Dipeptidyl peptidase 4 inhibitors and Inflammatory Bowel Disease: Real World Evidence in US Adults

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Disclosures

• The project was funded from the following sources:
  • R01 AG056479 from the National Institute on Aging
Background
Glucose Lowering Drugs (GLDs)

Monotherapy

Metformin

If A1C target not achieved after approximately 3 months

Dual therapy

Metformin +

- Sulfonylureas (SU)
- Thiazolidinedione (TZD)
- DPP-4 inhibitor (DPP4i)
- GLP-1 Receptor Agonist
- SGLT2 inhibitor
- Insulin

If A1C target not achieved after approximately 3 months

Triple therapy

Diabetes Care 2017;40(Suppl. 1);S64-S74.
Inflammatory Bowel Disease: UC, CD

- Ulcerative Colitis (UC) and Crohn’s Disease (CD)

**Ulcerative colitis** typically begins in the rectum and may extend continuously to involve the entire colon.

**Crohn disease** most commonly involves the end of the small intestine and beginning of the colon and may affect any part of the GI tract in a patchy pattern.

- Colon wall

- Normal
- Ulcerative colitis
- Crohn disease

Ulcerative colitis usually affects only the inner layer of the bowel wall.

Crohn disease may affect all layers of the bowel wall.
## DPP4i & IBD: evidence from the CPRD study

<table>
<thead>
<tr>
<th>Cohort study</th>
<th>Comparison</th>
<th>Drug</th>
<th>No. of Patients</th>
<th>No. of IBD Events</th>
<th>Median Use years:</th>
<th>IBD Rate per 100,000 pyrs</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abrahami et al.</td>
<td>DPP4i vs Other oral GLDs</td>
<td>DPP4i</td>
<td>7231</td>
<td>49</td>
<td>1.6</td>
<td>53.4</td>
<td>1.75 (1.22, 2.40)</td>
</tr>
<tr>
<td></td>
<td>Other oral GLDs</td>
<td>Other oral GLDs</td>
<td>133,939</td>
<td>159</td>
<td></td>
<td>34.5</td>
<td></td>
</tr>
</tbody>
</table>

UC: HR 2.23 (1.31, 3.76)
CD: HR 0.87 (0.37, 2.09)

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**Dipeptidyl peptidase-4 inhibitors and incidence of inflammatory bowel disease among patients with type 2 diabetes: population based cohort study**

Devin Abrahami,1,2 Antonios Douros,1,2,3 Hui Yim,1 Oriana Hoi Yun Yu,1,4 Christel Renoux,1,2,5 Alain Bitton,6,7 Laurent Azoulay1,2,8

**ABSTRACT**

**OBJECTIVE**
To assess whether the use of dipeptidyl peptidase-4 inhibitors is associated with the incidence of inflammatory bowel disease in patients with type 2 diabetes.

**DESIGN**
Population based cohort study.

**SETTING**
More than 700 general practices contributing data to the United Kingdom Clinical Practice Research Datalink.

**PARTICIPANTS**
A cohort of 161,170 patients, at least 18 years of age, starting antidiabetic drugs between 1 January 2007 and 31 December 2016, with follow-up until 30 June 2017.

**CONCLUSIONS**
In this first population based study, the use of dipeptidyl peptidase-4 inhibitors was associated with an increased risk of inflammatory bowel disease. Although these findings need to be replicated, physicians should be aware of this possible association.
Objective

- Conduct a large active-comparator, new-user (ACNU) cohort study to examine whether the use of DPP4i, as compared with therapeutic alternatives, is associated with an increased risk of IBD using data from US commercial administrative claims and fee-for-service Medicare plans.
Methods
Data source: MarketScan & Medicare

- **MarketScan:**
  - Primarily $18 \leq \text{age} < 65$ years old
  - Insured employees beneficiaries
    - Inpatient/Outpatient claims and encounters
    - Prescription dispensing

- **Medicare:**
  - Primarily 65 + years old
  - 20% random sample of all US fee-for-service Medicare beneficiaries
    - Part A/Part B (Inpatient/Outpatient services)
    - Part D (dispensed prescription drugs) benefits
Study Population

- Active-comparator, New-User cohort:
  - ≥ 1 year Continuous enrolment
  
  - New-users of DPP4i, SU, TZD from 2008 to 9/30/2015:
    - the 1st Rx after 1 year washout period
    - a 2nd Rx within (days supply of 1st Rx + 90-d grace period)

- Active-comparator: SU, TZD

| DPP4i vs Sulfonylurea (SU) | DPP-4i vs Thiazolidinedione (TZD) |
Exclusion criteria

- w/ the following diseases, IBD treatments, procedures

<table>
<thead>
<tr>
<th>Diseases</th>
<th>IBD treatment</th>
<th>Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBD (UC &amp; CD)</td>
<td>Aminosalicylates</td>
<td>Colectomy</td>
</tr>
<tr>
<td>Diverticulitis</td>
<td>anti-TNF</td>
<td>colostomy</td>
</tr>
<tr>
<td>ischemic colitis</td>
<td>azathioprine</td>
<td>ileostomy</td>
</tr>
<tr>
<td>pseudomenbraneous colitis</td>
<td>enteral budesonide</td>
<td>ostomy supplies</td>
</tr>
<tr>
<td>unspecific colitis</td>
<td>IV cyclosporine</td>
<td>colonoscopy &lt; age 50</td>
</tr>
</tbody>
</table>

Patients w/ heart failure when compared to TZD
Outcome definition

The majority of the first three diagnoses were used to distinguish between UC and CD.
Study design

Timeline to access the claim database

Jan 1, 2007 (Obtained Rx data)

365-day baseline period
Obtain baseline covariates

Index date (1st Rx)

Cohort entry date (2nd Rx)

January 1, 2008 (Earliest possible Index date)

September 30, 2015 (Latest possible Index date)

180-day induction period
IBD diagnosed in this period will be considered as prevalent IBD

Follow-up period
Outcome assessment

December 31, 2016
End of Study

180-day latent period

Change of initial Rx

Incident IBD

MarketScan
- 180-day latency after change of initial Rx
  1. Discontinuation
  2. Initiating the other drug in the drug pair that is being compared
- End of enrollment for MarketScan
- End of Study (December 31, 2016)

Medicare
- 180-day latency after change of initial Rx
  1. Discontinuation
  2. Initiating the other drug in the drug pair that is being compared
- Death
- End of Enrollment for Medicare Part A, B or D
- End of Study (December 31, 2016)

➢ A diagnosis code for IBD event
### Measured confounders: 58 covariates

#### Risk Factors of IBD
- Smoking
- Appendectomy
- Oral contraceptives

#### Other covariates

<table>
<thead>
<tr>
<th>Category</th>
<th>Covariates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic</td>
<td>Age, Gender, race (Medicare)</td>
</tr>
<tr>
<td>Autoimmune disease</td>
<td>Psoriasis, Rheumatoid arthritis, Systemic lupus erythematosus ...</td>
</tr>
<tr>
<td>Gastrointestinal diseases</td>
<td>Diseases Of Esophagus, Stomach, And Duodenum, Other Diseases Of Intestines And Peritoneum, Other Diseases Of Digestive System</td>
</tr>
<tr>
<td>Diabetes severity</td>
<td>Retinopathy, Neuropathy, Nephropathy</td>
</tr>
<tr>
<td>Comorbidities</td>
<td>HTN, Heart failure, depression, COPD, cancer...</td>
</tr>
<tr>
<td>Medications</td>
<td>Glucose lowering drugs, ACEI/ARB, CCB, Statin, diuretics, drugs may induce IBD</td>
</tr>
<tr>
<td>Health care use</td>
<td>No. of GI physician visit, No. physician visit, hospitalization...</td>
</tr>
<tr>
<td>Socioeconomic</td>
<td>Low income subsidy (Medicare)</td>
</tr>
</tbody>
</table>
Statistical analysis

- Propensity score (PS)
- Standardized Mortality/Morbidity Ratio weighting \(\left(\frac{PS}{1-PS}\right)\)
- Crude incidence rates = \(\frac{\text{No.of Patients with IBD event}}{\text{person time at risk}}\)
- Weighted Kaplan-Meier curves
- Cox proportional hazards models
- Random-effects meta-analysis to pool Hazard Ratios from
  - MarketScan population
  - 20% random sample of Medicare population
Secondary analysis: stratified by

- age at cohort entry
  - <50 and ≥50 years in MarketScan
  - <75 and ≥75 in Medicare
- sex
- gastroenterological disease
- autoimmune disease

- each individual DPP4i agent

- duration of follow-up
  - the first 12 months
  - after 12 months
Sensitivity analysis 1: different lag period

Timeline to access the claim database

- January 1, 2008 (Earliest possible Index date)
- September 30, 2015 (Latest possible Index date)

0, 90, 365-d

180-day induction period
IBD diagnosed in this period will be considered as prevalent IBD

365-day baseline period
Obtain baseline covariates

Follow-up period
Outcome assessment

180-day latent period
Change of initial Rx
Incident IBD

December 31, 2016
End of Study

THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL
Sensitivity analysis 2: initial-treatment analysis

Timeline to access the claim database

January 1, 2008 (Earliest possible Index date)

September 30, 2015 (Latest possible Index date)

365-day baseline period
Obtain baseline covariates

January 1, 2008 (Earliest possible Index date)

IBD diagnosed in this Period will be considered as prevalent IBD

Index date (1st Rx)

Change of initial Rx

Cohort entry date (2nd Rx)

Incident IBD

Follow-up period
Outcome assessment

4 years after Rx initiation

December 31, 2016 End of Study

➢ Censor at the earliest:

MarketScan
- 4 years after initial Rx
- End of enrollment for MarketScan
- End of Study (December 31, 2016)

Medicare
- 4 years after initial Rx
- Death
- End of Enrollment for Medicare Part A, B or D
- End of Study (December 30, 2016)

➢ A diagnosis code for IBD event
Sensitivity analysis 3: 1st Rx

- Follow-up start from the 1st Rx

Timeline to access the claim database:

- January 1, 2008 (Earliest possible Index date)
- September 30, 2015 (Latest possible Index date)
- January 1, 2007 (Obtained Rx data)
- December 31, 2016 End of Study

365-day baseline period
Obtain baseline covariates

180-day induction period
IBD diagnosed in this period will be considered as prevalent IBD

180-day latent period
Change of initial Rx
Incident IBD

Follow-up period
Outcome assessment

Censor at the earliest:

MarketScan
- 180-day latency after change of initial Rx
  ① Discontinuation
  ② Initiating the other drug in the drug pair that is being compared
- End of enrollment for MarketScan
- End of Study (December 31, 2016)

Medicare
- 180-day latency after change of initial Rx
  ① Discontinuation
  ② Initiating the other drug in the drug pair that is being compared
- Death
- End of Enrollment for Medicare Part A, B or D
- End of Study (December 31, 2016)

A diagnosis code for IBD event
Sensitivity analysis 4: Modified outcome

Primary outcome

- 180-day latent period
  - Cohort entry date (Second prescription)
  - The start of Follow-up
  - Colonoscopy
    - Sigmoidoscopy
  - Biopsy
  - IBD treatment
  - September 30, 2016
    - End of Study

Modified outcome 1

- 180-day latent period
  - Cohort entry date (Second prescription)
  - The start of Follow-up
  - Colonoscopy
    - Sigmoidoscopy
  - Biopsy
  - The 1st IBD Diagnosis
  - IBD treatment
  - September 30, 2016
    - End of Study

Modified outcome 2

- 180-day latent period
  - Cohort entry date (Second prescription)
  - The start of Follow-up
  - Colonoscopy
    - Sigmoidoscopy
  - The 1st IBD Diagnosis
  - IBD treatment
  - September 30, 2016
    - End of Study

Modified outcome 3

- 180-day latent period
  - Cohort entry date (Second prescription)
  - The start of Follow-up
  - Colonoscopy
    - Sigmoidoscopy
  - The 1st IBD Diagnosis
  - IBD treatment
  - September 30, 2016
    - End of Study

Modified outcome 4

- 180-day latent period
  - Cohort entry date (Second prescription)
  - The start of Follow-up
  - The 1st IBD Diagnosis
  - The 2nd IBD Diagnosis
  - The 3rd IBD Diagnosis
  - September 30, 2016
    - End of Study
Sensitivity analysis 5: relaxed exclusion criteria

- **Included:**
  - received abovementioned IBD treatments **except**
    - mesalamine;
    - Enteral budesonide
  - **Procedure:**
    - partial colectomy
    - Colostomy
    - Ileostomy
    - ostomy supplies;
  - MarketScan patients who received colonoscopy or sigmoidoscopy prior to age 50
Sensitivity analysis 6: censor Rx induce IBD

- Rx may induce IBD
  - Oral contraceptives
  - Hormonal replacement therapy
  - Aspirin
  - NSAIDs
  - Isotretinoin
  - Mycophenolate mofetil
  - Etanercept
  - Ipilimumab
  - Rituximab
Sensitivity analysis 7: Multivariable Regression

- Conventional multivariable-adjusted Cox regression
Sensitivity analysis 8:

- excluded patients who originally qualified for Medicare due to
  - end stage renal disease
  - disability
Results
Table 1. Key covariates for MarketScan population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DPP4i vs SU</th>
<th></th>
<th></th>
<th>DPP4i vs TZD</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DPP4i (N=137,130)</td>
<td>SU (N=234,503)</td>
<td>Weighted SU</td>
<td>DPP4i (N=171,311)</td>
<td>TZD (N=69,169)</td>
<td>Weighted TZD</td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>52.4 ± 8.32</td>
<td>51.0 ± 9.48</td>
<td>51.8 ± 8.88</td>
<td>52.4 ± 8.32</td>
<td>52.2 ± 8.52</td>
<td>52.4 ± 8.46</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>75,157 (54.8)</td>
<td>124,751 (53.2)</td>
<td>81,831 (53.0)</td>
<td>94,707 (55.3)</td>
<td>40,243 (58.2)</td>
<td>98,589 (54.4)</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>7,405 (5.4)</td>
<td>10,260 (4.4)</td>
<td>7,895 (5.1)</td>
<td>10,196 (6.0)</td>
<td>4,089 (5.9)</td>
<td>10,940 (6.0)</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>3,607 (2.6)</td>
<td>5,972 (2.5)</td>
<td>4,035 (2.6)</td>
<td>5,179 (3.0)</td>
<td>2,112 (3.1)</td>
<td>5,593 (3.1)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>6,734 (4.9)</td>
<td>10,079 (4.3)</td>
<td>7,231 (4.7)</td>
<td>9,845 (5.7)</td>
<td>3,580 (5.2)</td>
<td>10,661 (5.9)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>1,142 (0.9)</td>
<td>1,744 (0.8)</td>
<td>1,298 (0.8)</td>
<td>1,390 (0.8)</td>
<td>489 (0.7)</td>
<td>1,484 (0.8)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>738 (0.6)</td>
<td>1,102 (0.5)</td>
<td>799 (0.5)</td>
<td>805 (0.5)</td>
<td>257 (0.4)</td>
<td>868 (0.5)</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>284 (0.2)</td>
<td>439 (0.2)</td>
<td>350 (0.2)</td>
<td>291 (0.2)</td>
<td>103 (0.1)</td>
<td>376 (0.2)</td>
</tr>
<tr>
<td>Oral contraceptives / Hormones</td>
<td>7,085 (5.2)</td>
<td>12,378 (5.3)</td>
<td>8,870 (5.7)</td>
<td>8,330 (4.9)</td>
<td>3,258 (4.7)</td>
<td>9,445 (5.2)</td>
</tr>
</tbody>
</table>
# Table 1. Key covariates for Medicare population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>DPP4i vs SU*</th>
<th>DPP4i vs TZD*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DPP4i (N=46470)</td>
<td>SU (N=117830)</td>
</tr>
<tr>
<td>Age, mean ± SD</td>
<td>74.8 ± 7.29</td>
<td>74.4 ± 7.51</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>19,027 (40.9)</td>
<td>51,619 (43.8)</td>
</tr>
<tr>
<td>Retinopathy</td>
<td>6,385 (13.7)</td>
<td>12,073 (10.2)</td>
</tr>
<tr>
<td>Nephropathy</td>
<td>4,118 (8.9)</td>
<td>7,760 (6.6)</td>
</tr>
<tr>
<td>Neuropathy</td>
<td>8,910 (19.2)</td>
<td>16,960 (14.4)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>505 (1.1)</td>
<td>1,266 (1.1)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>1,279 (2.8)</td>
<td>2,585 (2.2)</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>152 (0.3)</td>
<td>290 (0.2)</td>
</tr>
<tr>
<td>Oral contraceptives / Hormones</td>
<td>830 (1.8)</td>
<td>1,717 (1.5)</td>
</tr>
</tbody>
</table>
### Table 2. As treated analysis (primary)

<table>
<thead>
<tr>
<th>Database</th>
<th>Cohort</th>
<th>No. of Patients</th>
<th>Follow-up years: median (IQR)</th>
<th>Person-yr</th>
<th>No. of IBD events</th>
<th>IBD Rate per 100,000 pyrs</th>
<th>Crude HR (95% CI)</th>
<th>PS weighting HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MarketScan</td>
<td>DPP-4i</td>
<td>117,451</td>
<td>1.21 (0.73-2.04)</td>
<td>146,162</td>
<td>35</td>
<td>23.9 (17.2-33.4)</td>
<td>1.08 (0.70-1.65)</td>
<td>1.08 (0.70-1.68)</td>
</tr>
<tr>
<td></td>
<td>SU</td>
<td>199,637</td>
<td>1.12 (0.66-1.96)</td>
<td>238,440</td>
<td>53</td>
<td>22.2 (17.4-29.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>DPP-4i</td>
<td>41,208</td>
<td>1.20 (0.74-2.27)</td>
<td>NA</td>
<td>NTSR</td>
<td>12.5 (6.0-26.3)</td>
<td>0.53 (0.24-1.17)</td>
<td>0.54 (0.23-1.23)</td>
</tr>
<tr>
<td></td>
<td>SU</td>
<td>105,969</td>
<td>1.42 (0.83-2.67)</td>
<td>168,942</td>
<td>39</td>
<td>23.1 (16.9-31.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MarketScan</td>
<td>DPP-4i</td>
<td>146,757</td>
<td>1.27 (0.75-2.13)</td>
<td>189,938</td>
<td>40</td>
<td>21.1 (15.4-28.7)</td>
<td>0.64 (0.39-1.06)</td>
<td>0.67 (0.36-1.24)</td>
</tr>
<tr>
<td></td>
<td>TZD</td>
<td>60,228</td>
<td>1.09 (0.67-1.88)</td>
<td>71,273</td>
<td>24</td>
<td>33.7 (22.6-50.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>DPP-4i</td>
<td>54,492</td>
<td>1.25 (0.76-2.30)</td>
<td>75,300</td>
<td>14</td>
<td>18.6 (11.0-31.4)</td>
<td>0.54 (0.25-1.16)</td>
<td>0.77 (0.31-1.93)</td>
</tr>
<tr>
<td></td>
<td>TZD</td>
<td>26,380</td>
<td>1.11 (0.72-2.02)</td>
<td>34,968</td>
<td>12</td>
<td>34.3 (19.5-60.4)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: Yr, year; IQR, interquartile range; HR, hazard ratio; PS, propensity score; CI, confidence interval; DPP4i, DPP-4 inhibitor; SU, Sulfonylurea; TZD, Thiazolidinedione; NTSR: numbers too small (<11) to report based on Center for Medicare and Medicaid Services (CMS) rules and data use agreement (Person-yr is not shown in this case to block the number of event).
**Table 2. As treated analysis (primary)**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Hazard ratio (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DPP4i vs SU</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MarketScan</td>
<td>1.08 (0.70, 1.68)</td>
<td>63.85</td>
</tr>
<tr>
<td>Medicare</td>
<td>0.54 (0.23, 1.23)</td>
<td>36.15</td>
</tr>
<tr>
<td>Random-effects model</td>
<td>0.84 (0.44, 1.61)</td>
<td>100.00</td>
</tr>
<tr>
<td>(I-squared = 51.5%, p = 0.151)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DPP4i vs TZD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MarketScan</td>
<td>0.67 (0.36, 1.24)</td>
<td>68.62</td>
</tr>
<tr>
<td>Medicare</td>
<td>0.77 (0.31, 1.93)</td>
<td>31.38</td>
</tr>
<tr>
<td>Random-effects model</td>
<td>0.70 (0.42, 1.17)</td>
<td>100.00</td>
</tr>
<tr>
<td>(I-squared = 0.0%, p = 0.805)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Decreased risk | Increased risk
DPP4i vs SU

Secondary analysis

Sensitivity analysis 1

Sensitivity analysis 2

Sensitivity analysis 3

Sensitivity analysis 4

Sensitivity analysis 5

Sensitivity analysis 6

Sensitivity analysis 7

Sensitivity analysis 8
Conclusions
Conclusion

- Our active-comparator, new-user cohort study of US adults showed DPP4i are not associated with an increased IBD risk compared with therapeutic alternatives.
Acknowledgements

- Jeff Y Yang
- John B Buse
- Virginia Pate
- Huilin Tang
- Edward Barnes
- Robert S. Sandler
- Til Stürmer
- UNC Pharmacoepidemiology Center
Thank you

tianwang@unc.edu
Discussion
The CPRD study

Scenario 1: initiating other oral GLDs, then switch/augment to DPP4i

1. Metformin
2. DPP4i
3. SGTL2i Switch
4. End of Follow-up

180 days lag

Scenario 2: initiating DPP4i, then switch/augment to other oral GLDs

1. DPP4i
2. Sulfonylurea
3. SGTL2i Switch
4. End of Follow-up

180 days lag

Scenario 3: initiating other oral GLDs and never switch/augment to DPP4i

1. Metformin
2. GLP1RA
3. SGTL2i Switch
4. End of Follow-up

180 days lag

Red = DPP4i exposed person-time
Blue = other oral GLD exposed person-time
<table>
<thead>
<tr>
<th>Year</th>
<th>T2D Patients</th>
<th>T2D Patients on SU</th>
<th>SU Prescriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>2001</td>
<td>25,000</td>
<td>15,000</td>
<td>15,000</td>
</tr>
<tr>
<td>2002</td>
<td>27,000</td>
<td>16,500</td>
<td>16,500</td>
</tr>
<tr>
<td>2003</td>
<td>29,000</td>
<td>18,000</td>
<td>18,000</td>
</tr>
<tr>
<td>2004</td>
<td>31,000</td>
<td>19,500</td>
<td>19,500</td>
</tr>
<tr>
<td>2005</td>
<td>33,000</td>
<td>21,000</td>
<td>21,000</td>
</tr>
</tbody>
</table>

Note: The number of T2D patients and SU prescriptions increased each year, with a corresponding increase in the number of patients on SU.