# 1. Primary outcome: insulin initiation + other diab outcomes

## 1.1. VTE Estimation

Table 1: VTE Estiamtes

| estimator | est | lower | upper |
|---|---|---|---|
| TMLE | 1e-03 | -5e-04 | 0.0026 |
| EE | 1e-04 | -9e-04 | 0.0011 |

## 1.2. VIM Estimation

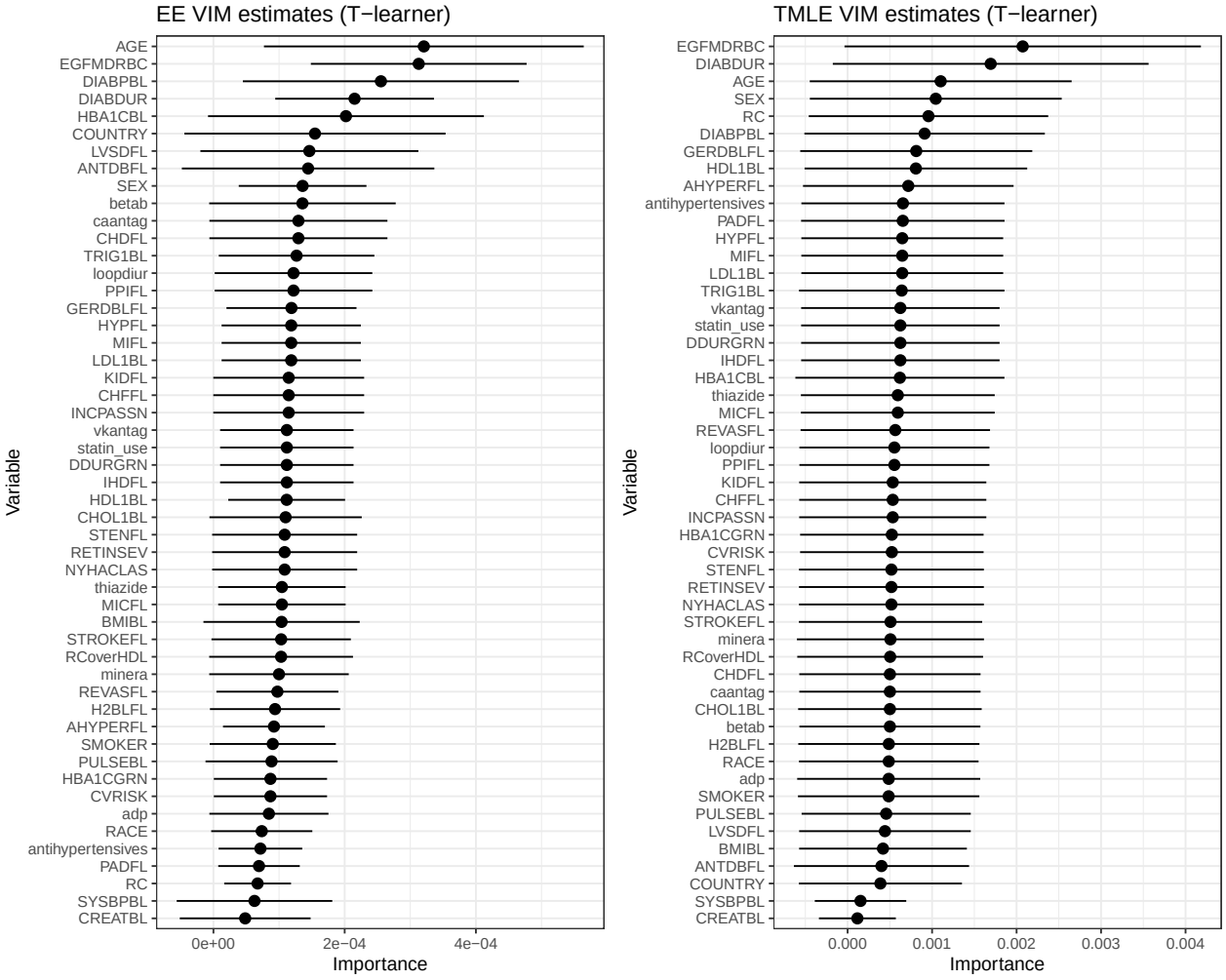


Figure 1: VIM Estiamtes

## 1.3 Stratified TMLE

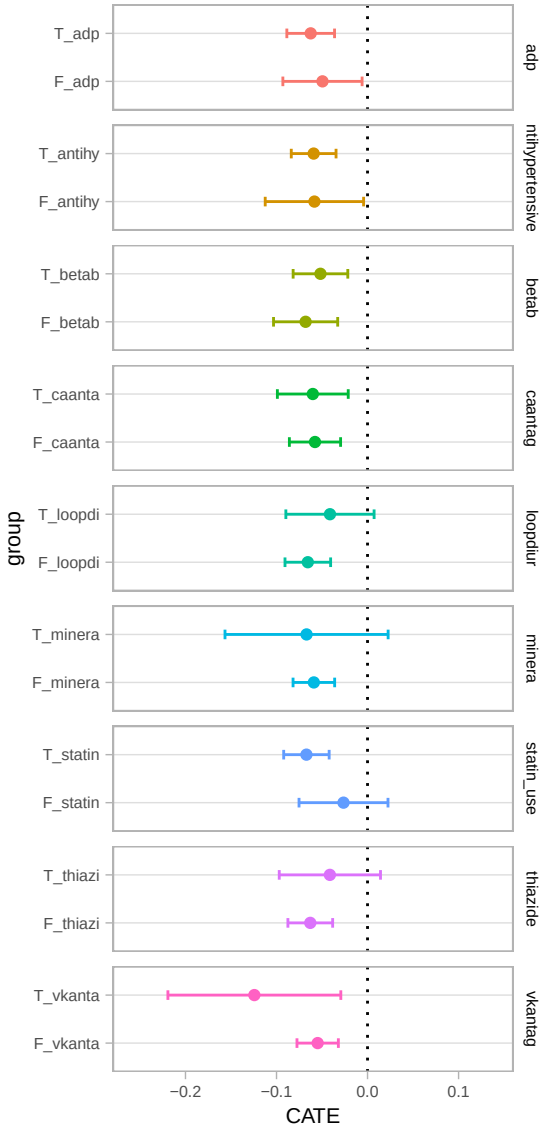


Figure 2: Stratified TMLE ATE Estiamtes

## 1.4. TMLE Effect Modification

Table 2: TMLE Effect Modification Estiamtes

| param | init_est | tmle_est | se | lower | upper |
|---|---|---|---|---|---|
| E[Y_{A=00}] | 0.1758 | 0.2105 | 0.0107 | 0.1896 | 0.2315 |
| E[Y_{A=01}] | 0.1824 | 0.1948 | 0.0088 | 0.1776 | 0.2121 |
| E[Y_{A=10}] | 0.1758 | 0.1586 | 0.0101 | 0.1388 | 0.1784 |
| E[Y_{A=11}] | 0.1418 | 0.1239 | 0.0076 | 0.1090 | 0.1388 |
| E[Y_{A=11}] - E[Y_{A=01}] | -0.0406 | -0.0710 | 0.0115 | -0.0935 | -0.0484 |
| E[Y_{A=10}] - E[Y_{A=00}] | 0.0000 | -0.0519 | 0.0146 | -0.0805 | -0.0233 |
| E[Y_{A=11}] - E[Y_{A=01}] - E[Y_{A=10}] - E[Y_{A=00}] | -0.0406 | -0.0191 | 0.0186 | -0.0555 | 0.0173 |

# 2. Alternative Primary outcome: insulin intesnfication + other diab outcomes

## 2.1. VTE Estimation

Table 3: VTE Estiamtes

| estimator | est | lower | upper |
|---|---|---|---|
| TMLE | 0.0017 | 2e-04 | 0.0032 |
| EE | 0.0015 | 1e-04 | 0.0029 |

## 2.2. VIM Estimation

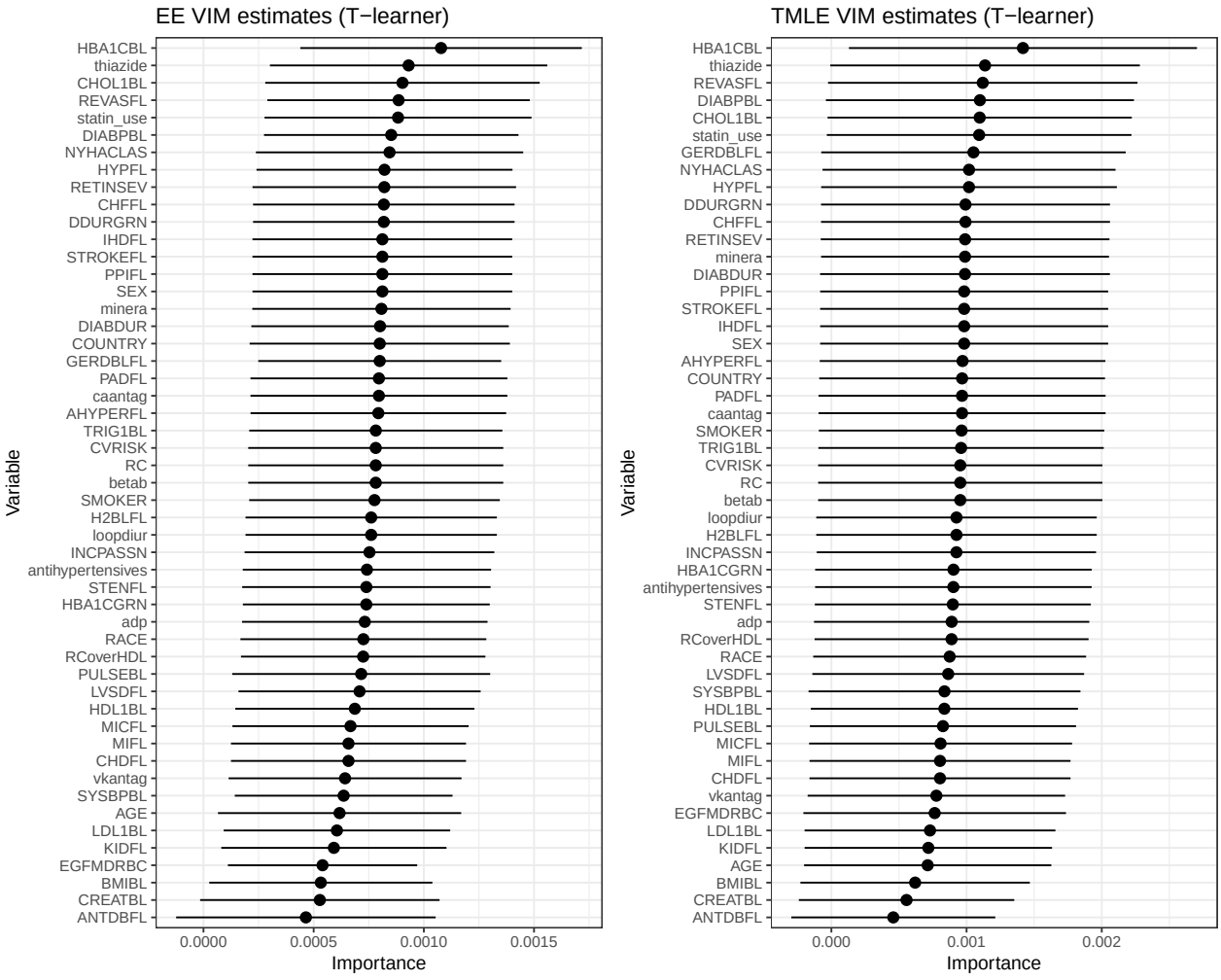


Figure 3: VIM Estiamtes

## 2.3 Stratified TMLE

```
## Warning: Removed 9 rows containing missing values (geom_hline).
```

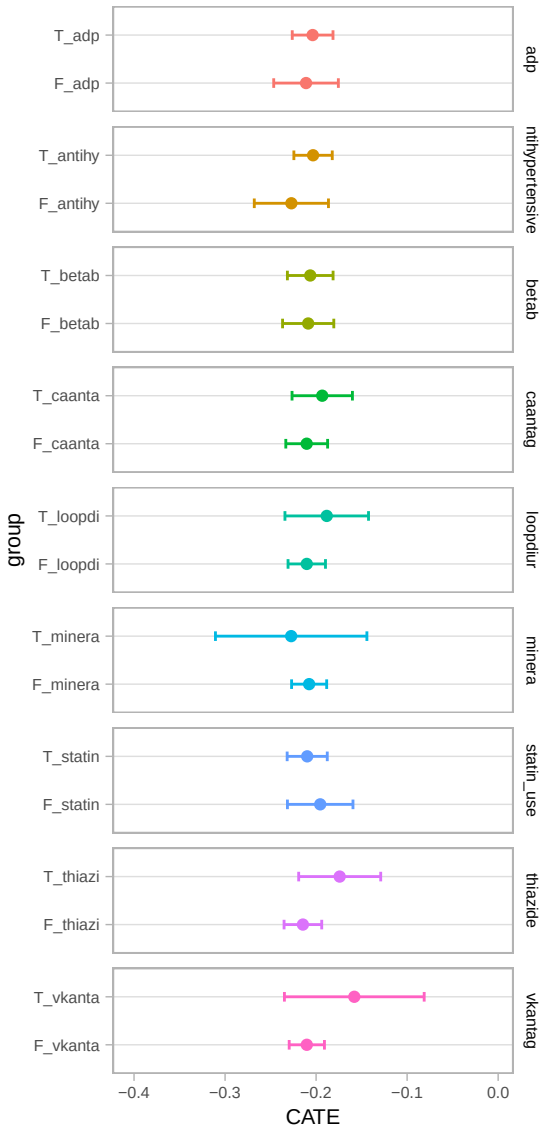


Figure 4: Stratified TMLE ATE Estiamtes

## 2.4. TMLE Effect Modification

Table 4: TMLE Effect Modification Estiamtes

| param | init_est | tmle_est | se | lower | upper |
|---|---|---|---|---|---|
| E[Y_{A=00}] | 0.4541 | 0.5239 | 0.0112 | 0.5020 | 0.5458 |
| E[Y_{A=01}] | 0.4893 | 0.4925 | 0.0079 | 0.4769 | 0.5080 |
| E[Y_{A=10}] | 0.3132 | 0.2784 | 0.0100 | 0.2588 | 0.2981 |
| E[Y_{A=11}] | 0.2885 | 0.2774 | 0.0071 | 0.2635 | 0.2913 |
| E[Y_{A=11}] - E[Y_{A=01}] | -0.2008 | -0.2150 | 0.0105 | -0.2355 | -0.1946 |
| E[Y_{A=10}] - E[Y_{A=00}] | -0.1409 | -0.2455 | 0.0149 | -0.2746 | -0.2163 |
| E[Y_{A=11}] - E[Y_{A=01}] - E[Y_{A=10}] - E[Y_{A=00}] | -0.0599 | 0.0304 | 0.0182 | -0.0052 | 0.0661 |

# 3. Secondary outcome: cv outcomes

## 3.1. VTE Estimation

Table 5: VTE Estiamtes

| estimator | est | lower | upper |
|---|---|---|---|
| TMLE | 0 | 0e+00 | 0e+00 |
| EE | 0 | -1e-04 | 1e-04 |

## 3.2. VIM Estimation

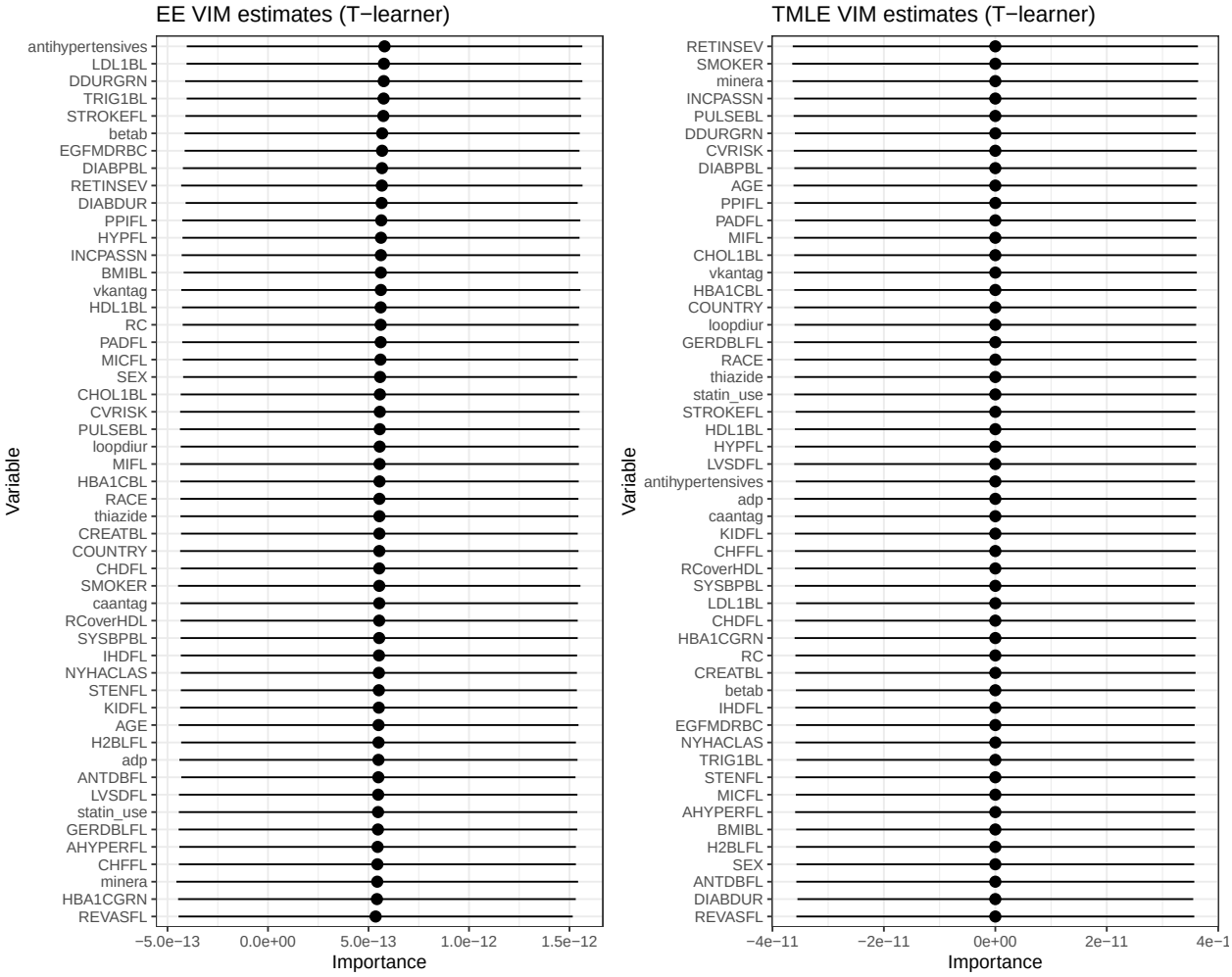


Figure 5: VIM Estiamtes

### 3.3 Stratified TMLE

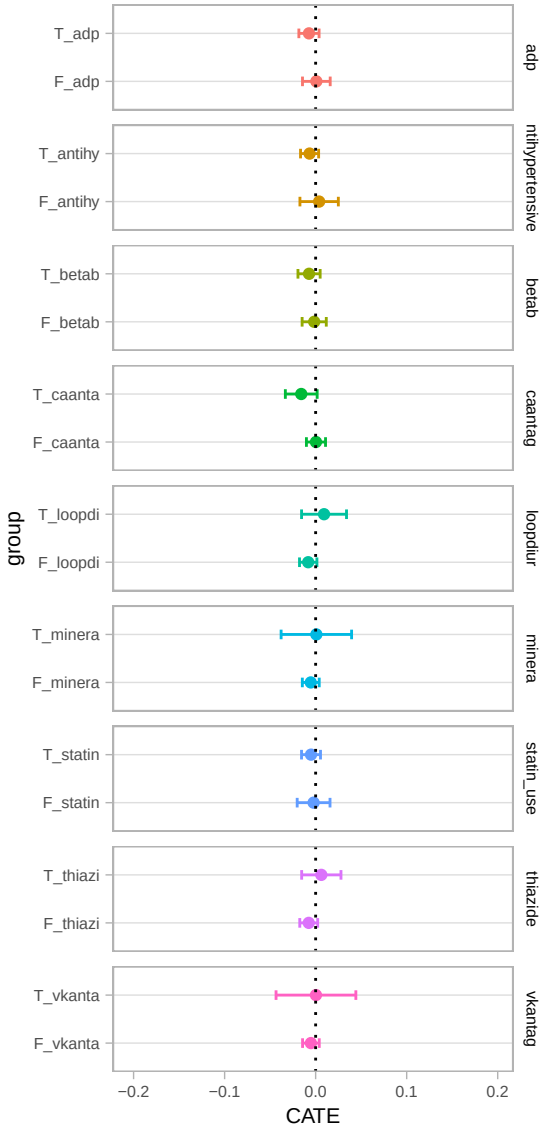


Figure 6: Stratified TMLE ATE Estiamtes

### 3.4. TMLE Effect Modification

Table 6: TMLE Effect Modification Estiamtes

| param | init_est | tmle_est | se | lower | upper |
|---|---|---|---|---|---|
| E[Y_{A=00}] | 0.052 | 0.0672 | 0.0057 | 0.0560 | 0.0783 |
| E[Y_{A=01}] | 0.052 | 0.0526 | 0.0036 | 0.0455 | 0.0596 |
| E[Y_{A=10}] | 0.052 | 0.0640 | 0.0054 | 0.0534 | 0.0747 |
| E[Y_{A=11}] | 0.052 | 0.0452 | 0.0033 | 0.0386 | 0.0517 |
| E[Y_{A=11}] - E[Y_{A=01}] | 0.000 | -0.0074 | 0.0048 | -0.0169 | 0.0021 |
| E[Y_{A=10}] - E[Y_{A=00}] | 0.000 | -0.0031 | 0.0078 | -0.0185 | 0.0122 |
| E[Y_{A=11}] - E[Y_{A=01}] - E[Y_{A=10}] - E[Y_{A=00}] | 0.000 | -0.0042 | 0.0092 | -0.0223 | 0.0138 |

# 4. Secondary outcome: HBA1C

## 4.1. VTE Estimation

Table 7: VTE Estiamtes

| estimator | est | lower | upper |
|---|---|---|---|
| TMLE | 0.0000 | -0.0006 | 0.0006 |
| EE | -0.0345 | -0.0530 | -0.0161 |

## 4.2. VIM Estimation

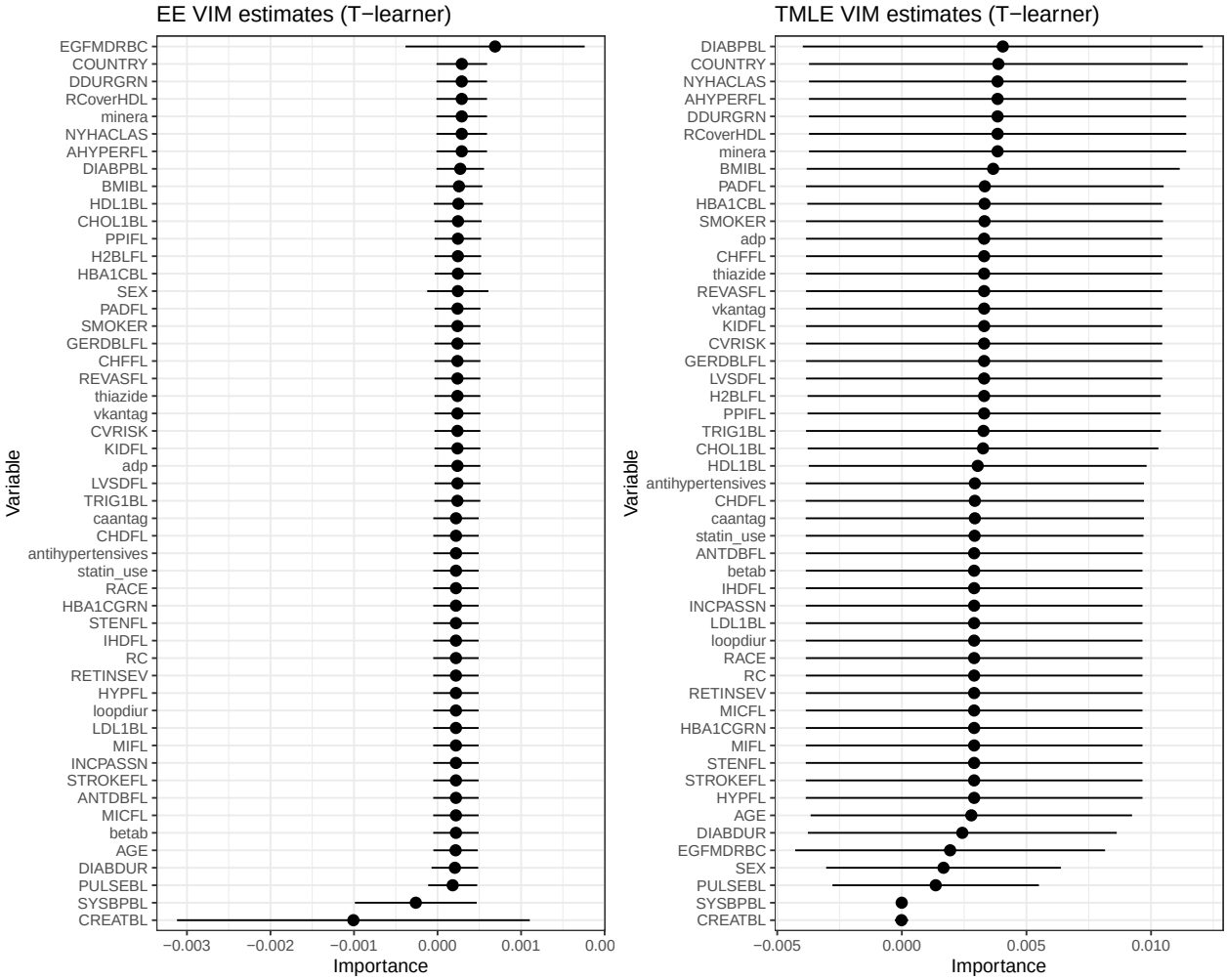


Figure 7: VIM Estiamtes

## 4.3 Stratified TMLE

```
## Warning: Removed 9 rows containing missing values (geom_hline).
```

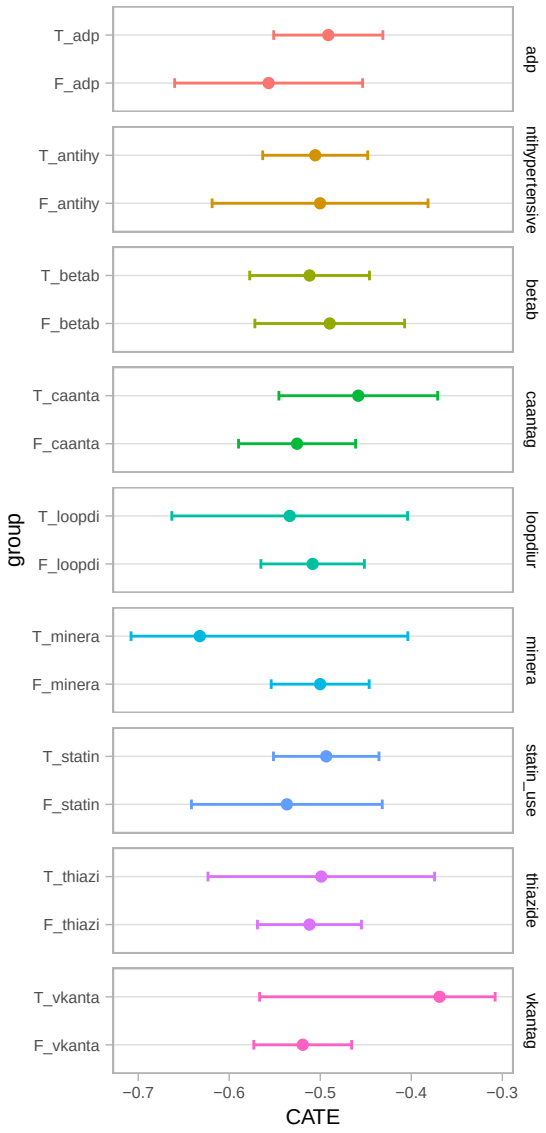


Figure 8: Stratified TMLE ATE Estiamtes

## 4.4. TMLE Effect Modification

Table 8: TMLE Effect Modification Estiamtes

| param | init_est | tmle_est | se | lower | upper |
|---|---|---|---|---|---|
| E[Y_{A=00}] | -0.9056 | -0.6855 | 0.0319 | -0.7479 | -0.6231 |
| E[Y_{A=01}] | -0.7974 | -0.7195 | 0.0227 | -0.7639 | -0.6751 |
| E[Y_{A=10}] | -1.1226 | -1.4267 | 0.0314 | -1.4882 | -1.3651 |
| E[Y_{A=11}] | -1.1693 | -1.2367 | 0.0231 | -1.2819 | -1.1915 |
| E[Y_{A=11}] - E[Y_{A=01}] | -0.3719 | -0.5172 | 0.0293 | -0.5746 | -0.4597 |
| E[Y_{A=10}] - E[Y_{A=00}] | -0.2170 | -0.7412 | 0.0425 | -0.8245 | -0.6579 |
| E[Y_{A=11}] - E[Y_{A=01}] - E[Y_{A=10}] - E[Y_{A=00}] | -0.1549 | 0.2240 | 0.0516 | 0.1228 | 0.3252 |