

Supporting Online Materials

METHODOLOGICAL APPROACH

Overview

We used Medicare claims to obtain annual skin biopsy rates for the population age 65 years and older who reside in each of the nine SEER areas. We then use multiple linear regression to explore how biopsy rates relate to the incidence of melanoma in these areas.

Data

We used Medicare Part B claims to obtain an annual population-based rate of skin biopsy in each of the nine SEER areas from 1986 to 2001. This entailed obtaining claims for the entire state of Connecticut, Hawaii, Iowa, New Mexico and Utah as well as the individual counties that make up the SEER registries in Atlanta, Detroit, San Francisco and Seattle. The numerator was the total number of skin biopsies (CPT code 11100 - single biopsy and CPT code 11101 - multiple biopsies, which includes a field for the total number of biopsies performed); the denominator was the mid-year Medicare Part B entitled population. Medicare beneficiaries under age 65 and those enrolled in risk-contract Health Maintenance Organizations (HMOs) were excluded (in the SEER areas, the proportion of beneficiaries age 65 and older enrolled in HMOs ranged from 14 to 27% during the years analyzed). Because Medicare claims were unavailable for two years (1991, 1992), a total of 14 biopsy rates were calculated for each of the nine SEER areas (N=126).

We used the National Cancer Institute's statistical software (SEER*Stat, Version 5.3.0) to obtain data on the annual incidence of melanoma in each of the nine SEER areas. The analysis was again restricted to the population age 65 and older. We obtained stage-specific incidence rates using SEER's four historic stages: in-situ, local, regional, and distant. We summed these rates to produce an incidence rate for all stages combined (a small proportion of melanoma is unstaged - ranging from 2% to 6% in any given year). To provide an overview of melanoma trends, we also performed an analysis of the nine SEER areas combined – both on the overall incidence of melanoma and disease-specific mortality (using SEER*Stat's incidence-based mortality method).

Analysis

We used multiple linear regression to explore the relationship between biopsy rate (the independent variable of interest) and melanoma rate (the dependent variable). The unit of analysis is the SEER area in an individual year (9 areas, 14 years, $N = 126$). All analyses reported here include an indicator variable for area, which is analogous to performing a panel analysis in which area is modeled as a fixed effect. In a sensitivity analysis, we repeated the analyses modeling area as a random effect - which had little impact on the coefficients reported here. However, because the p values were higher using the fixed effect models, we present the simpler, more conservative analyses.

Our baseline analysis predicts the effect of 1000 additional biopsies on the number of cases of melanoma after controlling for the effect of area. The implicit assumption here is that the true occurrence of melanoma may differ in different areas, but does not change over the period.

Subsequent analyses incorporate the effect of a potential underlying increase in the true occurrence of melanoma. We considered a number of functional forms to model how melanoma might be increasing over time (e.g. exponential, polynomial) and found that linear increase best fit the data (as is evident in Figure 1). To do this, we used year-area interaction terms which allows the melanoma incidence in each area to progress at its own rate (i.e. have its own slope and intercept).

Finally, we performed four stage-specific regressions using the same year-area interaction terms. The only change is that the dependent variable is no longer overall melanoma incidence, but is instead the incidence of a specific stage (i.e. in-situ, local, regional, distant). All analyses were carried out using Stata version 7.0 (College Station, Texas).

The output for the six models appear on the following pages:

Model #1: No change in true occurrence of disease

Unit of analysis: SEER area in an individual year (9 areas, 14 years, N = 126)

Dependent variable: melanoma incidence

Independent variable: biopsy rate

Control variables: indicator variables for each of the 9 SEER areas

```
. regress newmel newbx darea1-darea9
```

Source	SS	df	MS	Number of obs =	126
Model	66083.0692	9	7342.56324	F(9, 116) =	47.00
Residual	18121.4057	116	156.219014	Prob > F =	0.0000
-----				R-squared =	0.7848
-----				Adj R-squared =	0.7681
Total	84204.4748	125	673.635799	Root MSE =	12.499

newmel	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
newbx	12.62736	.7088533	17.81	0.000	11.22338	14.03133
darea1	-20.77837	5.092681	-4.08	0.000	-30.86507	-10.69168
darea2	.958757	4.89135	0.20	0.845	-8.729178	10.64669
darea3	-18.51631	4.799271	-3.86	0.000	-28.02187	-9.010752
darea4	(dropped)					
darea5	-12.9332	4.747709	-2.72	0.007	-22.33663	-3.529763
darea6	-4.672654	4.768985	-0.98	0.329	-14.11823	4.772922
darea7	-27.66929	5.217358	-5.30	0.000	-38.00293	-17.33566
darea8	-.7974728	4.860593	-0.16	0.870	-10.42449	8.829543
darea9	-4.805391	5.11005	-0.94	0.349	-14.92649	5.315707
_cons	18.84653	4.039023	4.67	0.000	10.84673	26.84632

Model #2: Increase in true occurrence of disease

Unit of analysis: SEER area in an individual year (9 areas, 14 years, N = 126)

Dependent variable: melanoma incidence

Independent variable: biopsy rate

Control variables: indicator variables for each of the 9 SEER areas, year-area interaction terms (to allows the melanoma incidence in each area to progress at its own rate)

```
. regress newmel newbx xta1-xta9 darea1-darea9
```

Source	SS	df	MS	Number of obs =	126
Model	77650.6826	18	4313.92681	F(18, 107) =	70.43
Residual	6553.7922	107	61.2503944	Prob > F =	0.0000
				R-squared =	0.9222
				Adj R-squared =	0.9091
Total	84204.4748	125	673.635799	Root MSE =	7.8263

newmel	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
newbx	6.93695	1.93542	3.58	0.000	3.100207 10.77369
xta1	.2530607	.9957486	0.25	0.800	-1.720895 2.227016
xta2	2.900757	1.019757	2.84	0.005	.8792077 4.922307
xta3	2.302365	.738589	3.12	0.002	.8381983 3.766531
xta4	3.560748	.471876	7.55	0.000	2.625309 4.496187
xta5	1.51586	.6738771	2.25	0.027	.1799775 2.851743
xta6	1.490887	.5322862	2.80	0.006	.4356917 2.546082
xta7	.7847641	.7687463	1.02	0.310	-.7391857 2.308714
xta8	3.242651	.7674312	4.23	0.000	1.721308 4.763994
xta9	4.835251	.5399297	8.96	0.000	3.764904 5.905599
darea1	6.61444	6.421179	1.03	0.305	-6.114798 19.34368
darea2	(dropped)				
darea3	-17.60559	6.344472	-2.77	0.007	-30.18276 -5.028414
darea4	-16.93779	6.793498	-2.49	0.014	-30.40511 -3.470471
darea5	-8.108062	6.270704	-1.29	0.199	-20.539 4.322877
darea6	1.815628	7.141718	0.25	0.800	-12.342 15.97325
darea7	-2.441251	7.967728	-0.31	0.760	-18.23634 13.35384
darea8	-5.758269	6.497389	-0.89	0.377	-18.63858 7.122046
darea9	-17.30093	9.381512	-1.84	0.068	-35.89868 1.296826
_cons	22.72739	4.589047	4.95	0.000	13.63014 31.82464

Model #3: Stage-specific analysis - increase in true occurrence of in-situ melanoma

Unit of analysis: SEER area in an individual year (9 areas, 14 years, N = 126)

Dependent variable: incidence of melanoma in-situ

Independent variable: biopsy rate

Control variables: indicator variables for each of the 9 SEER areas, year-area interaction terms (to allows the melanoma incidence in each area to progress at its own rate).

```
regress insitu newbx xta1-xta9 darea1-darea9
```

Source	SS	df	MS	Number of obs = 126		
Model	22817.6527	18	1267.64737	F(18, 107)	=	55.03
Residual	2464.61018	107	23.03374	Prob > F	=	0.0000
-----				R-squared	=	0.9025
-----				Adj R-squared	=	0.8861
Total	25282.2629	125	202.258103	Root MSE	=	4.7993

insitu	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]	
newbx	4.440318	1.186869	3.74	0.000	2.087488	6.793148
xta1	-.7271155	.6106291	-1.19	0.236	-1.937616	.4833854
xta2	1.42195	.625352	2.27	0.025	.1822623	2.661637
xta3	.9709697	.4529295	2.14	0.034	.0730898	1.86885
xta4	1.726939	.2893714	5.97	0.000	1.153294	2.300584
xta5	.5401914	.4132459	1.31	0.194	-.2790203	1.359403
xta6	.9157183	.3264172	2.81	0.006	.2686343	1.562802
xta7	.5140078	.471423	1.09	0.278	-.4205334	1.448549
xta8	1.65763	.4706166	3.52	0.001	.7246873	2.590572
xta9	2.456333	.3311045	7.42	0.000	1.799957	3.112709
darea1	10.18095	3.9377	2.59	0.011	2.374924	17.98698
darea2	(dropped)					
darea3	-4.487101	3.89066	-1.15	0.251	-12.19988	3.225678
darea4	.2787841	4.166019	0.07	0.947	-7.979862	8.537431
darea5	.785105	3.845423	0.20	0.839	-6.837997	8.408207
darea6	3.409261	4.37956	0.78	0.438	-5.272706	12.09123
darea7	.9208387	4.886099	0.19	0.851	-8.765283	10.60696
darea8	.2797695	3.984434	0.07	0.944	-7.618906	8.178445
darea9	-4.447645	5.753083	-0.77	0.441	-15.85246	6.95717
_cons	-3.238117	2.814169	-1.15	0.252	-8.81688	2.340645

Model #4: Stage-specific analysis - increase in true occurrence of localized melanoma

Unit of analysis: SEER area in an individual year (9 areas, 14 years, N = 126)

Dependent variable: incidence of local stage melanoma

Independent variable: biopsy rate

Control variables: indicator variables for each of the 9 SEER areas, year-area interaction terms (to allows the melanoma incidence in each area to progress at its own rate)

```
. regress local newbx xta1-xta9 darea1-darea9
```

Source	SS	df	MS	Number of obs =	126
Model	11505.2297	18	639.17943	F(18, 107) =	29.29
Residual	2335.19349	107	21.8242383	Prob > F =	0.0000
				R-squared =	0.8313
				Adj R-squared =	0.8029
Total	13840.4232	125	110.723386	Root MSE =	4.6716

localized	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
newbx	2.285205	1.155288	1.98	0.050	-.0050182 4.575429
xta1	.5744296	.5943808	0.97	0.336	-.603861 1.75272
xta2	1.204351	.608712	1.98	0.050	-.0023497 2.411051
xta3	.9340952	.4408775	2.12	0.036	.060107 1.808083
xta4	1.423739	.2816715	5.05	0.000	.8653578 1.98212
xta5	.7711066	.4022498	1.92	0.058	-.0263066 1.56852
xta6	.3918611	.3177315	1.23	0.220	-.2380045 1.021727
xta7	-.0123884	.4588789	-0.03	0.979	-.9220623 .8972856
xta8	1.188406	.4580939	2.59	0.011	.280288 2.096524
xta9	1.615089	.3222941	5.01	0.000	.9761781 2.253999
darea1	-.7953597	3.832921	-0.21	0.836	-8.393679 6.80296
darea2	(dropped)				
darea3	-9.157955	3.787133	-2.42	0.017	-16.6655 -1.650405
darea4	-13.03908	4.055165	-3.22	0.002	-21.07798 -5.000192
darea5	-8.030129	3.7431	-2.15	0.034	-15.45039 -.6098706
darea6	-.2851186	4.263024	-0.07	0.947	-8.736067 8.16583
darea7	-.8678054	4.756085	-0.18	0.856	-10.29619 8.560578
darea8	-4.10902	3.878412	-1.06	0.292	-11.79752 3.57948
darea9	-7.672381	5.599999	-1.37	0.174	-18.77372 3.428963
_cons	20.08942	2.739287	7.33	0.000	14.6591 25.51973

Model #5: Stage-specific analysis - increase in true occurrence of regional melanoma

Unit of analysis: SEER area in an individual year (9 areas, 14 years, N = 126)

Dependent variable: incidence of regional stage melanoma

Independent variable: biopsy rate

Control variables: indicator variables for each of the 9 SEER areas, year-area interaction terms (to allows the melanoma incidence in each area to progress at its own rate)

```
. regress regional newbx xta1-xta9 darea1-darea9
```

Source	SS	df	MS	Number of obs =	126
Model	513.837762	18	28.5465423	F(18, 107) =	10.71
Residual	285.301697	107	2.666371	Prob > F =	0.0000
				R-squared =	0.6430
				Adj R-squared =	0.5829
Total	799.139458	125	6.39311567	Root MSE =	1.6329

regional	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
newbx	.3066664	.4038136	0.76	0.449	-.493847 1.10718
xta1	.3028194	.2077569	1.46	0.148	-.1090345 .7146733
xta2	.1121469	.2127662	0.53	0.599	-.3096372 .5339311
xta3	.2522026	.1541021	1.64	0.105	-.0532869 .5576921
xta4	.3217822	.0984541	3.27	0.001	.1266084 .5169559
xta5	.2061461	.1406004	1.47	0.146	-.0725778 .48487
xta6	.0914983	.1110583	0.82	0.412	-.1286619 .3116584
xta7	.2084553	.1603943	1.30	0.197	-.1095077 .5264182
xta8	.2826096	.1601199	1.76	0.080	-.0348094 .6000286
xta9	.5349786	.1126531	4.75	0.000	.311657 .7583002
darea1	-2.749485	1.33974	-2.05	0.043	-5.405364 -.0936065
darea2	(dropped)				
darea3	-3.583627	1.323736	-2.71	0.008	-6.207779 -.9594756
darea4	-4.236004	1.417422	-2.99	0.003	-7.045879 -1.42613
darea5	-2.081836	1.308345	-1.59	0.115	-4.675477 .5118044
darea6	-1.795236	1.490076	-1.20	0.231	-4.749138 1.158667
darea7	-2.834087	1.662418	-1.70	0.091	-6.129637 .4614638
darea8	-1.950981	1.355641	-1.44	0.153	-4.638381 .7364189
darea9	-4.559081	1.957396	-2.33	0.022	-8.43939 -.6787718
_cons	4.562358	.9574769	4.76	0.000	2.664272 6.460444

Model #6: Stage-specific analysis - increase in true occurrence of distant melanoma

Unit of analysis: SEER area in an individual year (9 areas, 14 years, N = 126)

Dependent variable: incidence of distant stage melanoma

Independent variable: biopsy rate

Control variables: indicator variables for each of the 9 SEER areas, year-area interaction terms (to allows the melanoma incidence in each area to progress at its own rate)

```
. regress distant newbx xta1-xta9 darea1-darea9
```

Source	SS	df	MS	Number of obs =	126
Model	38.4588807	18	2.13660448	F(18, 107) =	2.46
Residual	93.0681829	107	.869796102	Prob > F =	0.0023
				R-squared =	0.2924
				Adj R-squared =	0.1734
Total	131.527064	125	1.05221651	Root MSE =	.93263

distant	Coef.	Std. Err.	t	P> t	[95% Conf. Interval]
newbx	-.09524	.2306372	-0.41	0.680	-.5524514 .3619714
xta1	.1029275	.1186599	0.87	0.388	-.1323019 .3381569
xta2	.1623099	.1215209	1.34	0.184	-.0785911 .403211
xta3	.1450973	.0880151	1.65	0.102	-.0293823 .319577
xta4	.088288	.0562318	1.57	0.119	-.0231851 .199761
xta5	-.0015836	.0803036	-0.02	0.984	-.1607761 .1576089
xta6	.0918095	.0634307	1.45	0.151	-.0339344 .2175535
xta7	.0746895	.0916088	0.82	0.417	-.1069143 .2562933
xta8	.114006	.0914521	1.25	0.215	-.0672871 .2952991
xta9	.2288518	.0643416	3.56	0.000	.1013022 .3564014
darea1	-.021669	.7651896	-0.03	0.977	-1.538568 1.49523
darea2	(dropped)				
darea3	-.3769055	.7560487	-0.50	0.619	-1.875684 1.121873
darea4	.0585161	.8095576	0.07	0.943	-1.546337 1.66337
darea5	1.218797	.7472581	1.63	0.106	-.2625546 2.700149
darea6	.4867213	.8510538	0.57	0.569	-1.200393 2.173836
darea7	.3398033	.9494865	0.36	0.721	-1.542443 2.222049
darea8	.0219624	.7742713	0.03	0.977	-1.51294 1.556865
darea9	-.62182	1.117962	-0.56	0.579	-2.83805 1.59441
_cons	1.313729	.5468607	2.40	0.018	.229641 2.397816