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Costs implications of pneumococcal vaccination of adults aged 30–60 with a recent diagnosis of diabetes

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Abstract

Objective: The 23-valent pneumococcal polysaccharide vaccine is routinely recommended for adults with diabetes, but little is known about adherence to this recommendation and how vaccination of these adults affects costs related to pneumococcal disease.

Research Design and Methods: We used data from a commercial insurance claims dataset to examine a cohort of non-elderly adults with a new diagnosis of diabetes and adults with no diagnosis of diabetes from 2005–2014. We examined rates of pneumococcal polysaccharide vaccination and the relationship between vaccination and pneumococcal disease costs, comparing results for persons with a diagnosis of diabetes and those with no diagnosis of diabetes.

Results: Overall rates of pneumococcal polysaccharide vaccination among adults 30–60 years old were <1%/year. Rates of pneumococcal polysaccharide vaccination were higher for adults with diabetes. Pneumococcal polysaccharide vaccination rates more than doubled from 2.9% per year in 2005 to 6.0% per year in 2014 for adults vaccinated during the same year as their diabetes diagnosis. Using a two-part differences-in-differences model on a propensity-score matched dataset, pneumococcal polysaccharide vaccination may reduce average annual per-person pneumococcal disease costs by $90.54 [95% CI: $183.59, −$2.49, (p=0.056)] in persons with diabetes from two years before to two years after vaccination.

Conclusions: Non-elderly adults with diabetes have low but rising rates of pneumococcal polysaccharide vaccination. Pneumococcal polysaccharide vaccination has a modest impact reducing overall costs of pneumococcal disease in this population.

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Author Contributions:

All authors were involved in conception and design of the work. JJP acquired and organized the data. DWH, JEM, WY, and JJP conducted the data analysis and interpretation. DWH, JEM, WY, and JJP drafted the article. All authors discussed the results, provided critical revision of the manuscript, and approved the version to be published. DWH takes overall responsibility for the contents of the article.

Introduction

Persons with diabetes are at increased risk of both acquiring pneumococcal disease and complications from it.[1] The Advisory Committee on Immunization Practices (ACIP) recommends that adults aged 19–64 years with diabetes receive the 23-valent pneumococcal polysaccharide vaccine (PPSV23) once before age 65 years.[2] Yet, little is known about adherence to this recommendation and the effect of vaccination on costs related to pneumococcal disease in this population.

The vaccine appears to be effective in preventing bacteremic pneumonia, but most cases of pneumonia are non-bacteremic and there is no consensus on PPSV23 effectiveness against non-bacteremic pneumonia.[3] A 2009 meta-analysis suggests little evidence for vaccine effectiveness against all-cause or pneumococcal pneumonia in adults with chronic illness[4].

The impact of vaccinating children appear to be clearer. A pneumococcal conjugate vaccine (PCV7, then PCV13) has been recommended for children since 2000[5] and the US has consistently had over 90% pneumococcal vaccine coverage in children[6,7]. Pneumococcal conjugate vaccine use in children has led to dramatic reductions in pneumococcal disease not only in children, but also adults, through indirect (or herd) effects[8,9]. However, the impact of pneumococcal immunization in adults is less clear. One study suggests PPSV23 vaccination may not be cost-effective in adults[10], but other studies suggest that PPSV23 vaccination for immunocompromised adults may be a part of a cost-effective comprehensive immunization strategy along with PCV13[11–13]. Increased pneumococcal polysaccharide vaccination of adults could reduce both incidence of pneumococcal disease and complications from pneumococcal disease,[14] and thus reduce costs associated with pneumococcal illness. The vaccination could also have an indirect impact on secondary bacterial pneumonia in those with influenza[15].

However, measuring the impact of pneumococcal vaccination on health care costs is challenging for three reasons. First, vaccinated patients are sicker and may have higher costs because they have more comorbidities and received more medical care prior to vaccination. Second, factors not recorded in insurance claims data may drive differences in costs for vaccinated patients (unobserved heterogeneity). Finally, modeling medical costs is challenging because many enrollees have zero pneumococcal disease costs in any particular year, and if they do have costs, they are right-skewed.

The purpose of this analysis was to use insurance claims data for adults with a recent diagnosis of diabetes to better understand rates of pneumococcal polysaccharide vaccination in this population and to understand the impact vaccination may have on costs related to pneumococcal disease in non-elderly adults with diabetes.

Research Design and Methods

Data Source

We created a retrospective cohort of enrollees with twelve years of continuous enrollment from 2003 to 2014 using the Truven Health MarketScan® Database (MarketScan)

commercial insurance inpatient and outpatient claims data. The cohort focuses on claims from 2005 to 2014. The cohort includes plan members ages 30–51 in 2005 with no prior history of diabetes. Over the course of the ten-year time period from 2005 to 2014, the age of the plan members becomes 39–60 by 2014. This age group was chosen as it is a time when type 2 diabetes is likely to be diagnosed and it also it not too close to age 65 when pneumococcal vaccination is recommended due to age. To identify confirmed diabetes diagnoses, we determined if the enrollee had more than one diabetes diagnosis thirty days or more apart in the outpatient file or a single diabetes diagnosis in the inpatient file. The dataset can track those with newly-diagnosed diabetes in each year and follow them after their diagnosis and compare them with individuals who do not develop diabetes. We identified individuals with diabetes using a single inpatient diabetes diagnosis or two outpatient diagnoses, thirty days or more apart.. A two-year washout period using claims from 2003–2004 was used to check for and remove enrollees with prior diabetes diagnoses and to indicate if individuals in the cohort received a PPSV23 vaccination during the washout period.

More on the dataset construction can be found in the supplement, including ICD-9 codes used to identify diabetes diagnoses, vaccination, and other health conditions indicating PPSV23 vaccination prior to age 65.

Analyses

Vaccination rates—We used two broad approaches to evaluate rates of pneumococcal vaccination in both persons with and without diabetes. The first was descriptive and the second used a regression analysis to identify factors associated with pneumococcal vaccination.

In the descriptive analysis, we examined rates of vaccination from 2005–2014, stratified by diabetes status. Enrollees were excluded from the denominator if they had pneumococcal vaccination in a prior year. We also made a distinction between those vaccinated in the year of their diabetes diagnosis (newly-diagnosed adults with diabetes) versus those vaccinated any time after their diabetes diagnosis.

Because one-time PPSV23 vaccination was recommended for adults under 65 years with diabetes, while PCV13 vaccination is not, we focused our analysis on rates of PPSV23 vaccination. We consider PCV13 along with PPSV23 starting in 2012 when recommendations for vaccination were made for other high risk conditions[2]. However, in our analysis, less than 1% of vaccines received by adults with diabetes were PCV13.

In the regression analysis evaluating predictors of vaccination in each year, we used logistic regression with PPSV23 (and/or PCV13 starting in 2012[1]) vaccination as the dependent variable with age, newly-diagnosed diabetes diagnosis in that year, prior diabetes diagnosis during the study period, and an indicator variable for having any condition other than diabetes indicated for PPSV23 pneumococcal vaccination (PPSV23 indication) as the

[1]We also captured PCV13 starting in 2012 when ACIP began recommending both PPSV23 and PCV13 for some conditions captured in the first alternative model

independent variables. As a robustness check, we used two alternative models to control for pneumococcal vaccine need. In the first alternative model we replaced the single indicator variable (PPSV23 indication) with multiple indicators for each of the individual conditions for which PPSV23 vaccination before age 65 is recommended (increased-risk conditions) (see Supplement for details). In the second alternative model, we replaced the indicator variable (PPSV23 indication) with variables corresponding to the more general individual components of the Charlson Comorbidity Index[16] that are not necessarily specifically indicated for pneumococcal vaccination (Supplement).

Pneumococcal Vaccination and Costs—We examined PPSV23 or PCV13 vaccination for this analysis. The main outcome variable is pneumococcal disease costs, which are identified according to diagnosis codes (Supplemental Table 3).

Our empirical approach employs three tools to address the challenges with selection, unobserved heterogeneity, and skewed costs (see Supplement for more details on cost categorization). First, we use propensity score matching to control for observed factors like diabetes status and to create a contemporaneous "control" group for subsequent analyses. This control group should be similar to the vaccinated individuals in all other characteristics except for being vaccinated. Second, we use a difference-in-differences approach to address selection based on unobserved, but time-invariant factors. Third, we employ a two-part model to address distributional issues with costs data. The two-part model first models the probability of having non-zero costs, and then, models costs in the group with non-zero costs.

Propensity-Score Matching—We first created matched groups in each year based on their propensity to get pneumococcal vaccination. The propensity score was based upon, age, age squared[2], sex, diabetes, other Charlson comorbidities, other increased-risk conditions, and numbers of inpatient and outpatient visits in each of the two years prior to matching (treatment). This approach assumes that these enrollee characteristics are important to the chance of getting vaccinated and pneumococcal disease costs. We matched those vaccinated in 2007 with those not vaccinated in 2007 and so forth for years 2007 through 2012 using one-to-one nearest-neighbor matching. We only matched a single time for each individual. We started with 2007 to allow us to evaluate two years prior to matching and two years after the matching to align with the 2005–2014 dataset. See supplement for additional technical details.

Difference-in-Differences—After matching enrollees with propensity scores, we evaluated the difference-in-differences in costs before and after matching between the vaccinated and unvaccinated individuals. We calculated the impact for persons with diabetes, those without diabetes, and both groups together. The assumption was that the matched unvaccinated person can serve as a control for the vaccinated person and that the control group's cost trends would have been observed in the vaccinated group had the vaccinated

[2]Age squared is introduced to allow for a more non-linear relationship with age.

group not been vaccinated. To assess this assumption, we created plots of cost trends before the year enrollees were matched to examine if the trends were parallel prior to vaccination.

In the difference-in-differences analysis, we included indicator variables for whether an enrollee was in the vaccinated group, the time (before or after matching), whether the enrollee had a diabetes diagnosis, and the interactions between these variables. Standard errors were robust and clustered by enrollee. Those with pneumococcal vaccination prior to the year of matching were filtered out of the analysis.

We evaluated the differences in costs from two years before and two years after matching/vaccination. We did not include costs in the year of vaccination as that year may have included costs of events that may have precipitated vaccination (e.g. pneumococcal disease may have led to pneumococcal vaccination). We evaluated the impact of vaccination on pneumococcal disease costs.

We used a two-part model to account for the large number of observations with zero annual pneumococcal disease costs and the skewed distribution of non-zero costs. We modeled the probability that an enrollee has non-zero costs in the first part and in the second part used a generalized linear model (GLM) to estimate the costs for those with positive cost. The GLM allows the expectation of the costs to be a (log link) function of the linear index of the covariates. This approach is considered appropriate for modeling health care expenditures.[17] In the end, this approach provides an estimate of the combined average overall effect on costs for all enrollees (with and without positive costs).

We conducted this analysis in Stata using Stata's twopm command[18] with robust cluster estimators (clustering on the enrollee because the data was longitudinal). We used bootstrapping with 300 bootstrap replications to compute confidence intervals.

The appendix includes additional technical details on the two-part model approach.

Robustness Check—To evaluate the robustness of the results, we conducted an additional analysis by estimating the two-part model with differences in differences on the full, unmatched sample. Because this analysis did not include matching, we controlled for age, age squared, sex, diabetes, other individual Charlson comorbidities, and other increased-risk conditions. We also evaluated robustness by estimating a conventional fixed effects model with beneficiary and year fixed effects.

Results

Cohort Characteristics

In the cohort, there were 547,337 person-years of adults with diabetes and 7,849,733 person-years of those without diabetes. The person-years of adults with a diabetes diagnosis were on average 3.4 years older and were more likely to have comorbidities (Table 1).

Rates of Vaccination

Overall annual rates of receiving pneumococcal vaccination were low (<1%), but they were higher for adults with diabetes and highest for those with newly-diagnosed diabetes. Annual pneumococcal vaccination rates more than doubled from 2.9% to 6.0% in newly-diagnosed adults with diabetes over the period studied (Figure 1a). Figure 1b shows the cumulative prevalence of pneumococcal vaccination.

Results of the logistic regressions predicting rates of PPSV23 vaccination showed that diabetes diagnosis and newly-diagnosed diabetes diagnosis were associated with statistically significant increases in the probability of pneumococcal vaccination. A diabetes diagnosis was associated with an odds ratio of 3.70 ($p<0.001$) for vaccination and a newly-diagnosed diabetes diagnosis further increased the odds ratio by 1.96 ($p<0.001$) for vaccination (Supplemental Table 4). When using individual increased-risk conditions or Charlson Comorbidity Index elements as controls, we saw similar results (Supplemental Tables 5–6). Most other increased-risk conditions and elements of the Charlson Comorbidity Index had positive relationships with pneumococcal vaccination (Supplemental Tables 4–6).

Cost impact of pneumococcal vaccination

Matching—Prior to matching, those who were vaccinated had more comorbidities and more inpatient and outpatient visits (Supplemental Table 7). The supplement has additional technical details (supplemental figures 1–6) on the propensity-score matching results. Although those who received pneumococcal vaccination had consistently higher costs both before and after vaccination, we found parallel trends in costs between the vaccinated and unvaccinated groups prior to the matching time points (Supplemental Table 8 and Supplemental Figure 7). These findings support our-difference-in-differences strategy. Matching methods leave substantial unobserved differences between vaccinated and control groups, but these unobserved differences are time-invariant.

Supplemental Table 7 shows that the vaccinated and unvaccinated groups became much more similar after matching. The average ages of both groups were within four months of each other. The fraction male and female were equal. And, the fraction of each group having comorbidities and conditions recommended for pneumococcal vaccination were within a few percentage points of each other after matching.

Differences-in-Differences Cost Analysis—We first examined the distributional properties of our cost data. More details of testing the appropriateness of the generalized linear model are in the supplement.

Raw probit and GLM results are reported in supplemental Table 9; the two coefficients represent first the log odds of having positive costs and then the magnitudes of cost differences. We computed the marginal effects of the differences-in-differences analysis to interpret the impact of vaccination on pneumococcal disease costs. When examining the overall population, the difference-in-differences analysis showed $61.40 [95% CI: $101.12, $21.67, $p=0.002$] in savings between the two years before and the two years after vaccination. When broken out by diabetes status, those without diabetes saw $51.26

[95% CI: $94.72, $7.79, p=0.021] in savings and those with diabetes saw $90.54 [95% CI: $183.59, −$2.49, p=0.056] in savings. The full results of the differences-in-differences analysis are in Table 2).

Matched Sample: The results from the differences-in-differences cost analysis are as follows. The first section of table 2 shows the results for the whole cohort, with and without diabetes; the second section shows results among adults without a diabetes diagnosis; and the third section shows results for those diagnosed with diabetes:

Robustness Check: Without Matching—Using the full, unmatched sample we found that the estimated vaccination savings were smaller, with savings of $8.63 overall, $8.87 for those without diabetes, and $5.69 for those with diabetes. None of these savings estimates were significantly different from zero. Detailed regression coefficient estimates may be found in supplemental tables 1–11.

Robustness Check: Conventional Fixed Effects—We also estimated a model with beneficiary and year fixed effects. The results were similar to those reported in Table 2. We found a $61.9 [95% CI of $88.2 to $35.6] spending reduction for nondiabetic beneficiaries as opposed to a $51 in our preferred specification and no significant savings for diabetic beneficiaries. We prefer the results of our two part model as the cost data are highly skewed and we can reject the parametric assumptions of a conventional regression model.

Discussion

Annual rates of pneumococcal vaccination uptake from 2005 to 2014 were low in non-elderly adults, both for those with and without increased-risk conditions. Rates were higher in newly-diagnosed adults with diabetes, but annual vaccination rates only rose to 6% by 2014, demonstrating that substantial numbers of adults with a recent diagnosis of diabetes are not receiving timely recommended pneumococcal vaccination. A cumulative 19% of persons with diabetes were vaccinated after 10 years. These low vaccination rates are consistent with a report that pneumococcal vaccination coverage amount high-risk, non-elderly adults is about 20%.[19] and are lower than Medicare enrollees over 65 with chronic conditions (including diabetes) where 60.5% had pneumococcal vaccination over a 7-year period. Diabetes is a complex disease that requires multifaceted care. Pneumococcal vaccination is one of many recommended interventions and preventive actions to avoid sequelae.

We found that pneumococcal vaccination was associated with modest pneumococcal disease cost savings. The lower ends of the confidence intervals were close to zero savings. This modest effect is plausible. Although vaccination is likely to reduce both incidence and severity of disease, there is little evidence PPSV23 vaccination prevents non-bacteremic pneumococcal disease, which accounts for 71% of adult pneumococcal disease in the U.S.[20] Although this is not a formal cost-effectiveness analysis, these savings over two years are close to the costs of the PPSV23 vaccine. Modest cost savings suggests that the recommendation to vaccinate adults with diabetes with the PPSV23 vaccine is valuable,

but the magnitude of the cost savings do not make it an urgent priority from an economic perspective.

We are not aware of other studies evaluating the economic impact of PPSV23 immunization using claims data. The results of our analysis may be relevant to future cost-effectiveness analyses. We find the cost-savings from PPSV23 immunization are modest and likely smaller than the cost of the vaccine itself. Our results are consistent with model-based cost-effectiveness studies of PPSV23 vaccination showing it is unlikely to be cost-saving[10–13,21].

This analysis has several limitations. It analyzed commercially-insured adults aged 30–60, so the conclusions may not be generalizable to children, younger adults, the elderly, or the uninsured or those on different insurance programs like Medicaid. The analysis excludes individuals with a prior diabetes diagnosis in the past two years and therefore focuses on those with a recent diabetes diagnosis. Although people with a prior diagnosis were excluded, we have no reason to believe their vaccination status would be substantially different than those with a new diagnosis so we believe the conclusions would still hold. Some unvaccinated individuals in the matched cost analysis became vaccinated in the post-matching period, diluting the estimate of the cost impact of vaccination. However, rates of vaccination were low, so the impact of this limitation was likely small. The cost impact of vaccination was estimated over a limited duration. In the propensity-score matched analysis, we only compared two years before with two years after vaccination. In the analysis on the full dataset, the maximum follow up was 9 years and longer-run findings remained modest but were statistically imprecise. However, the duration of protection with the PPSV23 vaccine is likely limited, so our analysis accounting for cost impact of short duration may be appropriate. The cost analysis excluded the year of vaccination, so vaccination costs were not considered. We used non-specific diagnostic codes incorporating etiologies other than pneumococcal disease because it was not possible to precisely identify pneumococcal disease in a claims dataset. Because of that, pneumococcal pneumonia may be over-or under-detected in our sample. Costs associated with non-pneumococcal diagnoses may be different if the pneumonia was due to other etiologies. Even knowing that, we did not see dramatic differences when examining overall costs. We did not account for receipt of influenza vaccination in this analysis as we did not feel influenza vaccination data in this claims dataset were reliable. But, it is plausible influenza vaccination could prevent secondary pneumococcal pneumonia, and thus influence costs associated with pneumococcal disease. Finally, the propensity-score matching and difference-in-differences approach rely on the assumptions that the covariates used to match are reasonable and that the cost trends are parallel.

Conclusions

Non-elderly adults with a recent diagnosis of diabetes have low pneumococcal vaccination uptake rates. Pneumococcal vaccination has a modest impact on overall pneumococcal disease costs. These cost savings may be more substantial among persons with diabetes. Given these modest effects, consideration should be given to low-cost interventions to improve timely pneumococcal vaccination rates among these adults, such as electronic health record reminders triggered by a diabetes diagnosis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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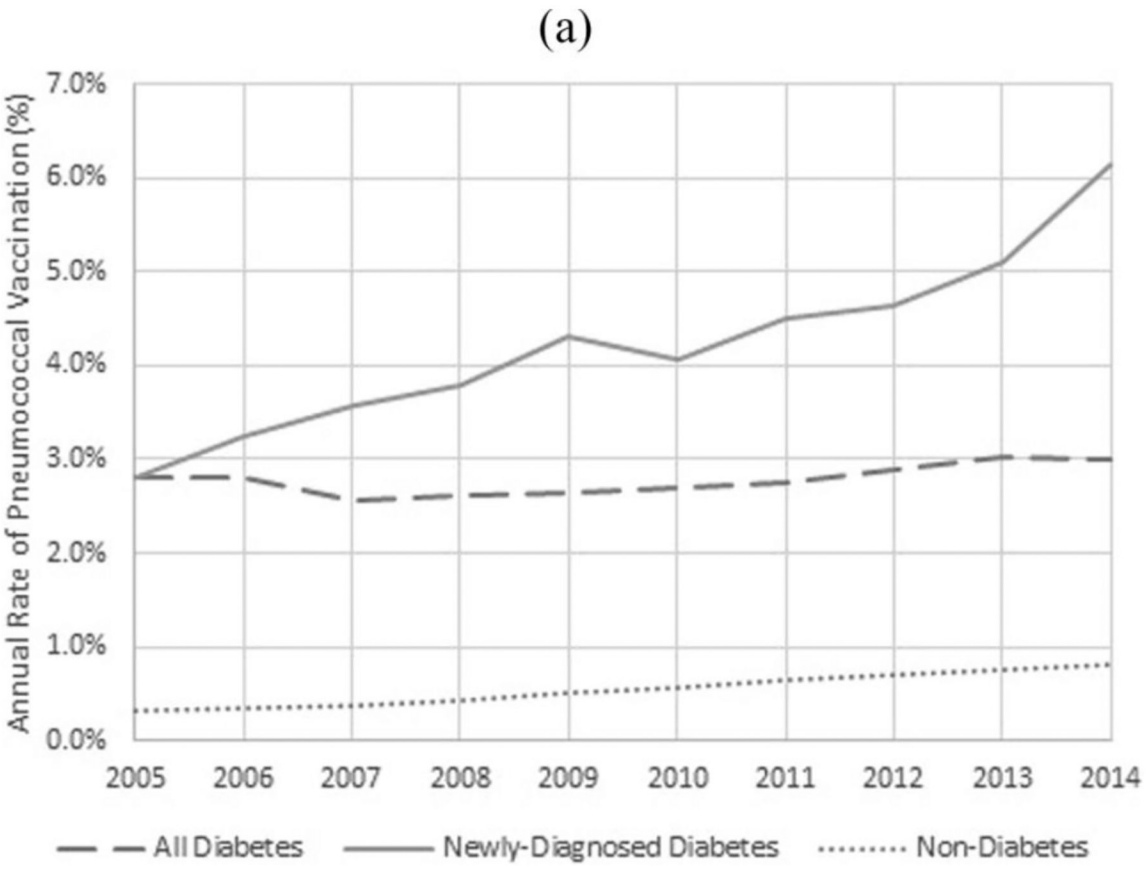

Fig. 1a.

Rates of Pneumococcal Vaccination. Panel a: The rates for diabetes and newly-diagnosed diabetes are equivalent in 2005 since all enrollees started without diabetes prior to 2005, so all identified adults with diabetes in 2005 were newly-diagnosed adults with diabetes.

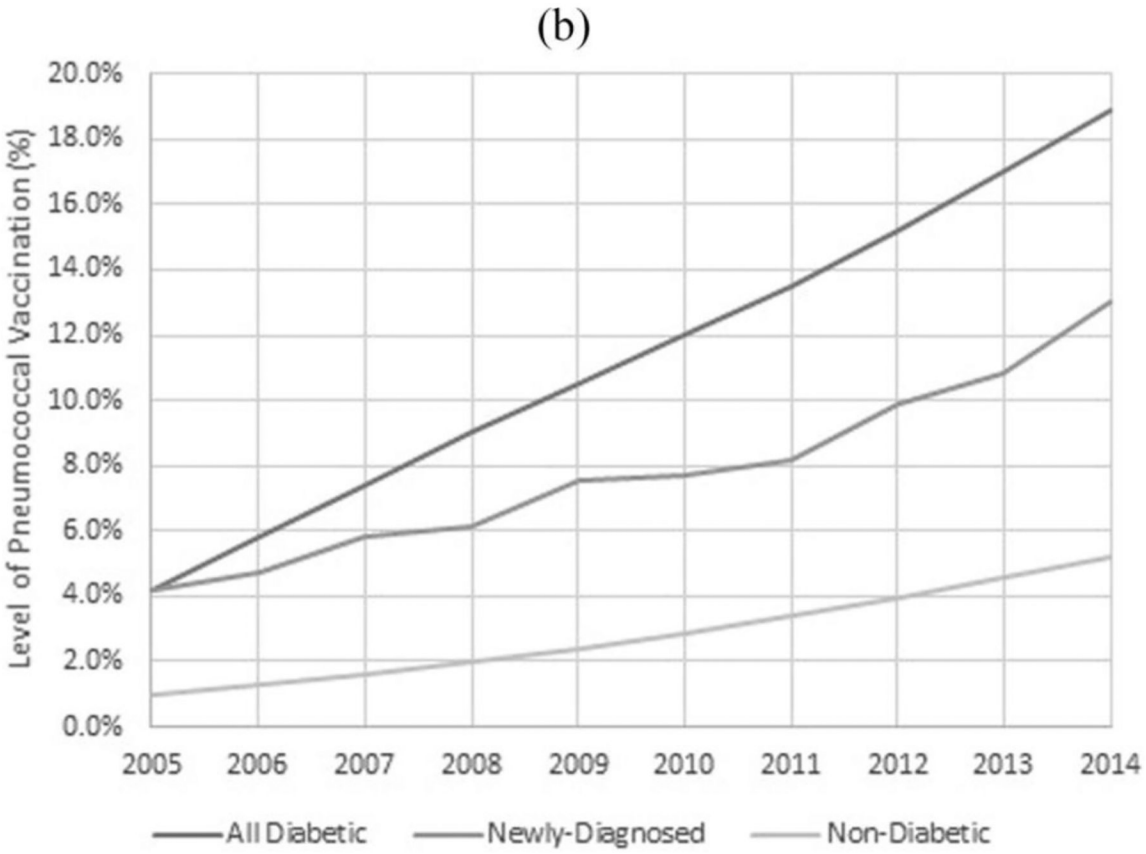

Fig. 1b.

Levels of Cumulative Uptake of Pneumococcal Vaccination. Panel b: This underestimates vaccination coverage as it does not include vaccination prior to 2005 and may miss immunizations not recorded by the health plan.

Table 1.

Demographic characteristics of the person-years in the cohort.

	Diabetes (547,337 person-years) Mean (95% CI)	**Non-diabetes (n = 7,849,733 person-years) Mean (95% CI)**
Age	49.82 (49.81,49.84)	46.4 (46.39,46.4)
Female (%)	51 (50.87,51.13)	55 (54.97,55.03)
Comorbidities (%)		
Myocardial Infarction	2.98 (2.93,3.02)	0.71 (0.7,0.71)
Congestive Heart Failure	5.99 (5.93,6.05)	1.27 (1.26,1.28)
Peripheral Vascular Disease	7.7 (7.63,7.77)	2.06 (2.05,2.07)
Cerebrovascular Disease	8.63 (8.55,8.7)	3.01 (3,3.03)
Dementia	0.19 (0.18,0.2)	0.06 (0.06,0.06)
Chronic Pulmonary Disease	25.91 (25.8,26.03)	14.01 (13.99,14.04)
Connective Tissue Disease-Rheumatic Disease	4.15 (4.1,4.2)	2.02 (2.01,2.03)
Peptic Ulcer Disease	2.25 (2.21,2.29)	0.97 (0.96,0.97)
Mild Liver Disease	13.62 (13.53,13.71)	4.06 (4.04,4.07)
Paraplegia and Hemiplegia	0.84 (0.81,0.86)	0.35 (0.35,0.36)
Renal Disease	4.31 (4.26,4.37)	0.87 (0.87,0.88)
Cancer	7.76 (7.69,7.83)	4.22 (4.21,4.24)
Moderate or Severe Liver Disease	0.43 (0.42,0.45)	0.1 (0.1,0.1)
Metastatic Carcinoma	1.05 (1.02,1.07)	0.52 (0.51,0.52)
AIDS/HIV	0.4 (0.38,0.41)	0.22 (0.21,0.22)

Table 2.

Differences-in-differences results.

Ever Received Pneumococcal Vaccination	Before/After	Marginal Effect ($)	Std. Err.	95% CI	P-value
For All, Regardless of Diabetes Status					
No	Before	168.53	9.65	149.61, 187.46	<0.001*
No	After	206.73	13.13	181, 232.46	<0.001*
Yes	Before	239.24	15.52	208.81, 269.67	<0.001*
Yes	After	216.04	10.42	195.62, 236.47	<0.001*
No	Change	38.20			
Yes	Change	−23.20			
Difference in Differences		−61.40		−101.12, −21.67	0.002†
Without Diabetes Diagnosis					
No	Before	169.12	11.07	147.42, 190.83	<0.001*
No	After	200.65	14.06	173.09, 228.22	<0.001*
Yes	Before	249.19	16.42	217.01, 281.38	<0.001*
Yes	After	229.46	12.69	204.6, 254.33	<0.001*
No	Change	31.53			
Yes	Change	−19.73			
Difference in Differences		−51.26		−94.72, −7.79	0.021†
With Diabetes Diagnosis					
No	Before	166.84	15.96	135.56, 198.12	<0.001*
No	After	224.21	29.57	166.26, 282.17	<0.001*
Yes	Before	210.62	33.09	145.76, 275.47	<0.001*
Yes	After	177.45	16	146.09, 208.81	<0.001*
No	Change	57.37			
Yes	Change	−33.17			
Difference in Differences		−90.54		−183.59, +2.49	0.056†

*p-value evaluates whether marginal effect was different from zero.

†p-value evaluates whether the difference in difference estimate was different from zero.