Medication Possession Ratio and Health Benefit Cost Comparisons in Type 2 Diabetes Patients Using Fixed- and Loose-Dose Thiazolidinedione Combination Products

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ABSTRACT

The objective of this study was to assess the impact of fixed- and loose-dose combination (FDC and LDC) thiazolidinedione (TZD) products on medication possession ratios (MPRs) and associated health benefit costs (HBCs) among type 2 diabetes mellitus (T2DM) patients.

The Human Capital Management Services Research Reference Database (HCMS RRDb) of United States (US) employees from 1/1/2001-12/31/2006 was used to study compliance and health-related costs in adult T2DM patients (ICD-9 codes of 250.X0 or .X2) prescribed a TZD along with metformin or a sulfonylurea either in separate (LDC) or combined (FDC) dosage forms. Costs were from claims for direct medical (inpatient, outpatient clinic/MD office, ER, laboratory, and other), prescription, sick leave, short- and long-term disability, and workers' compensation. Cohorts were matched 1:1 on demographics, job information, Charlson Comorbidity Index (CCI), and average co-payment. Index Date was assigned by first FDC TZD prescription or first occurrence of TZD within 45 days of metformin or sulfonylurea in the LDC component. Outcome measures included MPRs (days supply/days between fills), compared by the Woolf odds ratio test, and employer-paid HBCs. Costs were inflated to 2006 US dollars as appropriate and adjusted using regression modeling to control for age, gender, marital status, race, exempt status, full-time/part-time status, salary, location, CCI, insulin use, and the 1st digit of the patient's zip code.

Data were available for 163 matched subjects per cohort. Mean MPR was significantly higher for FDC (65%) than for LDC (50%) (P<0.0001). Pioglitazone and rosiglitazone LDC MPRs were similar. Total annual costs were lower for FDC users ($5360 FDC vs $6173 LDC), but not significantly different. Similar trends were seen in specific cost components: direct medical $2285 FDC vs $2666 LDC; prescription $2370 FDC vs $2678 LDC; sick leave $384 FDC vs $472 LDC; short-term disability $278 FDC vs $136 LDC; and Workers' Compensation $43 FDC vs $221 LDC.

Adherence to TZD combination therapy was significantly higher for those on FDC TZD compared with LDC TZD products based on MPRs. The adherence rates were congruent with those reported for other chronic oral medications. Although not significant, most study costs showed a lower trend among FDC users. This analysis showed the significant impact of FDCs on compliance and a trend toward reduction in costs.

BACKGROUND

- The prevalence of diagnosed diabetes mellitus is 7% in the US Population (all ages).[1] Type 2 diabetes mellitus (T2DM) accounts for 90% to 95% of all diagnosed cases of diabetes.[1]
- Persistence with prescription (Rx) therapy is often suboptimal among patients with T2DM, resulting in impaired glycemic control, poor health outcomes, and increased resource utilization. Many patients with T2DM that is managed by oral antidiabetic drugs (OADs) require polytherapy that may include combinations of:
  - A thiazolidinedione (TZD), such as pioglitazone HCl or rosiglitazone maleate.
  - Metformin, a biguanide.
  - Sulfonylureas, which include products such as glyburide or glipizide.
- Poor compliance and persistence with OADs has been documented, and when multiple OADs are needed to maintain glycemic control, nonpersistence may be exacerbated.
- The OAD market now includes TZD combination products for pioglitazone (pioglitazone+metformin and pioglitazone+glimepiride) and rosiglitazone (rosiglitazone+metformin and rosiglitazone+glimepiride).
- It is important to understand the impact that FDC therapies have on compliance and cost.

OBJECTIVES

- The goals of the current study were to assess the impact of fixed-dose (FDC) and loose-dose (LDC) combination TZD products on:
  - Medication Possession Ratio.
  - Health benefit costs, which include medical and pharmacy costs.

METHODS

- A retrospective analysis was performed on data (2001 to 2006) from the Human Capital Management Services (HCMS) Research Reference Database consisting of approximately 510,000 employees representing the retail, service, manufacturing, and financial industries.
- Patients with T2DM were identified based on the presence of International Classification of Diseases, 9th Revision (ICD-9) diagnostic codes of 250.X0 (Type II Diabetes, not stated as uncontrolled) or 250.X2 (Type II Diabetes, uncontrolled).

METHODS

- Patients with an Rx claim for metformin or a sulfonylurea, concurrent with a TZD (LDC) or combined with a TZD (FDC), were matched on demographics, job information, geography, and co-payment in a 1:1 ratio.
- Index Date was assigned by the first FDC TZD Rx or the first occurrence of TZD within 45 days of metformin or sulfonylurea in the LDC component.
  - Index Dates before 31 May 2004 were required to avoid the FDC rosiglitazone+metformin supply shortage between June 2005 and July 2006.
- Employees included in the analysis were required to be continuously employed and eligible for health benefits for at least 12 months after their Index Date.
- Because of the 12-month eligibility requirement and the timeframe of the study, the FDC cohort is represented by rosiglitazone+metformin only as it was the FDC with sufficient data during the study period.
- It is assumed that the FDC cohort is representative of the TZD class, and pioglitazone+metformin specifically.
- Comparisons were made between 2 groups (FDCs and LDCs).
- Medication Possession Ratio is defined as the sum of the days supply of medicine divided by the days in the time period (365).
- Employee outcomes for both groups were compared over the 12 months following the Index Date and included:
  - Medication Possession Ratio.
  - Number of months of therapy was defined as the months of supply purchased during the 12 months following the Index Date.
  - Health benefit cost was defined as direct medical and prescription costs as well as indirect costs associated with payments for absences (sick leave, short- and long-term disability, and workers' compensation).
    - Costs were inflation-adjusted to 2006 US dollars.

Statistical Analysis

- Employees in the LDC and FDC cohorts were matched 1:1 using logistic regression and propensity scores for age, tenure (years with current employer), sex, marital status, race, exempt/non-exempt status (exempt employees are not paid on an hourly basis and are not paid for overtime work), full-time/part-time status, salary, region (defined by first digit of employee's postal zip code), employer, and average co-payment.
- Comparisons between groups were made using Woolf odds ratio tests for Medication Possession Ratio, and Chi-square tests for months-supply distributions, percent of employees reaching 90 days without a gap in supply.
- Two-part regression analysis was used to model the cost differences between the FDC and LDC cohorts using separate regression models for direct medical costs, prescription drug costs, and absence (indirect) costs.
  - The models controlled for population differences in age, tenure (years with current employer), sex, marital status, race, exempt/non-exempt status (exempt employees are not paid on an hourly basis and are not paid for overtime work), full-time/part-time status, salary, Charlson Comorbidity Index,[2] and geography (defined by the first digit of the employee's postal zip code).
  - Only employees eligible for each specific benefit were included in the regression models for that benefit.
  - Indirect costs were summed over all absence claims initiated at any point during the year following the Index Date.
    - Differences were considered significant if P<0.05.

RESULTS

- Data were available for 163 matched subjects per cohort with no significant baseline differences **(Table 1)**.
  - All subjects in the FDC cohort used rosiglitazone as a TZD component.
  - Among the LDC cohort, 54% used pioglitazone and 49% used rosiglitazone.
- Following propensity-score matching, both cohorts averaged 41 years of age, were predominantly male (74% for FDC and 69% for LDC), were predominantly married (>66%), and worked full-time (>98%). The majority of employees in both cohorts were White (>50%).
- Medication Possession Ratio was significantly better (P<0.0001) for the FDC cohort at 65% MPR compared with the LDC cohort at 50% MPR **(Figure 1).**
- The number of months supply was shifted towards more days for the FDC cohort **(Figure 2)**.
- All health benefit costs **(Table 2)** were similar between the cohorts:
  - Overall costs as well as direct medical costs, prescription drug costs, and indirect costs due to sick leave and workers' compensation all trended lower for the FDC cohort.
  - Neither group had any long-term disability claims.

Table 1. Descriptive Statistics

Variable	Diabetes Treated with TZD FDC Cohort (N=163) Mean (SE) or Percent (%)	Diabetes Treated with TZD LDC Cohort (N=163) Mean (SE) or Percent (%)
Age (years at Index Date)	46.00 (0.66)	47.57 (0.74)
Tenure (years at Index Date)	9.63 (0.69)	10.54 (0.81)
Annual Salary (US dollars)	49,228 (2,291)	47,060 (2,002)
Charlson Comorbidity Index Score	1.45 (0.09)	1.58 (0.10)
Female, %	26.4	30.7
Married, %	66.4	71.6
White, %	52.1	54.6
Black, %	19.2	19.1
Hispanic, %	23.3	19.9
Exempt, %	22.7	20.2
Full Time, %	98.8	98.8
Geography, 1st digit zip code		
0, %	5.5	6.7
1, %	3.1	4.3
2, %	9.2	9.8
3, %	20.2	15.3
4, %	2.5	3.7
5, %	1.2	0.0
6, %	4.3	1.8
7, %	42.9	49.1
8, %	4.9	4.3
9, %	6.1	4.9

Figure 1. Medication Possession Ratios: FDC vs Matched LDC Cohorts

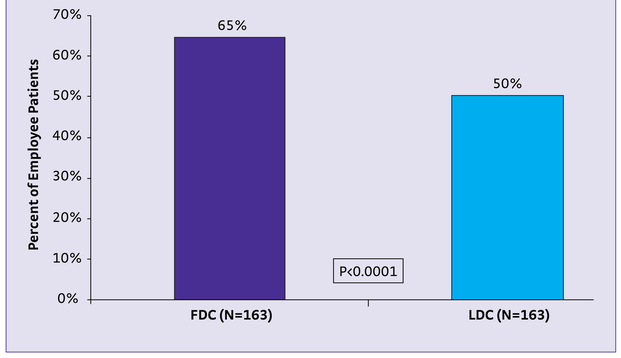
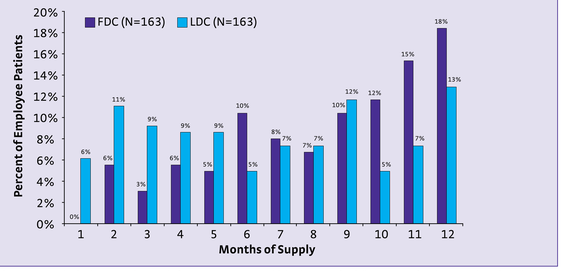


Figure 2. Number of Months Supply by FDC and LDC Cohorts



Note: FDC patients were required to have an Index Date before 31 May 2004 to avoid the shortage of rosiglitazone+metformin. LDC patients (matched on demographics, salary, and average co-payment) were required to have a supply of both the TZD and either metformin or a sulfonylurea.

Table 2. Annual Health Benefit Costs per Employee

Cost Category	Diabetes Treated with TZD FDC Cohort (N=163) N	Diabetes Treated with TZD FDC Cohort (N=163) Adjusted Mean Cost	Diabetes Treated with TZD LDC Cohort (N=163) N	Diabetes Treated with TZD LDC Cohort (N=163) Adjusted Mean Cost	Difference in Means
Medical costs	163	$2,285	163	$2,666	-$381
Prescription Drug	163	$2,370	163	$2,678	-$308
Sick Leave	95	$384	86	$472	-$88
Short-term Disability	112	$278	81	$136	$142
Workers' Compensation	160	$43	156	$221	-$178
Total		$5,360		$6,174	-$814

All comparisons nonsignificant (P>0.05). Costs are in 2006 US dollars.

LIMITATIONS

- Data availability at this time limits the composition of the FDC cohort.
- The composition of the FDC cohort serves as a surrogate for pioglitazone+metformin.

SUMMARY AND CONCLUSIONS

- Adherence as measured by Medication Possession Ratio with FDC combination therapy was significantly better than with LDC.
- FDC TZD therapies provide an advantage for patients with T2DM.
- T2DM is associated with substantial direct and indirect cost (burden) of illness, which can be a large financial liability to employers.
- Individuals with T2DM managed by OAD that includes TZDs who are more compliant may have lower costs.
- These results indicate an opportunity for improved management of patients with T2DM, which may result in reduced costs from an employer perspective.
- This study suggests that:
  - T2DM patients achieve compliance benefits from reduced medication burden by using FDC.
  - Additional research is needed with newer data in these cohorts to further inform us on the long-term impact on compliance and cost.

REFERENCES

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