SUPPLEMENTARY DATA

Supplementary Table 1. Distribution of insulin-use in cases and controls.

| | Cases | Controls | p value |
|----------------------------|----------------|----------------|---------|
| Cumulative insulin therapy | (n=12248) | (n=12248) | |
| φ30 days | 10026 (81.86%) | 10100 (82.46%) | 0.2168 |
| > 30 days | 2222 (18.14%) | 2148 (17.54%) | |

Supplementary Table 2. Subgroup analysis of TZD use and adjusted odds ratios of colorectal cancer among patients with diabetes.

| | | Duration of TZDs Therapy (Day) | | | | | | |
|-------------------------|------|---|-----------------|-----------------|--------|--|--|--|
| | 0 | 1–90 | 91-270 | >270 | | | | |
| | | Adjusted Odds Ratio (95% Confidence Interval) | | | | | | |
| Main model [†] | 1.00 | 0.90(0.78-1.04) | 0.86(0.74-1.01) | 0.84(0.75-0.95) | 0.0007 | | | |
| Subgroup effects‡ | | | | | | | | |
| Insulin 30 days | 1.00 | 0.91(0.74-1.12) | 0.90(0.73-1.12) | 0.80(0.68-0.94) | 0.0043 | | | |

TZDs = thiazolidinediones. †Main model = Adjusted for urbanization, income, colorectal polyp disorder, inflammatory bowel disease, hypertension, hyperlipidemia, biliary stone disease, alcohol related disease, chronic kidney disease, diabetes related complications, ischemic heart disease, cerebrovascular disease, heart failure, chronic obstructive pulmonary disease and hormone therapy. ‡The models were adjusted for covariates in the main model. §Test of linear dose-response effect of cumulative TZDs exposure

Supplementary Table 3. Distribution between use of TZD and diagnosis of colorectal polyp before index date in cases and controls.

| | | Cases n=12248 | | | | | Controls | | | |
|-------------------------------|------|------------------|-------|---------------|--------|------|-----------|-------|---------------|--------|
| | | | | | | | n=12248 | | | |
| | TZD | TZD users | | TZD non-users | | TZD | TZD users | | TZD non-users | |
| | n | (%) | n | (%) | p | n | (%) | n | (%) | p |
| | 1634 | (13.34) | 10614 | (86.66) | | 1753 | (14.31) | 10495 | (85.69) | |
| Diagnosis of colorectal polyp | | | | | 0.1641 | | | | | 0.3882 |
| Never | 1472 | (12.02) | 9674 | (78.98) | | 1716 | (14.01) | 10305 | (84.14) | + |
| Ever | 162 | (1.32) | 940 | (7.67) | | 37 | (0.30) | 190 | (1.55) | |

SUPPLEMENTARY DATA

Supplementary Table 4. Subgroup analysis of TZD use and adjusted odds ratios of colorectal cancer among patients with diabetes.

| | 0 | 1–90 | 91-270 | >270 | | | | |
|---------------------------------------|------|---|-----------------|-----------------|--------|--|--|--|
| | | Adjusted Odds Ratio (95% Confidence Interval) | | | | | | |
| Main model [†] | 1.00 | 0.90(0.78-1.04) | 0.86(0.74-1.01) | 0.84(0.75-0.95) | 0.0007 | | | |
| Subgroup effects‡ | | | | | | | | |
| Never diagnosed with colorectal polyp | 1.00 | 0.89(0.76-1.03) | 0.87(0.74-1.02) | 0.83(0.74-0.93) | 0.0005 | | | |

TZDs = thiazolidinediones. †Main model = Adjusted for urbanization, income, colorectal polyp disorder, inflammatory bowel disease, hypertension, hyperlipidemia, biliary stone disease, alcohol related disease, chronic kidney disease, diabetes related complications, ischemic heart disease, cerebrovascular disease, heart failure, chronic obstructive pulmonary disease and hormone therapy. ‡The models were adjusted for covariates in the main model as well as each additional listed covariate. §Test of linear dose-response effect of cumulative TZDs exposure

SUPPLEMENTARY DATA

Supplementary Figure 1. Meta-analysis of use of thiazolidinediones and the risk of colorectal cancer in patients with diabetes in previously reported studies and in this study.

