Diabetes care & risk of kidney disease in Medicare elderly patients with diabetes: an instrumental variable analysis

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Introduction

Background

- In patients age 25-65 with type 2 diabetes (DM), increased glycemic control has been shown to reduce the risk of renal failure by 27% , of myocardial infarction by 16%, and of microvascular complication by 25%.[1]
- In patients age 13-39 with type 1 DM, increased glycemic control also reduces the risk of microalbuminuria by 39%, of albuminuria by 54%, and of macrovascular disease by 41%.[2]
- American Diabetes Association (ADA) standards for diabetes care include at least two HbA1c tests a year.[3]

Objective

- To examine the effect of HbA1c testing as a surrogate for glycemic control on the risk of chronic kidney disease (CKD) in DM patients older than 65.

Hypothesis

- HbA1c testing is associated with a reduction in the risk of CKD in elderly DM patients.

1. UKPDS Group: Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes. The Lancet, 352:837-853, 1998

2. DCCT Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The New England Journal of Medicine, 329:977-986, 1993

3. American Diabetes Association. Standards of medical care for patients with diabetes mellitus. Diabetes Care 26 (Suppl. 1): S33-S50, 2003

Methods

- Population and data sources
  - 1998-99 Medicare patients with newly reported DM, age 65+, non-HMO, non-ESRD, part A and B eligible, w/o CVD prior to 1998, and alive at least 2 yrs after reported DM
  - 5% Medicare claims data
- Study design
  - Two-year entry period with baseline data and HbA1c test (CPT code 83036) collected in the 2 years
  - Four-year follow-up with CKD complication and death data
- Analytical model – instrumental variable (IV) analysis
  - IV- ADA Diabetes Education Programs (DEP) – to account for selection bias in observational study
  - Stage 1: Logistic regression

    $HbA1c = \alpha_0 + \alpha_1 \cdot IV$
  - Stage 2: Cox regression

    $CKD = \beta_0 + \beta_1 \cdot X + \beta_2 \cdot HbA1c\hat{} + \mu$

    X: individual, social, & healthcare variables

    HbA1c^: predicted HbA1c test rate from stage 1

Results

- Overall characteristics: among 13,282 DM patients:
  - Mean age: 72.64 ± 5.63
  - White, 86.4% and black, 8.6%
  - Female: 60.5%
  - Medicaid eligible: 15.1%
  - Hypertension: 66.4%
  - Mean Follow-up after reported DM: 3.2 yrs
- Validating the IV
  - Evidence of selection bias (*Table 1*)
  - IV assumption 1 – IV affects HbA1c testing rate
    - F-value from stage 1: 10.31
    - IV affects receiving DM training and DM care (*Tables 2-3*)
  - IV assumption 2 – IV is uncorrelated with baseline characteristics and health status, therefore no direct effect on outcome (*Table 4*)
- Effect on risk of CKD from controlled variables (*Table 5*)
- Effect of HbA1c testing on the risk of CKD from IV analysis and comparing result from UKPDS and DCCT (*Table 6*)

Table 1 Distribution of baseline characteristics in patients receiving or not receiving HbA1c test

Group	No HbA1c Test	With HbA1c Test	P-chisq
N	4,056	9,226	
Age (yrs)	73.3	72.3	<0.0001
Male (%)	37.8	40.3	0.0058
White (%)	83.0	87.9	<0.0001
Black (%)	10.6	7.7	<0.0001
Hypertension (%)	63.0	67.9	<0.0001
Anemia (%)	21.3	12.0	<0.0001
COPD* (%)	14.6	10.8	<0.0001
Hospitalization^	3.3	1.5	<0.0001

* chronic obstructive pulmonary disease
^ mean hospitalization in days in 2 yrs entry period

Table 2 DM training in patients residing outside and within an ADA DM Education Program (DEP)

	Percent with DM Self-Management Training (DSMT) (%)		
Patient group	1998	1999	2000
Outside DEP	0.81	3.51	7.28
Within DEP^	0.94	4.28	11.76

^ patient and DEP have the same Zip code

Table 3 DM standard care in patients with and without DM self-management training (DSMT)

	Percent Receiving DM Care (%)				
Patient group	HbA1c Test	Eye Exam	Kidney Screen	Lipid Profile	Glucose Monitoring
No DSMT	68.6	54.3	66.1	71.3	20.1
Within DSMT	95.3	66.7	79.1	81.8	64.0

Table 4 Distribution of baseline characteristics in patients residing outside and within an ADA DM Education Program (DEP)

Group	No DEP	With DEP	P-chisq
N	2,690	10,592	
Age (yrs)	72.6	72.9	0.0097
Male (%)	39.5	39.5	0.9691
White (%)	86.3	87.0	0.3206
Black (%)	8.4	9.3	0.1331
Hypertension (%)	66.5	65.9	0.5130
Anemia (%)	14.9	14.5	0.5605
COPD* (%)	12.1	11.6	0.4476
Hospitalization^	2.0	2.3	0.6233

* chronic obstructive pulmonary disease
^ mean hospitalization in days in 2 yrs entry period

Table 5 Effect on risk of CKD for controlled variables

Variables	RR	Lower	Upper	P-value
Age (years)	1.04	1.03	1.06	<.0001
Male (vs. female)	1.64	1.46	1.85	<.0001
Anemia (yes vs. no)	1.28	1.10	1.49	0.0015
COPD (yes vs. no)	1.28	1.09	1.51	0.0032
Hypertension (yes vs. no)	1.47	1.29	1.67	<.0001
Liver disease (yes vs. no)	1.81	1.25	2.61	0.0016
No hospitalization in entry period	1.00			
Hospital days: 1-6	1.03	0.86	1.23	0.7712
Hospital days: 7+	1.07	0.87	1.32	0.5333
Black (vs. white)	1.26	1.04	1.52	0.0169
Other race (vs. white)	1.02	0.79	1.33	0.8561
Medicaid (yes vs. no)	1.39	1.19	1.62	<.0001
Median family income < $28,449	1.00			
Income $28,449 – $32,769	1.10	0.85	1.41	0.4536
Income $32,769 – $37,655	1.08	0.86	1.37	0.4902
Income $37,655 – $43,198	1.19	0.94	1.50	0.1445
Income $43,198 – $53,382	1.18	0.92	1.51	0.2014
Income >= $53,382	0.96	0.73	1.26	0.7969
Physician visits				
General practice (yes vs. no)	0.98	0.83	1.14	0.7583
Family practice (yes vs. no)	0.99	0.88	1.12	0.8833
Internal medicine (yes vs. no)	0.82	0.72	0.93	0.0019
Endocrinology (yes vs. no)	1.24	0.95	1.61	0.1074
Rural (vs. urban)	0.92	0.77	1.11	0.3927
Mid-W/W (vs. North-east/South)	1.01	0.89	1.14	0.9166
DM visits <=2 in entry period	1.00			
DM visits 3-4 times	1.12	0.96	1.31	0.1586
DM visits 5-7 times	1.10	0.94	1.29	0.2287
DM visits 8+	1.43	1.23	1.67	<.0001
DM training (yes vs. no)	1.20	0.83	1.73	0.3399
DM diagnosed yr (99 vs. 98)	1.03	0.91	1.16	0.6962
No. of providers visited < 8	1.00			
No. of providers visited 8+	1.02	1.00	1.03	0.0081
Size of providers ^ <-2,597	1.00			
Size of providers ^ >= 2,598	1.02	0.90	1.15	0.7692
Lipid test (yes vs. no)	0.95	0.83	1.08	0.4145
Flu vaccination (yes vs. no)	0.88	0.78	0.99	0.0338

^ measured by total patients cared by all providers visited in 2 yrs entry period

Table 6 Effect of glycemic control on risk of kidney disease with IV analysis and controlled for individual, social, and healthcare system variables

Glycemic Control/monitoring	RR	Lower	Upper	P-value
HbA1c test rate increases 3.19%*	0.80^	0.74	0.86	0.0035
HbA1c test (yes vs. no)~	0.94	0.82	1.07	0.3334
Glycemic control vs. standard care in UKPDS[1]	0.73	0.25	2.14	0.45
Glycemic control vs. standard care in DCCT[2] reduced risk in albuminuria by 54% (19%-74%) and risk in microalbuminuria by 39% (21%-52%)				

* Predicted HbA1c test rates for patients reside outside and within an ADA DM Program are 68.82% and 72.01%, respectively
^ RR = $EXP^{coefficient * 3.19}$ with IV analysis
~ Cox regression without IV analysis and controlled for same variables as in the analysis with IV

Conclusions

- Among 13,282 Medicare elderly DM patients, HbA1c test rates were 68.82% and 72.01% in the first 2 years, and rates of CKD were 9.57% and 7.92% in the third to sixth years of DM for patients outside and within an ADA Diabetes Education Program (DEP), respectively.
- An increased HbA1c test rate due to access to a DEP was associated with a reduction of CKD risk. A one percent increase in the HbA1c test rate caused a 6.79% decrease in CKD risk in the four-year follow up. This effect is attributable to the subgroup who received an HbA1c test due to a DEP.
- It is verified that this result was corrected for selection bias in the observational study due to two facts: this finding is consistent with DCCT and UKPDS findings, and is more preferable than the naïve estimate (Table 6).
- Healthcare system characteristics play an important role in implementing the standards of diabetes care and affecting diabetes-related outcomes such as CKD.
- This study implies that access to care measured by HbA1c testing may be an appropriate measure in determining the effect of care processes on patient outcomes if corrected for selection bias such as an IV analysis in observational study.

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