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Reductions in Mortality Among Medicare Beneficiaries Following the Implementation of Medicare Part D

April P. Semilla, MS; Fang Chen, PhD; Timothy M. Dall, MS

Abstract

Medicare Part D is a prescription drug program that provides seniors and disabled individuals enrolled in Medicare with outpatient drug coverage benefits. Part D has been shown to increase access to medicines and improve medication adherence; however, the effect of Part D on health outcomes has not yet been extensively studied. In this study, we used a published and validated Markov-based microsimulation model to quantify the relationships among medication use, disease incidence and severity, and mortality. Based on the simulation results, we estimate that since the implementation of Part D in 2006, nearly 200,000 Medicare beneficiaries have lived at least 1 year longer. Reductions in mortality have occurred because of fewer deaths associated with medication-sensitive conditions such as diabetes, congestive heart failure, stroke, and myocardial infarction. Improved access to medication through Medicare Part D helps patients improve blood pressure, cholesterol, and blood glucose levels, which in turn can prevent or delay the onset of disease and the incidence of adverse health events, thus reducing mortality.

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BACKGROUND AND OBJECTIVES

In 2003, Medicare Part D, a prescription drug program providing outpatient drug coverage benefits to seniors and disabled individuals enrolled in Medicare, was signed into law. A large body of literature documents the positive impact that Part D has had on increasing access to medicines and improving medication adherence; however, the effect of Part D on health outcomes has not yet been extensively studied.[1-9]

While life expectancy among the population 65 years and older has increased since 2006,[10] 4 studies that have examined Part D's impact on mortality report mixed findings.[5,11-13] Kaestner et al and Briesacher et al found no statistically significant association between Part D and mortality.[5,11] Huh and Reif estimated that Part D reduced overall mortality among beneficiaries by 2.2% annually, with the effect driven primarily by a decrease in cardiovascular-related deaths.[12] Similarly, Dunn and Shapiro found that Part D

reduced cardiovascular-related mortality, but that mortality associated with noncardiovascular disease remained unchanged.[13] Dunn and Shapiro estimate that between 21,800 and 25,500 individuals were still alive in mid-2007 because of Part D's implementation in 2006. These 4 studies were limited to a narrow time frame of analysis or made strong assumptions regarding the continuation of historical trends pre- and post Part D. The goal of this study is to further explore Part D's effect on mortality from 2006 to the present.

STUDY DESIGN

This study used a published and validated Markov-based microsimulation model to quantify the relationships among medication use, disease incidence and severity, and mortality. Information on the model design, data, assumptions, methods, and validation results have been published elsewhere.[14,15] A microsimulation approach was chosen based on its ability to model changes in health and disease states longitudinally based on individual demographics (age, sex, race, ethnicity), biometrics (body mass index [BMI], systolic blood pressure [SBP], diastolic blood pressure [DBP], total cholesterol, high-density lipoprotein cholesterol [HDL-C], and glycated hemoglobin [A1C]), smoking status, and presence of approximately 30 diseases to predict mortality as an individual ages. The model incorporates the expected impact of medication use on changes in blood pressure, cholesterol, and A1C levels, and simulates the resulting implications on disease incidence and severity that in turn impact the cause and timing of beneficiary mortality.

METHODS

Population

We created a representative sample of the Medicare population using data from the 2005 to 2012 National Health and Nutrition Examination Survey (NHANES) files.[16] The combined files contain data for 3621 Medicare beneficiaries 65 years and older, including demographic and biometric information required for use in the microsimulation model. Using NHANES sample weights to dictate the probability of selection, we used Monte Carlo simulation, which involves repeated random sampling of the population, to produce a nationally representative simulation sample of 100,000 observations representative of the estimated 22.5 million beneficiaries enrolled in Medicare Part D in 2006.[17] We added 20,000 additional observations in each year of the simulation to represent new enrollees in Part D. This annual number of observations added to the simulation population reflected that net enrollment in Part D grew by approximately 6.5% annually between 2006 and 2014 after factoring in mortality, and the assumption that once enrolled in Part D beneficiaries did not drop Part D coverage unless death occurred.[18]

Using this model, we simulated outcomes for this population under 2 scenarios over the 2006 to 2014 period:

1. ***Medicare Part D scenario:*** An estimated 25% of Part D enrollees would not have had comprehensive drug coverage in the absence of Part D.[19,20] Beneficiaries who gained comprehensive coverage under Part D increased their use of medication.[3,4,6,21,22] For modeling purposes, we used findings from Zhang et al, which showed that drug possession rates increased by 29%, 31%, and 22%, respectively, for people diagnosed with hyperlipidemia, diabetes, and hypertension.[23]
2. ***Status Quo scenario:*** In this scenario, there were no changes in drug coverage among the Medicare population. As a result, there were no changes in medication use, and natural progression of disease and mortality was maintained.

Results for both scenarios were then scaled to simulate total Part D enrollment.

Model Parameters and Disease States

For each beneficiary, the previous year's health status was used to predict the current year's outcomes, with this process repeated through 2014 or until death. Prediction equations dictating the transition probabilities for various cardiovascular conditions (congestive heart failure [CHF], ischemic heart disease, stroke, myocardial infarction [MI]), diabetes, chronic kidney disease, renal failure, and other diseases modeled were obtained from published studies including the Framingham Heart Study, the United Kingdom Prospective Diabetes Study, and various clinical trials and observational studies.[24-30] Annual changes in body weight were estimated based on national trends by age, sex, and current weight.[14,15] Annual changes in DBP, SBP, HDL-C and total cholesterol were determined based on each beneficiary's age, sex, and change in BMI,[14,15,24,31,32] while changes in A1C were predicted based on BMI, age, and total cholesterol (if beneficiary did not have diabetes) and years since diagnosis and previous year's A1C (if diabetic).[14,15,28]

Annual mortality rates associated with the chronic diseases modeled, acute events such as MI and stroke, and "all other causes" were estimated from published sources and based on demographics, biometrics, smoking status, and presence of adverse medical conditions.[14,15,28,33,34]

Coverage and Drug Effect

To simulate the impact of gaining comprehensive drug coverage under the Part D scenario, enrollees with high cholesterol (total cholesterol >240 mg/dL), high blood pressure (SBP >140 mm Hg or DBP ≥90 mm Hg), and high A1C levels (≥6.5%) were assumed to increase their medication use, resulting in improvements on these measurements. We performed sensitivity

analyses using published 95% CIs for key parameters used in the model. We modeled that statins would reduce total blood cholesterol by 34.42 mg/dL (CI, 22.04-46.40), and anti-hypertensives would reduce SBP by 14.5 mm Hg (CI, 14.2-14.8) and DBP by 10.7 mm Hg (CI, 10.5-10.8).[35,36] These reductions were assumed to occur entirely within the first year of therapy. Oral diabetes medications were assumed to reduce A1C by 1 percentage point (CI, 0.5-1.25) annually across every year of the analysis until diabetes control was reached at A1C of 7.5%.[37] (Most patients with high A1C levels see their A1C levels fall to 7.5% or lower within 1 year.) Medication use and drug effect were assumed to remain unchanged in the status quo scenario.

Table 1. Simulation Population Characteristics (2006)

Characteristic/Risk Factor	Values
Means	
Age	73.6
Glycated hemoglobin	5.9
Body mass index	28.4
Systolic blood pressure	135.9
HDL cholesterol	55.5
Total cholesterol	193.8
Percentages	
Female	55.5%
Diabetes prevalence	25.1%
Prediabetes prevalence	60.0%
History of hypertension (controlled or uncontrolled)	74.4%
History of hypercholesterolemia (controlled or uncontrolled)	58.6%

HDL indicates high-density lipoprotein.

RESULTS

A nationally representative sample of Medicare beneficiaries 65 years and older served as the baseline simulation population in this study. The initial (2006) sample was 55.5% female, with an average BMI of 28.4, and an average age of 73.6 years (Table 1). Controlled or uncontrolled hypertension (74.4%) and hypercholesterolemia (58.6%), prediabetes (60.0%), and diabetes (25.1%) were highly prevalent among this population. The CDC reports similar characteristics for Medicare beneficiaries in 2006, but reports a greater proportion of individuals 85 years and older (14.0% vs 2.2% in our sample) and a lower prevalence of hypertension (62.8%).[38]

In the status quo scenario, the prevalence of uncontrolled hypertension remained fairly constant at about 41% from 2006 to 2014. We observed a lower prevalence under the Part D scenario (ranging from 38.8% to 39.6%), which translates into an estimated 550,000 fewer beneficiaries with uncontrolled hypertension between 2006 and 2014 (Table 2). Cumulative over this period, there were 180,000 fewer new cases of CHF, 210,000 fewer MIs, and 830,000 more people with tightly controlled diabetes (defined by A1C level <7%).

The results of the simulation suggest that about 198,800 Part D beneficiaries lived at least 1 year longer following the implementation of the program. The average increase in longevity was 3.3 years. On average, approximately 22,100 lives were saved annually between 2006 and 2014. The number of lives saved each year increased from 2006 to 2009, but declined in the later years as deaths that might have occurred sooner eventually occurred in later years (Figure).

Mortality reductions were primarily attributable to fewer deaths from medication-sensitive conditions, particularly diabetes and cardiovascular diseases (Table 3). We estimate that between 2006 and 2014, total deaths associated with diabetes declined by 100,400, deaths associated with CHF declined by 53,100, deaths from stroke declined by 40,400, and deaths from MI declined by 25,100.

These mortality reductions may potentially be offset by complications arising from medications or polypharmacy in the population examined. While the classes of medications modeled in our analysis do pose risk for adverse events (eg, muscle toxicity and increased liver enzymes from statin use; hypotension, in general, from antihypertensive use; gastrointestinal issues from oral diabetes medication use), it is widely accepted that safety profiles are good for these medications and the drugs are well tolerated.[39-41] The implicit modeling assumption is that patients experiencing complications from medication will work with their doctors to modify their medication regimens.

We conducted several sensitivity analyses in which we varied our assumptions about the impact of medication use among beneficiaries gaining comprehensive drug coverage as a result of Part D. Improving A1C levels by 0.5 to 1.25 percentage points while holding all else constant resulted in a range of approximately 181,200 to 205,000 lives saved over 9 years. Similar analyses varying the efficacy of lipid lowering drugs showed a range of approximately 196,400 to 201,400 lives saved, while the estimated range for antihypertensive drugs was 196,600 to 199,900 lives saved over the same 9-year period.

Table 2. Simulation of Cumulative Outcomes for Selected Conditions: 3-, 5-, and 9-year Impact

Disease Incidence and Prevalence	Status Quo Scenario (million beneficiaries)			Part D Scenario (million beneficiaries)			Part D Impact (million beneficiaries)		
	3-year Impact	5-year Impact	9-year Impact	3-year Impact	5-year Impact	9-year Impact	3-year Impact	5-year Impact	9-year Impact
Uncontrolled hypertension (P)	10.41	11.26	15.36	9.93	10.76	14.81	–0.48	–0.50	–0.55
Ischemic heart disease (I)	1.64	2.68	4.73	1.60	2.62	4.65	–0.04	–0.06	–0.08
Myocardial infarction (I)	1.18	2.07	4.05	1.13	1.95	3.83	–0.05	–0.11	–0.21
Congestive heart failure (I)	2.69	4.28	7.11	2.62	4.15	6.94	–0.08	–0.13	–0.18
Stroke (I)	2.07	3.72	7.80	2.03	3.65	7.71	–0.04	–0.06	–0.09
Controlled diabetes, A1C ≤7 % (P)	N/A						+0.75	+0.89	+0.83

A1C indicates glycated hemoglobin; I, incidence; N/A, not applicable; P, prevalence.

DISCUSSION

Our analysis suggests that implementation of Part D in 2006 prolonged life by at least 1 year for nearly 200,000 Medicare beneficiaries through lower mortality associated primarily with diabetes, CHF, stroke, and MI. The simulated impact on mortality was greatest in the initial years following program inception, a trend also observed in similar studies.[12,13] The gradual rise in numbers of lives saved, followed by lower estimates in later years, may reflect the large number of individuals gaining comprehensive drug coverage in the initial years (with smaller numbers of beneficiaries enrolling in Part D in later years), as well as delayed onset of morbidity and mortality associated with better access to medicines under Part D.

The largest contribution to lives saved came from a reduction in deaths attributable to diabetes, CHF, MI, and stroke. Studies have shown that the use of medications to treat diabetes and cardiovascular conditions increased significantly in the post Part D period. Although estimates vary by source, the use of diabetes medicines increased by an estimated 3.7% to 17.9%.[21,42] Similarly, utilization rates for statins are reported to have increased by 13% to 22%, and antihypertensive utilization rates by 14% to 29%.[7,21]

Other studies that have examined the impact of Part D on mortality have been confined to a narrow window of analysis, often focusing only on the effects of the program in the first year or two following implementation.[5,12,13] The Briesacher et al study analyzed data through 4 years following Part D implementation, but made strong assumptions regarding the continuation of falling mortality trends from 2000 to 2010.[11] The magnitude of our findings is generally consistent with other studies. We estimated a 1.2% decline in annual mortality over 9 years. Huh and Reif estimated a 2.2% decline in the first 2 years of Part D, similar to our finding that the mortality effect was higher in the first few years of Part D.[12] Briesacher et al found a decline of approximately 1% in mortality, though their result is not statistically significant.[11] Dunn and Shapiro estimated that 21,800 to 25,500 individuals with cardiovascular disease were still alive in mid-2007 because of Part D.[13] We estimated that about 20,000 lives were saved in 2006 and 26,000 lives were saved in 2007; this number includes people with diabetes as well as cardiovascular disease.

Strengths and Limitations

Our study is unique in that it uses a microsimulation approach to estimate how improved access to pharmaceuticals that can lower blood pressure, cholesterol levels, and blood glucose levels can reduce the incidence of adverse health events that contribute to mortality. The strengths of using a microsimulation model include the ability to explain the pathway by which Part D benefits those participants who otherwise would have lower access to medications. This approach controls for patient health risk factors to isolate the timing and magnitude of medication use on reducing mortality.

Limitations are largely driven by data challenges. Part D beneficiaries who otherwise would not have comprehensive access to medications cannot directly be identified and observed, so this study used a microsimulation approach that uses published data to make assumptions regarding increased use of medications and effect on health outcomes.

The model does not take into account possible declines in medication persistence. That is, the documented increases in medication use tied to Part D (ie, 29%, 31%, and

Table 3. Causes of Simulated Mortality (cumulative over 9 years)

	Mortality Rate (per 100,000)			
	Status Quo	Part D	Number of Lives Saved	% Lives Saved
Diabetes	703	683	100,400	50%
Congestive heart failure	392	382	53,100	27%
Stroke	129	120	40,400	20%
Myocardial infarction	561	556	25,100	13%
End-stage renal disease	114	111	15,500	8%
Cervical cancer	27	27	1400	<1%
Gallbladder cancer	15	15	800	<1%
Liver cancer	14	14	800	<1%
Stomach cancer	14	13	600	<1%
Coronary heart disease	11	11	600	<1%
Prostate cancer	2	2	200	<1%
Esophageal cancer	2	2	0	<1%
Pancreatic cancer	31	31	–600	<1%
Leukemia	25	25	–800	<1%
Multiple myeloma	23	23	–1000	<1%
Pulmonary embolism	21	22	–1000	<1%
Endocrine cancer	16	16	–1200	<1%
Kidney cancer	12	12	–1400	<1%
Ovarian cancer	9	10	–1600	<1%
Non-Hodgkin lymphoma	1	2	–1800	–1%
Colorectal cancer	112	113	–2600	–2%
Breast cancer	109	110	–2800	–2%
All other causes	1776	1781	–25,300	–11%
Total	**4119**	**4081**	**198,800**	**100%**

22% increases in drug possession rates observed for patients diagnosed with hyperlipidemia, diabetes, and hypertension, respectively)[23] might not be sustained over time, thus overestimating the mortality benefits of Part D.[43] A more detailed discussion of the strengths and limitations of this microsimulation model are described in depth elsewhere.[14,15]

CONCLUSIONS

Since the implementation of Part D in 2006, nearly 200,000 Medicare beneficiaries have lived at least 1 year longer, with an average 3.3 year increase in longevity. Reductions in mortality have occurred because of fewer deaths associated with medication-sensitive conditions such as diabetes, CHF, stroke, and MI.

Author affiliations: IHS Life Sciences, Washington, DC (FC, TMD, APS).

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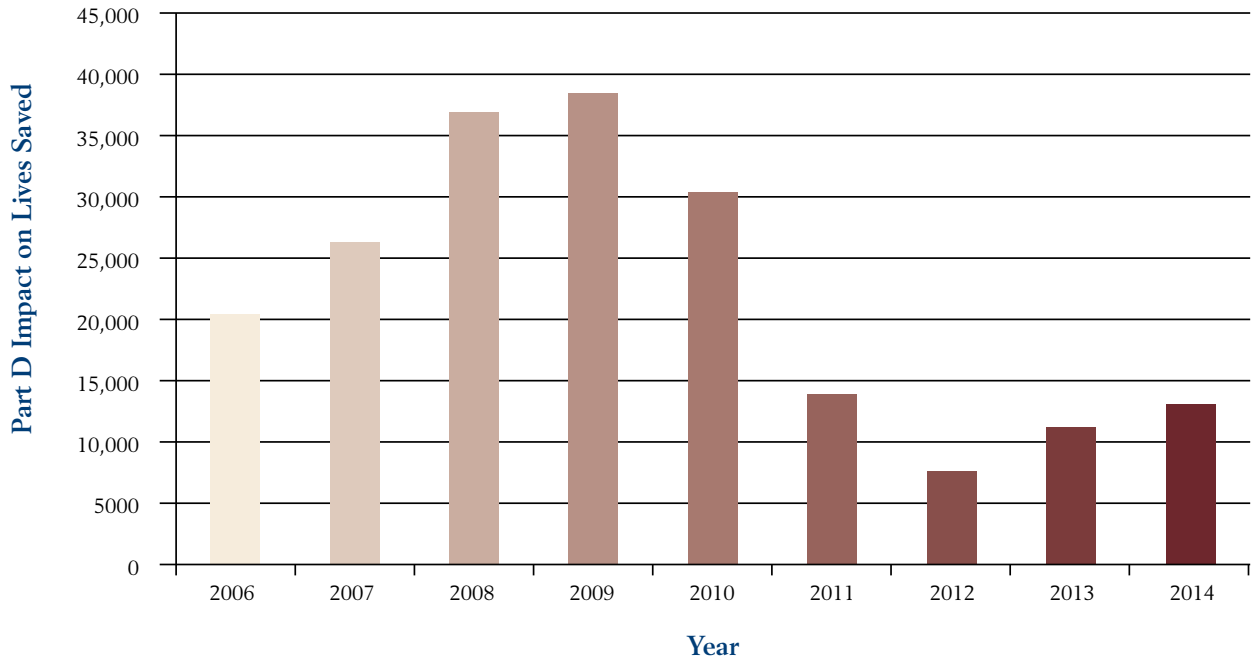
Address correspondence to: April P. Semilla, MS, 1150 Connecticut Ave NW, Suite 401, Washington, DC 20036. E-mail: april.semilla@ihs.com.

Figure. Medicare Part D Impact on Lives Saved per Year (2006-2014)[a]



[a]The reduction in lives saved after 2009 suggests a delay in mortality of several years. For example, the lower number of lives saved in 2012 may reflect delays in mortality for individuals who might have died in 2006 to 2011 absent Part D.

REFERENCES

1. Joyce GF, Goldman DP, Vogt WB, Sun E, Jena AB. Medicare Part D after 2 years. *Am J Manag Care*. 2009;15(8):536-544.

2. Duggan M, Morton FS. The effect of Medicare Part D on pharmaceutical prices and utilization. National Bureau of Economic Research; 2008.

3. Lichtenberg FR, Sun SX. The impact of Medicare Part D on prescription drug use by the elderly. *Health Aff (Millwood)*. 2007;26(6):1735-1744.

4. Yin W, Basu A, Zhang JX, et al. The effect of the Medicare Part D prescription benefit on drug utilization and expenditures. *Ann Intern Med*. 2008;148(3):169-177.

5. Kaestner R, Long C, Alexander GC. Effects of prescription drug insurance on hospitalization and mortality: evidence from Medicare Part D. National Bureau of Economic Research; 2014.

6. Liu FX, Alexander GC, Crawford SY, et al. The impact of Medicare Part D on out-of-pocket costs for prescription drugs, medication utilization, health resource utilization, and preference-based health utility. *Health Serv Res*. 2011;46(4):1104-1123.

7. Schneeweiss S, Patrick AR, Pedan A, et al. The effect of Medicare Part D coverage on drug use and cost sharing among seniors without prior drug benefits. *Health Aff (Millwood)*. 2009;28(2):w305-w316.

8. Ayyagari P, Shane D. Does insurance coverage improve health? evidence from Medicare Part D. College of Business at Illinois website. https://business.illinois.edu/nmiller/mhec/Ayyagari.pdf. Published April 2014. Accessed June 24, 2015.

9. Ketcham JD, Simon KI. Medicare Part D's effects on elderly patients' drug costs and utilization. *Am J Manag Care*. 2008;14(11, suppl):SP14-SP22.

10. CDC. Life tables. CDC website. http://www.cdc.gov/nchs/products/life_tables.htm. Accessed June 24, 2015.

11. Briesacher BA, Madden JM, Zhang F, et al. Did Medicare Part D affect national trends in health outcomes or hospitalizations? a time-series analysis. *Ann Intern Med*. 2015;162(12):825-833.

12. Huh J, Reif J. Did Medicare Part D reduce mortality? Julian Reif website. http://www.julianreif.com/research/medicare_d_mortality.pdf. Accessed June 24, 2015.

13. Dunn A, Shapiro AH. Does Medicare Part D save lives? Federal Reserve Bank of San Francisco website. http://www.frbsf.org/economic-research/files/wp2015-04.pdf. Accessed June 24, 2015.

14. Dall TM, Storm MV, Semilla AP, et al. Value of lifestyle intervention to prevent diabetes and sequelae. *Am J Prev Med*. 2015;48(3):271-280.

15. Su W, Huang J, Chen F, et al. Modeling the clinical and economic implications of obesity using microsimulation. *J Med Econ*. 2015:1-27.

16. National Center for Health Statistics. Continuous NHANES Web Tutorial. CDC website. http://www.cdc.gov/nchs/tutorials/NHANES/index_continuous.htm. Accessed June 24, 2015.

17. Kroese DP, Taimre T, Botev ZI. *Handbook of Monte Carlo Methods*. Hoboken, NJ: John Wiley & Sons; 2011.

18. Hoadley J, Summer L, Hargrave E, Cubanski J, Neuman T. Medicare Part D in its ninth year: the 2014 marketplace and key trends, 2006-2014. Kaiser Family Foundation website. http://kff.org/report-section/medicare-part-d-in-its-ninth-year-section-1-part-d-enrollment-and-plan-availability. Accessed June 24, 2015.

19. Afendulis CC, Chernew ME. State-level impacts of Medicare Part D. *Am J Manag Care*. 2011;17(suppl 12):S.

20. Kaiser Family Foundation. Total number of Medicare beneficiaries-2006. Kaiser Family Foundation website. http://kff.org/medicare/state-indicator/total-medicare-beneficiaries. Accessed June 24, 2015.

21. Kaestner R, Khan N. Medicare Part D and its effect on the use of prescription drugs, use of other health care services and health of the elderly. *J Policy Anal Manage*. 2012;31(2):253-279.

22. Madden JM, Graves AJ, Zhang F, et al. Cost-related medication nonadherence and spending on basic needs following implementation of Medicare Part D. *JAMA*. 2008;299(16):1922-1928.

23. Zhang Y, Lave JR, Donohue JM, et al. The impact of Medicare Part D on medication adherence among older adults enrolled in Medicare-Advantage products. *Med Care*. 2010;48(5):409-417.

24. Wilson PW, Anderson KM, Harris T, Kannel WB, Castelli WP. Determinants of change in total cholesterol and HDL-C with age: the Framingham Study. *J Gerontol*. 1994;49(6):M252-M257.

25. Wilson PW, Bozeman SR, Burton TM, et al. Prediction of first events of coronary heart disease and stroke with consideration of adiposity. *Circulation*. 2008;118(2):124-130.

26. D'Agostino RB, Wolf P, Belanger A, Kannel W. Framingham heart study: risk score profiles. Framingham Heart Study website. https://www.framinghamheartstudy.org/risk-functions/cardiovascular-disease/10-year-risk.php. Accessed June 24, 2015.

27. National Institutes of Health. The Framingham study: an epidemiological investigation of cardiovascular diseases: section 34: some risk factors related to the annual incidence of cardiovascular disease and death using pooled repeated biennial measurements: Framingham heart study, 30 year followup. Biologic Specimen and Data Repository Information Coordinating Center website. https://biolincc.nhlbi.nih.gov/static/studies/fhsc/30-Year_Followup_(Section_34).pdf. Accessed June 24, 2015.

28. Clarke PM, Gray AM, Briggs A, et al. A model to estimate the lifetime health outcomes of patients with type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS no. 68). *Diabetologia*. 2004;47(10):1747-1759.

29. Nichols GA, Reinier K, Chugh SS. Independent contribution of diabetes to increased prevalence and incidence of atrial fibrillation. *Diabetes Care*. 2009;32(10):1851-1856.

30. Hippisley-Cox J, Coupland C. Predicting the risk of chronic kidney disease in men and women in England and Wales: prospective derivation and external validation of the QKidney Scores. *BMC Fam Pract*. 2010;11:49.

31. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. *Hypertension*. 2003;42(5):878-884.

32. Heianza Y, Arase Y, Fujihara K, et al. Longitudinal trajectories of HbA1c and fasting plasma glucose levels during the development of type 2 diabetes: the Toranomon Hospital Health Management Center Study 7 (TOPICS 7). *Diabetes Care*. 2012;35(5):1050-1052.

33. Schaufelberger M, Swedberg K, Köster M, Rosén M, Rosengren A. Decreasing one-year mortality and hospitalization rates for heart failure in Sweden; Data from the Swedish Hospital Discharge Registry 1988 to 2000. *Eur Heart J*. 2004;25(4):300-307.

34. CDC, National Center for Health Statistics. Underlying cause of death 1999-2010. http://wonder.cdc.gov/ucd-icd10.html. Accessed July 1, 2013.

35. Taylor F, Huffman MD, Macedo AF, et al. Statins for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev*. 2013;1:CD004816.

36. Baguet JP, Legallicier B, Auquier P, Robitail S. Updated meta-analytical approach to the efficacy of antihypertensive drugs in reducing blood pressure. *Clin Drug Investig*. 2007;27(11):735-753.

37. Sherifali D, Nerenberg K, Pullenayegum E, Cheng JE, Gerstein HC. The effect of oral antidiabetic agents on A1C levels: a systematic review and meta-analysis. *Diabetes Care*. 2010;33(8):1859-1864.

38. Centers for Medicare & Medicaid Services. Medicare current beneficiary survey (MCBS): 2006 health and health care of the Medicare population. http://www.cms.gov/Research-Statistics-Data-and-Systems/Research/MCBS/Data-Tables-Items/CMS1253265.html?DLPage=1&DLSort=0&DLSortDir=descending. Accessed June 24, 2015.

39. Escobar C, Echarri R, Barrios V. Relative safety profiles of high dose statin regimens. *Vasc Health Risk Manag*. 2008;4(3):525-533.

40. Trinder Y. Common and less common adverse effects of antihypertensives: a general practitioner's perspective: SA Hypertension Society supplement. *S Afr Fam Pract*. 2012;54(2):S31-S32.

41. Diabetes Prevention Program Research Group. Long-term safety, tolerability, and weight loss associated with metformin in the Diabetes Prevention Program Outcomes Study. *Diabetes Care*. 2012;35(4):731-737.

42. Karaca Z, Streeter SB, Barton V, Nguyen K, Norris K. The impact of Medicare Part D on beneficiaries with type 2 diabetes: drug utilization and out-of-pocket vosts. Avalere Health LLC; 2008.

43. Viswanathan M, Golin CE, Jones CD, et al. Interventions to improve adherence to self-administered medications for chronic diseases in the United States: a systematic review. *Ann Intern Med*. 2012;157(11):785-795. ■

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