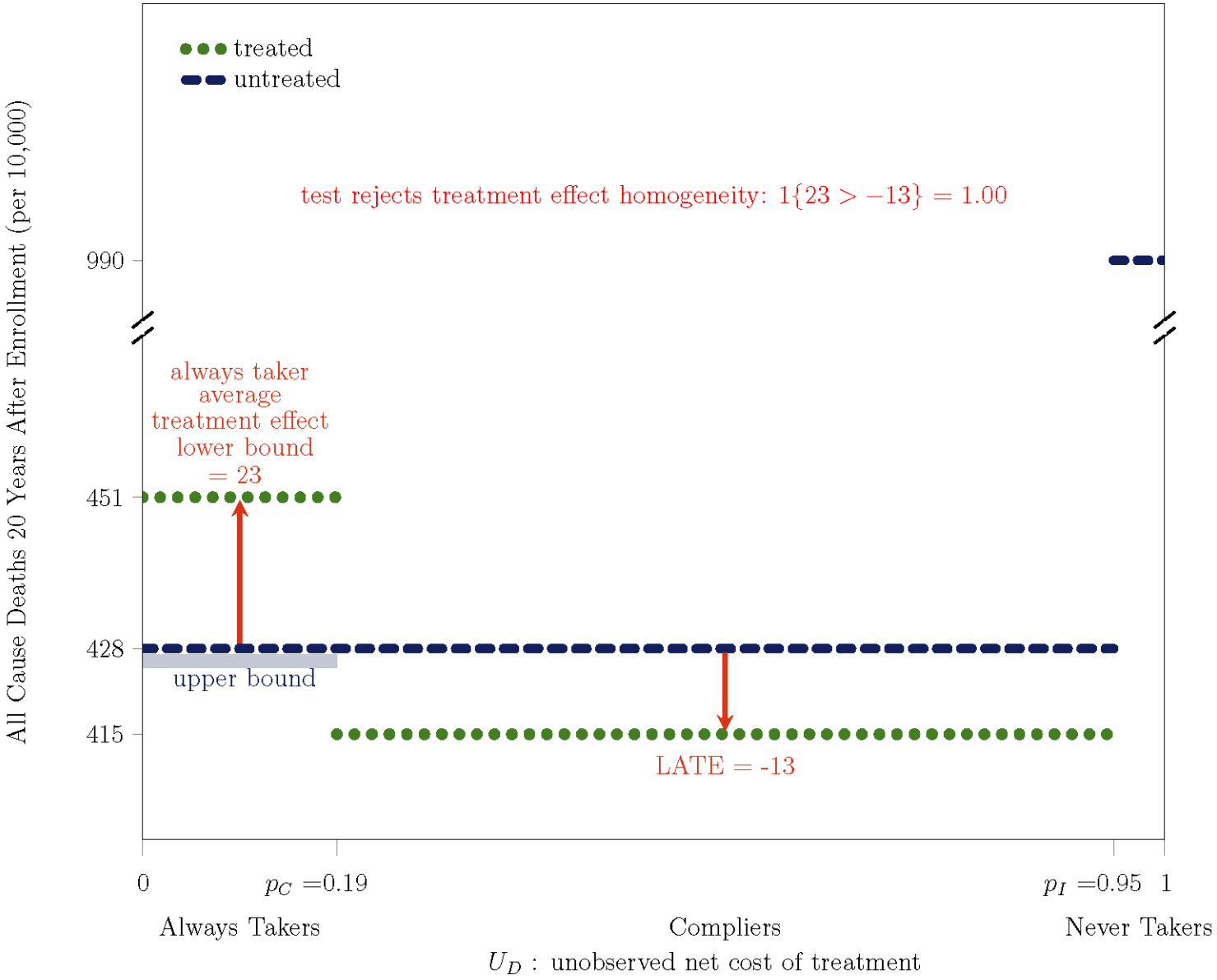
**Ancillary Assumption - Weak Monotonicity of the MUO Function**

For all $p_1, p_2 \in [0,1]$ such that $p_1 < p_2$ :
$\mathrm{E}[Y_U \,|\, U_D = p_1] \leq \mathrm{E}[Y_U \,|\, U_D = p_2]$ or $\mathrm{E}[Y_U \,|\, U_D = p_1] \geq \mathrm{E}[Y_U \,|\, U_D = p_2]$

(Brinch, Mogstad, and Wiswall (2017).)


treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
990
451
428
415
untreated outcome test: -562*** ≠ 0
LATE = -13
0
$p_C$ =0.19
$p_I$ =0.95
1
Always Takers
Compliers
Never Takers
$U_D$ : unobserved net cost of treatment


treated
untreated
All Cause Deaths 20 Years After Enrollment (per 10,000)
990
451
428
415
upper bound
LATE = -13
0
$p_C$ =0.19
$p_I$ =0.95
1
Always Takers
Compliers
Never Takers
$U_D$ : unobserved net cost of treatment


treated
untreated
test rejects treatment effect homogeneity: $1\{23 > -13\} = 1.00$
All Cause Deaths 20 Years After Enrollment (per 10,000)
990
451
428
415
always taker average treatment effect lower bound = 23
upper bound
LATE = -13
0
$p_C$ =0.19
$p_I$ =0.95
1
Always Takers
Compliers
Never Takers
$U_D$ : unobserved net cost of treatment

*"I never, though, had a patient whose worry about those side effects came close to her worry about the disease. Being preoccupied with saving one's life produces a myopia, in which other worries unrelated to one's possibly imminent death fall away."*

-Brown, New York Times, October 28, 2017

*"And so, unable to say whether any particular patient will benefit, we have no choice but to overtreat."*

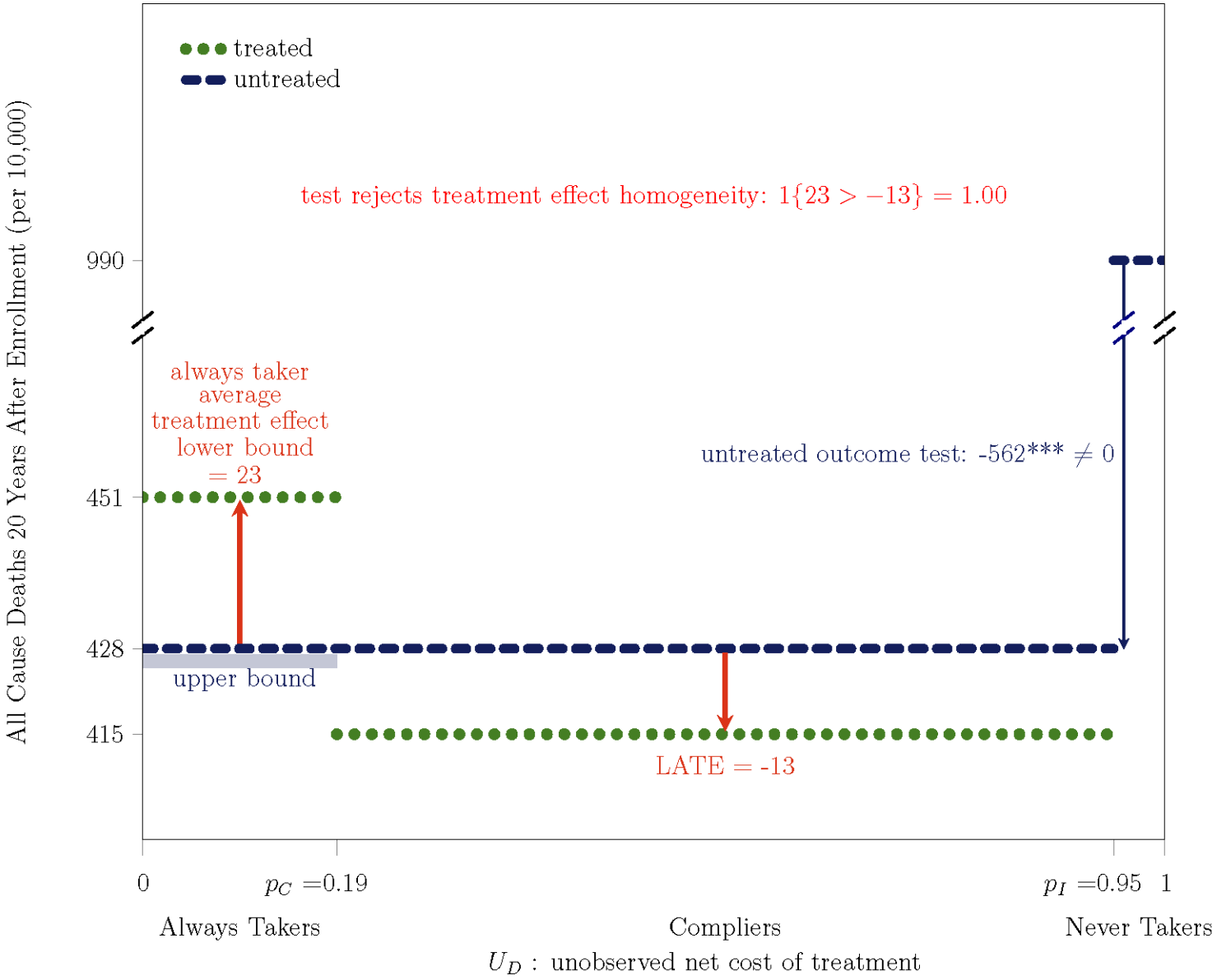
-Mukherjee, New Yorker, September 11, 2017

# Baseline Covariates Support Ancillary Assumption

| | Means | | |
|---|---|---|---|
| | Always Takers | Compliers | Never Takers |
| **Baseline Socioeconomic Status** | | | |
| University, trade or business school | 0.50 | 0.46 | 0.39 |
| In work force | 0.65 | 0.64 | 0.65 |
| Age at first birth | 24.28 | 23.98 | 23.57 |
| No live birth | 0.16 | 0.15 | 0.13 |
| Married | 0.80 | 0.81 | 0.75 |
| Husband in work force / alive | 0.81 | 0.81 | 0.76 |
| **Baseline Health Behavior** | | | |
| Non-Smoker | 0.78 | 0.75 | 0.63 |
| Body Mass Index | 23.87 | 24.42 | 24.48 |
| Used oral contraception | 0.74 | 0.71 | 0.67 |
| Used estrogen | 0.13 | 0.13 | 0.15 |
| Mammograms prior to enrollment | 0.23 | 0.13 | 0.13 |
| Practiced breast self examination | 0.47 | 0.44 | 0.38 |

# Behavior within a Clinical Trial and Implications for Mammography Guidelines

- Model
  - First Stage: Mammography
  - Second Stage: Mortality
- Results
  1. Selection Heterogeneity
     - *Women more likely to receive mammograms are healthier*
  2. Treatment Effect Heterogeneity
     - *Women more likely to receive mammograms are more likely to be harmed by them*
- **Robustness**
- Conclusions


treated
untreated
test rejects treatment effect homogeneity: $1\{23 > -13\} = 1.00$
All Cause Deaths 20 Years After Enrollment (per 10,000)
990
451
428
415
always taker average treatment effect lower bound = 23
untreated outcome test: -562*** $\neq 0$
upper bound
LATE = -13
0
$p_C$ =0.19
$p_I$ =0.95
1
Always Takers
Compliers
Never Takers
$U_D$ : unobserved net cost of treatment

# Main Specification For Comparison

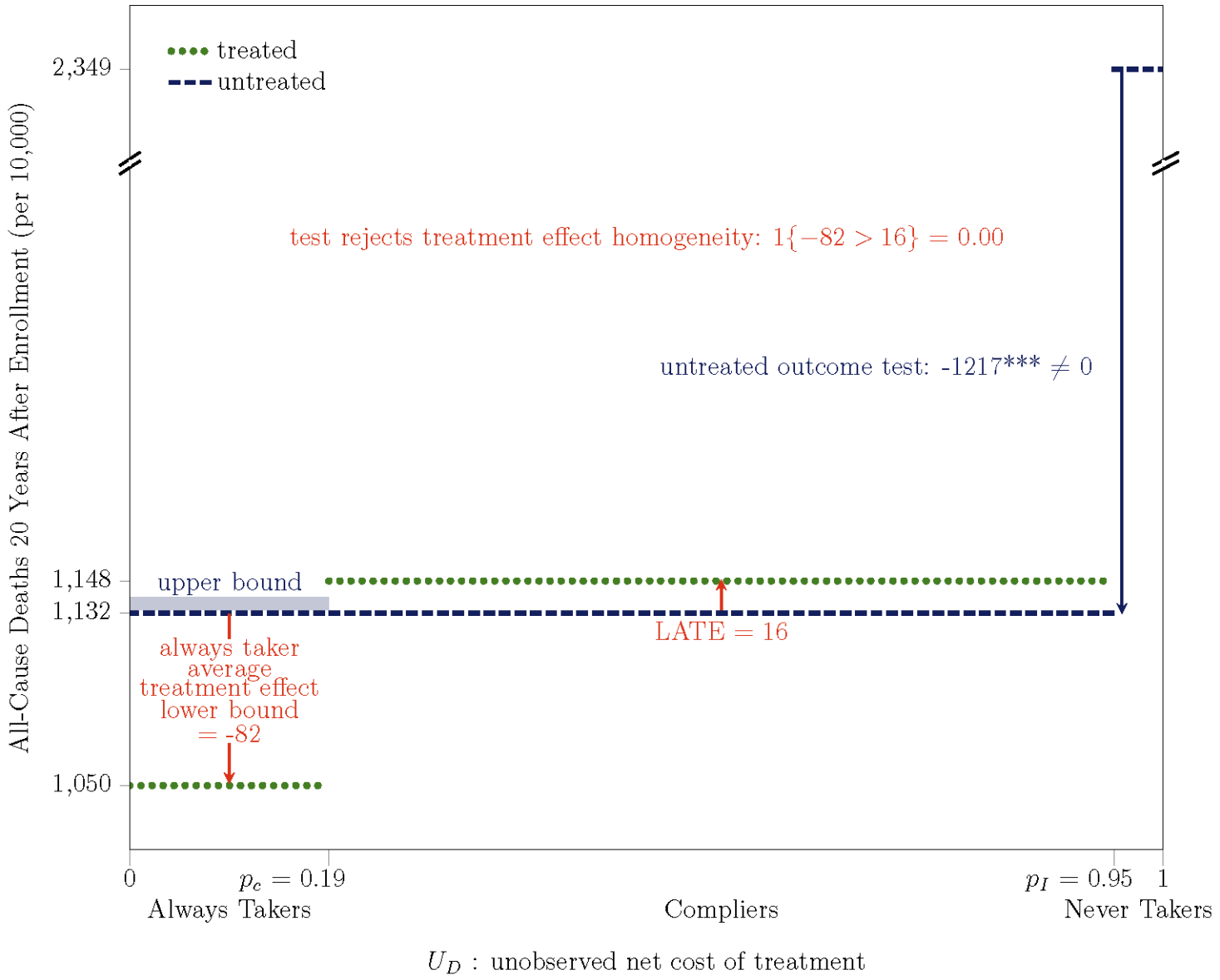
| | N | Untreated Outcome Test | Always Taker Average Treatment Effect Lower Bound | LATE | Test Rejects Treatment Effect Homogeneity |
|---|---|---|---|---|---|
| **Main Specification** | | | | | |
| Main Specification | 19,505 | -562<br>(147) | 23<br>(59) | -13<br>(38) | 1.00<br>(0.48) |

# Results Are Robust Along Many Dimensions

- **Sample Restrictions**
  - **Excluded participants aged 40-49**
  - **All participants aged 40-49**
  - **All participants aged 50-59**
- Definitions of mammography
  - Narrower
  - Broader
- Outcomes
  - Breast cancer mortality
  - Mortality at alternative follow-up lengths

# Robust to Alternative Sample Restrictions

| | N | Untreated Outcome Test | Always Taker Average Treatment Effect Lower Bound | LATE | Test Rejects Treatment Effect Homogeneity |
|---|---|---|---|---|---|
| **Main Specification** | | | | | |
| Main Specification | 19,505 | -562<br>(147) | 23<br>(59) | -13<br>(38) | 1.00<br>(0.48) |
| **Alternative Sample Restrictions** | | | | | |
| All excluded participants aged 40-49 at enrollment | 30,925 | -759<br>(135) | 60<br>(39) | 27<br>(40) | 1.00<br>(0.47) |
| All participants aged 40-49 at enrollment | 50,430 | -672<br>(103) | 53<br>(31) | 9<br>(27) | 1.00<br>(0.34) |
| All participants aged 50-59 at enrollment | 39,405 | -1,216<br>(154) | -83<br>(51) | 15<br>(46) | 0.00<br>(0.26) |


treated
untreated
2,349
test rejects treatment effect homogeneity: $1\{-82 > 16\} = 0.00$
untreated outcome test: -1217*** $\neq 0$
1,148
upper bound
1,132
LATE = 16
always taker average treatment effect lower bound = -82
1,050
All-Cause Deaths 20 Years After Enrollment (per 10,000)
0
$p_c = 0.19$
$p_I = 0.95$
1
Always Takers
Compliers
Never Takers
$U_D$ : unobserved net cost of treatment

# Results Are Robust Along Many Dimensions

- Sample Restrictions
  - Excluded participants aged 40-49
  - All participants aged 40-49
  - All participants aged 50-59
- **Definitions of mammography**
  - **Narrower**
  - **Broader**
- Outcomes
  - Breast cancer mortality
  - Mortality at alternative follow-up lengths

# Robust to Alternative Definitions of Mammography

| | N | Untreated Outcome Test | Always Taker Average Treatment Effect Lower Bound | LATE | Test Rejects Treatment Effect Homogeneity |
|---|---|---|---|---|---|
| **Main Specification** | | | | | |
| Mammogram in at least one year after enrollment during the active study period, missing in year = no mammogram in year | | | | | |
| Main specification | 19,505 | -562 | 23 | -13 | 1.00 |
| | | (147) | (59) | (38) | (0.48) |
| **Narrower Definitions of Mammography** | | | | | |
| Mammogram in more than one year after enrollment during the active study period, missing in year = no mammogram in year | | | | | |
| At least two active study period years | 19,505 | -465 | -27 | -12 | 0.00 |
| | | (106) | (77) | (35) | (0.49) |
| At least three active study period years | 19,505 | -420 | 56 | -12 | 1.00 |
| | | (94) | (145) | (36) | (0.48) |
| All active study period years | 19,505 | -225 | -135 | -15 | 0.00 |
| | | (75) | (138) | (42) | (0.37) |
| **Broader Definition of Mammography** | | | | | |
| Mammogram in at least one year after enrollment during the active study period | | | | | |
| Missing in year = mammogram in year | 19,505 | -776 | 103 | -24 | 1.00 |
| | | (835) | (43) | (69) | (0.43) |

# Results Are Robust Along Many Dimensions

- Sample Restrictions
  - Excluded participants aged 40-49
  - All participants aged 40-49
  - All participants aged 50-59
- Definitions of mammography
  - Narrower
  - Broader
- **Outcomes**
  - **Breast cancer mortality**
  - Mortality at alternative follow-up lengths

# Robust to Alternative Outcomes

| | N | Untreated Outcome Test | Always Taker Average Treatment Effect Lower Bound | LATE | Test Rejects Treatment Effect Homogeneity |
|---|---|---|---|---|---|
| **Main Specification** | | | | | |
| Main Specification | 19,505 | -562<br>(147) | 23<br>(59) | -13<br>(38) | 1.00<br>(0.48) |
| **Alternative Outcome** | | | | | |
| Breast Cancer Mortality | 19,505 | -43<br>(47) | 30<br>(25) | -12<br>(13) | 1.00<br>(0.43) |

# Results Are Robust Along Many Dimensions

- Sample Restrictions
  - Excluded participants aged 40-49
  - All participants aged 40-49
  - All participants aged 50-59
- Definitions of mammography
  - Narrower
  - Broader
- **Outcomes**
  - Breast cancer mortality
  - **Mortality at alternative follow-up lengths**

# Robust to Mortality at Alternative Follow-Up Lengths: 11-20

| Years Since Enrollment | N | Untreated Outcome Test | Always Taker Average Treatment Effect Lower Bound | LATE | Test Rejects Treatment Effect Homogeneity |
|---|---|---|---|---|---|
| Main specification: 20 | 19,505 | -562 | 23 | -13 | 1.00 |
| | | (147) | (59) | (38) | (0.48) |
| 19 | 19,505 | -485 | 50 | -13 | 1.00 |
| | | (142) | (58) | (37) | (0.40) |
| 18 | 19,505 | -492 | 54 | -8 | 1.00 |
| | | (139) | (56) | (35) | (0.41) |
| 17 | 19,505 | -456 | 18 | -8 | 1.00 |
| | | (135) | (50) | (33) | (0.48) |
| 16 | 19,505 | -471 | 15 | -16 | 1.00 |
| | | (134) | (46) | (31) | (0.47) |
| 15 | 19,505 | -480 | -11 | -15 | 1.00 |
| | | (131) | (42) | (31) | (0.50) |
| 14 | 19,505 | -396 | -38 | -21 | 0.00 |
| | | (121) | (38) | (30) | (0.45) |
| 13 | 19,505 | -365 | -30 | -24 | 0.00 |
| | | (115) | (36) | (28) | (0.49) |
| 12 | 19,505 | -334 | -23 | -27 | 1.00 |
| | | (106) | (32) | (27) | (0.50) |
| 11 | 19,505 | -351 | -30 | -10 | 0.00 |
| | | (105) | (28) | (25) | (0.42) |

# Robust to Mortality at Alternative Follow-Up Lengths: 1 - 10

| Years Since Enrollment | N | Untreated Outcome Test | Always Taker Average Treatment Effect Lower Bound | LATE | Test Rejects Treatment Effect Homogeneity |
|---|---|---|---|---|---|
| 10 | 19,505 | -306 | -41 | -15 | 0.00 |
| | | (97) | (25) | (23) | (0.37) |
| 9 | 19,505 | -314 | -35 | -12 | 0.00 |
| | | (97) | (21) | (20) | (0.36) |
| 8 | 19,505 | -340 | -14 | -2 | 0.00 |
| | | (97) | (21) | (18) | (0.44) |
| 7 | 19,505 | -351 | -15 | -6 | 0.00 |
| | | (97) | (18) | (17) | (0.46) |
| 6 | 19,505 | -317 | -24 | -5 | 0.00 |
| | | (93) | (16) | (15) | (0.33) |
| 5 | 19,505 | -269 | -12 | -5 | 0.00 |
| | | (86) | (15) | (13) | (0.45) |
| 4 | 19,505 | -218 | -3 | -9 | 1.00 |
| | | (77) | (14) | (11) | (0.49) |
| 3 | 19,505 | -209 | -3 | -6 | 1.00 |
| | | (76) | (11) | (9) | (0.50) |
| 2 | 19,505 | -194 | -3 | -3 | 1.00 |
| | | (67) | (9) | (9) | (0.50) |
| 1 | 19,505 | -55 | -5 | -5 | 0.00 |
| | | (40) | (5) | (5) | (0.00) |

# Behavior within a Clinical Trial and Implications for Mammography Guidelines

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  1. Selection Heterogeneity
     - *Women more likely to receive mammograms are healthier*
  2. Treatment Effect Heterogeneity
     - *Women more likely to receive mammograms are more likely to be harmed by them*
- Robustness
- **Conclusions**

# U.S. Preventive Services Task Force (USPSTF) 2016 Guidelines for Women in 40's:

*"The decision to start screening mammography in women prior to age 50 years should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin biennial screening between the ages of 40 and 49 years"*

# U.S. Preventive Services Task Force (USPSTF)

## "C recommendation"

*"The USPSTF recommends selectively offering this service to individual patients based on professional judgment and patient preferences"*

# Appendix

# CNBSS Protocols Varied by Age

- Patients aged 40-49:
  - Intervention group: mammography + physical examination each year for 4-5 years, then return to usual care
  - Control group: usual care
- Patients aged 50-59:
  - Intervention group: mammography + physical examination each year for 4-5 years, then return to usual care
  - Control group: physical examination each year for 4-5 years, then return to usual care

# USPSTF Recommendations Differ for Women in 40's and 50's

- The U.S. Preventive Services Task Force (USPSTF) Assigns "grades"
  - "A" and "B" grades fully-covered under ACA
- Different grades for 40's and 50+ (Siu, 2016)
  - "The decision to start screening mammography in women prior to age 50 years should be an individual one. (Grade C recommendation)"
  - "The USPSTF recommends biennial screening mammography for women aged 50 to 74 years. (Grade B recommendation)"