

Article

Estimating Cost Savings from Early Cancer Diagnosis

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Abstract: We estimate treatment cost-savings from early cancer diagnosis. For breast, lung, prostate and colorectal cancers and melanoma, which account for more than 50% of new incidences projected in 2017, we combine published cancer treatment cost estimates by stage with incidence rates by stage at diagnosis. We extrapolate to other cancer sites by using estimated national expenditures and incidence rates. A rough estimate for the U.S. national annual treatment cost-savings from early cancer diagnosis is in 11 digits. Using this estimate and cost-neutrality, we also estimate a rough upper bound on the cost of a routine early cancer screening test.

Keywords: cancer; costs; incidence; stage; early diagnosis; treatment; data

1. Introduction

According to the Centers for Medicare & Medicaid Services (CMS), the U.S. national health expenditure (NHE) in 2015 was \$3.2 trillion and accounted for 17.8% of gross domestic product (GDP); NHE is projected to grow at an average rate of 5.6% per year in 2016–2025 [1]. Cancer care is projected to account for up to \$177 billion in 2017 [2], or nearly 1% of GDP.¹ The American Cancer Society estimates 1.7 million new cases of cancer and 600 thousand deaths in 2017 [3]. Although overall incidence rates for new cancer cases have been falling on average 1.1% each year over the last 10 years, and death rates have been falling on average 1.5% each year over 2005–2014 [4], the impact of population changes in the U.S. on cancer prevalence may exceed the impact of declining cancer incidence rates. Also, the population in the U.S. is expected to become much older; by 2030, more than 20% of the U.S. residents are projected to be aged 65 and over, compared with 13% in 2010 [5]. Since cancer incidence

¹ The \$177B figure is a high estimate assuming incidence/survival rate trends and 5% cost increases [2].

typically is higher in the elderly, the aging population and costly advancements in treatment options will impact cancer survival and care expenditures, both of which are likely to increase in the future. Overall, the cancer costs do tend to rise [2].

Detecting and treating cancer at an early stage can and does save lives. Survival rates improve dramatically when cancer is diagnosed early and the disease is confined to the organ of origin before it has had a chance to spread, and the cancer is more likely to be treated successfully [6,7]. Conversely, a late stage diagnosis essentially means that the cancer has spread, making treatment much more difficult, thereby reducing chances of survival. Thus, according to [8], more than 9 in 10 bowel cancer patients will survive the disease for more than 5 years if diagnosed at the earliest stage; more than 90% of women diagnosed with breast cancer at the earliest stage survive their disease for at least 5 years compared to around 15% for women diagnosed with the most advanced stage of disease; more than 90% of women diagnosed with the earliest stage ovarian cancer survive their disease for at least 5 years compared to around 5% for women diagnosed with the most advanced stage of disease; around 70% of lung cancer patients will survive for at least a year if diagnosed at the earliest stage compared to around 14% for people diagnosed with the most advanced stage of disease. The importance of diagnosing cancer early for survival cannot be overstated.

Another important aspect relating to early diagnosis is treatment costs. Thus, cancer patient costs of care in the last year of life are sizably higher than during earlier stages [9]. Further, in many cases, it is much less costly to treat cancer when it is diagnosed early.² Considering that the wealth of nations is not limitless, one of our better chances to reduce staggering cancer treatment costs is through early detection and intervention. Traditionally, cancer research has focused on treatments for late-stage disease, encompassing an estimated 85% of the annual allocation [10]. Thus, global oncology drug costs reached \$107 billion in 2015 and are projected to exceed \$150 billion by 2020 [11]. Such trends appear to be producing a shift in thinking amongst various stakeholders, such as policy makers, payers, providers, and consumers, in reorienting research toward prevention³ and early detection. Recent high fund-raising figures by companies such as Grail, Inc., which raised close to \$1B in its recent series B funding round [12], and Guardant Health, which recently raised \$360M from investors (bringing its total raised to \$550M) [13] speak volumes in this regard. Therefore, here we ask the following question: *What are the estimated cost-savings from early cancer diagnosis?*

Our goal is to arrive at a *conservative* estimate. Therefore, we define cost-savings from early diagnosis by assuming that all stage III and IV cases are detected at stages I or II, with the current incidence rates for this. We specifically exclude stage 0. The requisite data is scarce, incomplete and scattered. We use costs and incidence rates data available for four and 19 cancer sites, respectively, and extrapolate to various other cancers. We focus on U.S. expenditures. While healthcare costs in other countries are in many cases lower than in the U.S., the estimates apply directionally worldwide. Finally, the cost-savings estimates hereof are limited to direct costs for treatment only. When conducting health economic analyses, a critical piece of the evaluation is the question “What is the value of health, both to the individual patient and to the overall system as a whole?” In considering this question, the indirect financial costs of cancer treatment can be an additional burden to the people diagnosed with cancer, their families, their employers, and the society in general, and the added costs can be significant. However, as mentioned above, we are after a conservative estimate and such considerations would only add to it. Our estimate, \$26B/year, is by no means “precise” as it is extrapolated. However, it is likely correct within a factor of 2.

The remainder is organized as follows. Section 2 discusses (i) a methodology for estimating cost-savings from early cancer diagnosis and (ii) data based on commercial claims for breast cancer as reported in [14] and on incidence rates by stage at diagnosis as reported in [15]. Section 3 discusses

² E.g., later-stage melanoma, chemotherapy, etc., sizably increase costs [19] (see Table V therein).

³ Reducing exposure to known carcinogens [20,21] such as tobacco, etc., is important. However, cancer occurs at the DNA level via somatic mutations (see [22–24] and referenced therein) and is not always preventable.

incidence rate data for 19 cancer sites as reported in [16] (and also [17]). Section 4 discusses Medicare claims data as reported in [18] for four cancer sites. Section 5 discusses melanoma data as reported in [19]. Section 6 discusses (i) extrapolation to other cancer sites and (ii) national expenditure estimates as reported in [2]. Section 7 briefly concludes. Table 1 through 11 contain data utilized in our analysis.

2. Breast Cancer

2.1. Costs by Stage at Diagnosis: Commercially Insured Population Study

[14] analyzes commercially insured U.S. women aged 18 to 64 years who were newly diagnosed with breast cancer in 2010.⁴ Table 1, which is adapted from [14], summarizes their results. The average per-patient allowed costs in the 12 months following diagnosis are \$60,637, \$82,121, \$129,387 and \$134,682 for stages 0, I/II, III, and IV at diagnosis, respectively. The average per-patient allowed costs in the 24 months following diagnosis are \$71,909, \$97,066, \$159,442 and \$182,655 for stages 0, I/II, III, and IV at diagnosis, respectively. These costs are not adjusted for inflation or any other temporal changes.

Table 1. Average per-patient allowed costs, by disease stage at diagnosis, for breast cancer patients studied in [14].

Stage at Diagnosis	# of Patients at Diagnosis	0–6 Months Post-Diagnosis	0–12 Months Post-Diagnosis	0–18 Months Post-Diagnosis	0–24 Months Post-Diagnosis
0	2300	\$48,477	\$60,637	\$67,450	\$71,909
I/II	4425	\$61,621	\$82,121	\$91,109	\$97,066
III	1134	\$84,481	\$129,387	\$147,470	\$159,442
IV	501	\$89,463	\$134,682	\$162,086	\$182,655
All	8360	\$62,774	\$85,772	\$96,499	\$103,735

2.2. Incidence Rates by Stage at Diagnosis

[15] analyzes various data for 452,215 women diagnosed with invasive breast cancer from 2004 to 2011 who were identified in the Surveillance, Epidemiology, and End Results (SEER) 18 registries database.⁵ This study focuses on stages I, II, III and IV, specifically excluding in situ stage 0 and stage unknown cases.⁶ Table 2, which is adapted from [15], summarizes the data for breast cancer incidence rates (in %) by stage (I, II, III and IV only) at diagnosis, including aggregated numbers as well as those broken down by eight racial/ethnic groups, across which there is some degree of variability, which should be kept in mind when interpreting cost-savings estimates. We will use the figures (column 2, Table 2) aggregated across all racial/ethnic groups: 48%, 34.6%, 12.4% and 5% for stages I, II, III and IV, respectively.

⁴ This study utilizes the Truven Health MarketScan[®] commercial claims database using 2010 as the index year, 2009 as a look-back year, and 2011 and 2012 as the 24-month look-forward period. It infers the stage—to wit, stage 0, I/II, III, or IV—at diagnosis based on identification of stage-specific treatments recommended in the National Comprehensive Cancer Network (NCCN) treatment guidelines [25]. Cases at stages I and II are combined as the NCCN treatment recommendations are interchangeable for these stages. See [14] for details.

⁵ According to [26]: the SEER 18 registries consist of the SEER 13, plus Greater California, Greater Georgia, Kentucky, Louisiana, and New Jersey; the SEER 13 registries consist of the SEER 9 plus Los Angeles, San Jose-Monterey, Rural Georgia and the Alaska Native Tumor Registry; the SEER 9 registries are Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, and Utah. The SEER 18 covers about 28% of the total U.S. population (based on the 2010 Census) [15].

⁶ It also excludes a small fraction of cases with borderline, undetermined or unknown estrogen receptor status, and those with prior history of any cancer, leaving 373,563 cases in the study [15].

Table 2. Breast cancer incidence rates (in %) by stage at diagnosis from 2004 to 2011 for women who were identified in the Surveillance, Epidemiology, and End Results (SEER) 18 registries database, as reported in [15]. Columns 3–10 correspond to the eight racial/ethnic groups identified therein. Column 2 corresponds to all racial/ethnic groups.

Stage at Diagnosis	Total	Non-Hispanic White	Hispanic White	Black	Chinese	Japanese	South Asian	Other Asian	Other
I	48.0	50.8	40.1	37.0	50.1	56.1	40.4	45.2	43.6
II	34.6	33.2	38.7	38.6	35.7	32.4	38.7	38.1	37.2
III	12.4	11.4	15.9	16.6	10.7	8.5	15.3	12.4	13.5
IV	5.0	4.6	5.3	7.8	3.5	3.0	5.6	4.3	5.7

2.3. Cost-Savings Estimates

To estimate cost-savings of early (stages I and II) vs. late (stages III and IV) diagnoses, we use the 12-month and 24-month average per-patient allowed costs for stages I/II, III and IV from [14] (see Section 2.1 and columns 4 and 6 of Table 1) and incidence rates by stage at diagnosis (see Section 2.2 and column 2 in Table 2) from [15]. The average 12 and 24-month estimated per-patient cost-savings from early diagnosis are given by

$$S_{12-mo} = (X_{III} - X_{I,II}) \times R_{III} + (X_{IV} - X_{I,II}) \times R_{IV} \tag{1}$$

$$S_{24-mo} = (Y_{III} - Y_{I,II}) \times R_{III} + (Y_{IV} - Y_{I,II}) \times R_{IV} \tag{2}$$

where $X_{I,II} = \$82,121$, $X_{III} = \$129,387$ and $X_{IV} = \$134,682$ are the 12-month average per-patient allowed costs for stages I/II, III and IV, respectively; $Y_{I,II} = \$97,066$, $Y_{III} = \$159,442$ and $Y_{IV} = \$182,655$ are the 24-month average per-patient allowed costs for stages I/II, III and IV, respectively. The incidence rates by stage at diagnosis are $R_I = 48.0\%$, $R_{II} = 34.6\%$, $R_{III} = 12.4\%$ and $R_{IV} = 5.0\%$ for stages I, II, III and IV, respectively. Thus, in Equations (1) and (2), we are estimating average savings by assuming that all stage III and IV cases are diagnosed early, at stage I or II. With these assumptions, the estimated cost-savings are $S_{12-mo} = \$8489$ and $S_{24-mo} = \$12,014$ (these figures are rounded to the nearest integer). It is also instructive to estimate relative (as opposed to absolute) cost-savings compared with average per-patient costs across all stages. The latter can be estimated as

$$C_{12-mo} = X_{I,II} \times (R_I + R_{II}) + X_{III} \times R_{III} + X_{IV} \times R_{IV} \tag{3}$$

$$C_{24-mo} = Y_{I,II} \times (R_I + R_{II}) + Y_{III} \times R_{III} + Y_{IV} \times R_{IV} \tag{4}$$

These estimates, $C_{12-mo} = \$90,610$ and $C_{24-mo} = \$109,080$, are based on stage I, II, III and IV cases only. However, if we include in situ stage 0 cases, then the average per-patient costs are lower. To estimate these costs, we need the incidence rate for stage 0 cases. Thus, according to [27], the estimated number of new in situ (stage 0) female breast cancer cases in the U.S. in 2017 is 63,410, whereas the estimated number of new invasive (stages I, II, III and IV) female breast cancer cases in the U.S. in 2017 is 252,710. We will take $\tilde{R}_0 = 63,410 / (252,710 + 63,410) = 20.1\%$ as the incidence rate for stage 0. Accordingly, the incidence rates for stage I-IV cases are given by $\tilde{R}_K = (1 - \tilde{R}_0) \times R_K$ with $K = I, II, III, IV$. Note that $R_I + R_{II} + R_{III} + R_{IV} = 100\%$, and, therefore, $\tilde{R}_0 + \tilde{R}_I + \tilde{R}_{II} + \tilde{R}_{III} + \tilde{R}_{IV} = 100\%$.

The average per-patient costs across all stages including stage 0 then are given by

$$\tilde{C}_{12-mo} = X_0 \times \tilde{R}_0 + X_{I,II} \times (\tilde{R}_I + \tilde{R}_{II}) + X_{III} \times \tilde{R}_{III} + X_{IV} \times \tilde{R}_{IV} \tag{5}$$

$$\tilde{C}_{24-mo} = Y_0 \times \tilde{R}_0 + Y_{I,II} \times (\tilde{R}_I + \tilde{R}_{II}) + Y_{III} \times \tilde{R}_{III} + Y_{IV} \times \tilde{R}_{IV} \tag{6}$$

here $X_0 = \$60,637$ and $Y_0 = \$71,909$ (see Section 2.1), so $\tilde{C}_{12-mo} = \$84,598$ and $\tilde{C}_{24-mo} = \$101,624$, which are 6.6% and 6.8% lower than C_{12-mo} and C_{24-mo} , respectively.

The relative cost-savings are defined as

$$E_{12-mo} = S_{12-mo} / C_{12-mo} \quad (7)$$

$$E_{24-mo} = S_{24-mo} / C_{24-mo} \quad (8)$$

$$\tilde{E}_{12-mo} = \tilde{S}_{12-mo} / \tilde{C}_{12-mo} = (1 - \tilde{R}_0) \times S_{12-mo} / \tilde{C}_{12-mo} \quad (9)$$

$$\tilde{E}_{24-mo} = \tilde{S}_{24-mo} / \tilde{C}_{24-mo} = (1 - \tilde{R}_0) \times S_{24-mo} / \tilde{C}_{24-mo} \quad (10)$$

These estimated relative cost-savings are $E_{12-mo} = 9.37\%$, $E_{24-mo} = 11.01\%$, $\tilde{E}_{12-mo} = 8.02\%$, $\tilde{E}_{24-mo} = 9.45\%$. So, roughly, we expect around 8–11% savings from early diagnosis. When we include stage 0, in Equations (9) and (10) the average 12- and 24-month estimated per-patient cost-savings \tilde{S}_{12-mo} and \tilde{S}_{24-mo} are computed via Equations (1) and (2), respectively, but with R_{III} and R_{IV} replaced by \tilde{R}_{III} and \tilde{R}_{IV} , hence the factor $(1 - \tilde{R}_0)$. Therefore, including stage 0 reduces the absolute costs-savings and also to a lesser degree the average costs, so overall the relative cost-savings are also reduced. Thus, we have $\tilde{E}_{12-mo} / E_{12-mo} = 85.59\%$, and $\tilde{E}_{24-mo} / E_{24-mo} = 85.83\%$, so including stage 0 reduces the relative cost-savings by about 14–15%. Generally, stage unknown can also alter these figures, but to a lesser degree.

3. Incidence Rates by Stage at Diagnosis: 19 Cancers

[16] provides detailed data for stage at diagnosis for Californian adults aged 20 and older diagnosed with cancer during 2005–2009. Their data contains 19 cancer sites. We compile their data into Table 3, which provides (for each of the 19 cancer sites) the total number of cases, numbers of cases for stages 0–IV and stage unknown, and the corresponding incidence rates (in %), both including and excluding stage 0 and stage unknown. For some cancer sites, stage 0 data is not available (NA). For the bladder, stage 0 and stage I are combined.

Comparing incidence rates in columns 15–18 of Table 3 (these correspond to stages I–IV only, with stage 0 and stage unknown excluded) for breast cancer, we see that they are very close to the incidence rates in column two of Table 2 obtained from [15], which is based on the SEER 18 database (see Section 2.2) and includes various other U.S. regions.

[16] also provide data for various racial/ethnic and age groups. We compile their data for breast cancer into Table 4. The last four rows correspond to the incidence rates by stage at diagnosis with stage 0 and stage unknown excluded. The racial/ethnic group incidence rates are consistent with those in Table 2, which are based on the SEER 18 [15].

A Sanity Check: 5 Cancers

[17] analyzes data by stage at diagnosis, quality of treatment, and survival among persons diagnosed with breast, colon, rectal, lung, and prostate cancer in California between 2004 and 2012. We compile their data into Table 5. The last 4 columns of Table 5 are consistent with those in Table 3. A notable difference exists for prostate cancer, for which there are relatively few cases at stage I in Table 3, and a more sizable number in Table 5, but the stage I + II incidence rates from Table 3 (85.5%) and Table 5 (84.64%) are still consistent.

Table 3. Incidence numbers (column two = total; columns 3–7 = stages 0-IV; column eight = stage unknown or “?”; for each row, columns three through eight add up to column two), incidence rates in % for stages 0-IV and stage unknown (columns 9–13 = stages 0-IV, column 14 = stage unknown, for each row columns 9 through 14 add up to 100% up to rounding to two digits), and incidence rates for stages I-IV only with stage 0 and stage unknown specifically excluded (columns 15–18 = stages I-IV, for each row columns 15 through 18 add up to 100% up to rounding to two digits). The incidence numbers are based on the data for California adults aged 20 and older diagnosed with the cancers listed in column 1 during 2005–2009 as reported in [16]. Some cancer sites in column one are abbreviated as follows: Breast = female breast, Cervix = cervix uteri, Rectum = rectum and rectosigmoid junction, Kidney = kidney and renal pelvis, liver = liver and intrahepatic bile ducts, Lung = lung and bronchus, Melanoma = melanoma of the skin, Oral = oral cavity and pharynx, Bladder = urinary bladder, Uterine = uterine corpus. For Bladder, stage I includes stage 0 (stage I = stage 0/I).

Cancer	Total	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage
	#	0, #	I, #	II, #	III, #	IV, #	?, #	0, %	I, %	II, %	III, %	IV, %	?, %	I, %	II, %	III, %	IV, %
Breast	141,654	27,344	51,515	37,083	13,360	5415	6937	19.3	36.37	26.18	9.43	3.82	4.9	47.98	34.54	12.44	5.04
Cervix	7454	NA	3516	894	1402	942	700	NA	47.17	11.99	18.81	12.64	9.39	52.06	13.23	20.76	13.95
Colon	55,378	4872	11,342	13,393	12,000	9849	3922	8.8	20.48	24.18	21.67	17.79	7.08	24.35	28.74	25.76	21.15
Rectum	22,468	2045	5132	3825	4631	3406	3429	9.1	22.84	17.02	20.61	15.16	15.26	30.2	22.5	27.25	20.04
Esophagus	6786	118	1098	959	1063	2154	1394	1.74	16.18	14.13	15.66	31.74	20.54	20.82	18.18	20.15	40.84
Kidney	23,664	373	12,100	2193	3084	4070	1844	1.58	51.13	9.27	13.03	17.2	7.79	56.42	10.23	14.38	18.98
Larynx	4803	402	1647	644	606	1080	424	8.37	34.29	13.41	12.62	22.49	8.83	41.41	16.2	15.24	27.16
Liver	15,246	NA	3964	2126	2682	2433	4041	NA	26	13.94	17.59	15.96	26.51	35.38	18.97	23.94	21.72
Lung	86,954	34	14,847	3083	18,639	37,467	12,884	0.04	17.07	3.55	21.44	43.09	14.82	20.05	4.17	25.18	50.61
Melanoma	59,676	23,920	22,250	3990	1910	1355	6251	40.08	37.28	6.69	3.2	2.27	10.47	75.39	13.53	6.47	4.59
Oral	18,434	445	3272	2074	2463	6415	3765	2.41	17.75	11.25	13.36	34.8	20.42	23	14.58	17.31	45.1
Ovary	14,295	NA	3427	870	3984	2995	3019	NA	23.97	6.09	27.87	20.95	21.12	30.39	7.72	35.33	26.56
Pancreas	19,545	77	1248	3995	1331	9054	3840	0.39	6.39	20.44	6.81	46.32	19.65	7.99	25.56	8.52	57.93
Prostate	109,601	NA	134	84,673	7283	7097	10,414	NA	0.12	77.26	6.65	6.48	9.5	0.13	85.37	7.35	7.16
Stomach	13,566	140	2855	1269	1319	5014	2969	1.03	21.05	9.35	9.72	36.96	21.89	27.31	12.13	12.61	47.95
Testis	4809	11	3249	454	717	0	378	0.23	67.56	9.44	14.91	0	7.86	73.51	10.27	16.22	0
Thyroid	17,968	NA	11,375	1466	2134	1890	1103	NA	63.31	8.16	11.88	10.52	6.14	67.45	8.69	12.66	11.21
Bladder	31,628	—	22,875	3434	1401	2331	1587	—	72.33	10.86	4.43	7.37	5.02	76.15	11.43	4.66	7.76
Uterus	21,710	242	13,366	1537	2546	1447	2572	1.11	61.57	7.08	11.73	6.67	11.85	70.74	8.13	13.48	7.66

Table 4. Incidence numbers (column two = total; columns 3–7 = stages 0-IV; column eight = stage unknown or “?”; for each row, columns three through eight add up to column two), incidence rates in % for stages 0-IV and stage unknown (columns 9–13 = stages 0-IV, column 14 = stage unknown, for each row columns 9 through 14 add up to 100% up to rounding to two digits), and incidence rates for stages I-IV only with stage 0 and stage unknown specifically excluded (columns 15–18 = stages I-IV, for each row columns 15 through 18 add up to 100% up to rounding to two digits). The incidence numbers are based on the data for California women aged 20 and older diagnosed with Breast Cancer during 2005–2009 as reported in [16]. The demographic groups are abbreviated as follows: NHW = Non-Hispanic White, PI = Pacific Islander.

Group	Total	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage
	#	0, #	I, #	II, #	III, #	IV, #	?, #	0, %	I, %	II, %	III, %	IV, %	?, %	I, %	II, %	III, %	IV, %
NHW	91,951	17,315	36,067	23,185	7899	3304	4181	18.83	39.22	25.21	8.59	3.59	4.55	51.19	32.91	11.21	4.69
Black	8804	1634	2548	2533	1073	549	467	18.56	28.94	28.77	12.19	6.24	5.3	38.01	37.79	16.01	8.19
Hispanic	22,856	4155	6887	6663	2915	988	1248	18.18	30.13	29.15	12.75	4.32	5.46	39.46	38.18	16.7	5.66
Asian/PI	16,251	3818	5515	4353	1359	525	681	23.49	33.94	26.79	8.36	3.23	4.19	46.93	37.04	11.56	4.47
Age 20–44	16,560	3071	4245	5466	2445	627	706	18.54	25.63	33.01	14.76	3.79	4.26	33.21	42.76	19.13	4.9
Age 45–64	69,521	15,088	24,218	18,211	6812	2590	2602	21.7	34.84	26.19	9.8	3.73	3.74	46.72	35.14	13.14	5
Age 65+	55,573	9185	23,052	13,406	4103	2198	3629	16.53	41.48	24.12	7.38	3.96	6.53	53.91	31.35	9.6	5.14

Table 5. Incidence numbers and rates with the same conventions for columns 2–18 as in Table 4. The incidence numbers are based on the data for persons diagnosed with breast, colon, rectal, lung, and prostate cancer in California during 2004–2012 as reported in [17]. Some cancer sites in column 1 are abbreviated as follows: Breast = female breast, Rectum = rectum and rectosigmoid junction, Lung = lung and bronchus.

Cancer	Total	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage	Stage
	#	0, #	I, #	II, #	III, #	IV, #	?, #	0, %	I, %	II, %	III, %	IV, %	?, %	I, %	II, %	III, %	IV, %
Breast	260,590	49,540	96,601	67,953	24,317	10,382	11,797	19.01	37.07	26.08	9.33	3.98	4.53	48.48	34.1	12.2	5.21
Colon	97,947	8235	20,085	23,615	21,597	17,961	6454	8.41	20.51	24.11	22.05	18.34	6.59	24.12	28.36	25.94	21.57
Rectum	30,334	2814	7536	4794	6081	4242	4867	9.28	24.84	15.8	20.05	13.98	16.04	33.27	21.16	26.84	18.73
Lung	155,820	142	27,008	7381	31,097	69,944	20,248	0.09	17.33	4.74	19.96	44.89	12.99	19.94	5.45	22.96	51.65
Prostate	198,043	NA	16,113	135,698	14,194	13,359	18,679	NA	8.14	68.52	7.17	6.75	9.43	8.98	75.66	7.91	7.45

4. Medicare Data: Four Cancers

[18] provides Medicare spending estimates for breast, colorectal, lung and prostate cancers in California between 2007–2011. One of the reasons cited in [18] for focusing on Medicare spending is that “Medicare data, unlike data from other payers, are readily accessible”. We compile the data from [18] into Table 6 (mean per-patient Medicare spending in the first year after diagnosis by stage at diagnosis) and Table 7 (mean per-patient Medicare spending in the last year of life by stage at diagnosis). The costs in Table 7 in the last year of life are relatively uniform with the stage at diagnosis. However, the costs in Table 6 in the first year after diagnosis increase considerably with the stage at diagnosis.

Table 6. Medicare spending per patient in the first year after diagnosis (columns 2–5) and fractions of patients (columns 6–9) by stage at diagnosis based on California beneficiaries diagnosed in 2007–2011 and followed through 2012, as reported in [18]. Spending estimates are based on Medicare fee-for-service patients only and are adjusted for inflation to 2013 dollars. For prostate cancer stages I and II are combined due to small numbers for stage I.

Cancer	Stage I, \$	Stage II, \$	Stage III, \$	Stage IV, \$	Stage I, %	Stage II, %	Stage III, %	Stage IV, %
Breast	29,377	40,989	57,155	67,038	52	32	10	6
Prostate	—	26,505	30,541	44,591	—	84	8	8
Lung	60,038	73,509	84,726	93,166	22	4	26	48
Colorectal	49,189	66,613	83,980	108,599	25	29	26	20

Table 7. Medicare spending per patient in the last year of life (columns 2–5) and fractions of patients (columns 6–9) by stage at diagnosis based on California beneficiaries who were diagnosed in 2007–2011 and died in 2007–2012, as reported in [18]. Estimates include the full year of Medicare spending prior to and including the month of death, irrespective of when the patient was diagnosed. Spending estimates are based on Medicare fee-for-service patients only and are adjusted for inflation to 2013 dollars. For prostate cancer stages I and II are combined due to small numbers for stage I.

Cancer	Stage I, \$	Stage II, \$	Stage III, \$	Stage IV, \$	Stage I, %	Stage II, %	Stage III, %	Stage IV, %
Breast	64,889	70,931	71,555	70,057	27	32	19	22
Prostate	—	66,160	82,621	71,704	—	66	5	29
Lung	82,621	78,091	74,186	65,907	13	3	27	57
Colorectal	83,135	84,098	86,789	79,552	14	21	26	39

For the first year after diagnosis, we can use the same methodology as in Section 2.3 to estimate cost-savings from early (stages I and II) vs. late (stages III and IV) diagnosis. Here we can estimate the following quantities: C_{12-mo} (average per-patient cost in the first 12 months after diagnosis based on stages I-IV) using Equation (3); S_{12-mo} (average per-patient cost-savings from early diagnosis in the first 12 months from diagnosis) using Equation (1); and E_{12-mo} (the relative cost-savings) using Equation (7). In Equations (1) and (3) the quantity (the stage I/II cost)

$$X_{I,II} = (X_I \times R_I + X_{II} \times R_{II}) / (R_I + R_{II}) \tag{11}$$

where X_K is the stage K cost from Table 6 (columns 2–5), and R_K is the stage K fraction from Table 6 (columns 6–9) with $K = I, II, III, IV$. For prostate cancer, we set $R_I = 0$, so $X_{I,II} = X_{II}$.

The results are summarized in Table 8. For breast cancer, the relative savings (11.35%) are consistent with our estimates in Section 2.3 for commercially insured patients. Note that the fractions in columns 6–9 of Table 6 are somewhat different from all-age incidence rates in, for example, Table 3. For instance, for breast cancer in Table 6, we have 52% for stage I, while in Table 3 we have about 48%. This difference appears to be due to the age group (Medicare). Thus, for age 65+ we have the incidence rate close to 54% for breast cancer in Table 4. Also, let us note that the average per-patient costs reported

in [18] in the graph at p.9 are somewhat lower⁷ than those in column 2 of Table 8 (which are computed based on the data in Table 6 as set forth above). This difference may be due to stage 0 and/or stage unknown contributions. There is not enough information to determine this; however, the difference is small (<7.52%).

Table 8. Estimated average costs (second column), absolute cost-savings (third column) and relative cost-savings (in %, fourth column). These estimates are based on the data in Table 6.

Cancer	Average Costs, \$	Average Cost-Savings, \$	Average Cost-Savings, %
Breast	38,130	4330	11.35
Prostate	28,275	1770	6.26
Lung	82,897	20,787	25.08
Colorectal	75,170	16,623	22.11

Finally, let us mention that our estimate for the average 12-month cost for breast cancer for Medicare (see Table 8) is \$38,130, while the analogous estimate for the commercially insured population from Section 2.3 is \$90,610; i.e., the Medicare figure is about 42% of the commercial insurance figure.⁸ However, this ratio is by no means “precise” as the commercial insurance figures in [14] are from 2010 diagnoses, whereas the Medicare data in [18] is from 2007–2011 diagnoses, so the actual ratio could be higher. However, the ballpark appears to be correct. Thus, according to Appendix D of [28],⁹ in 2004 the cancer population was 63,935 (commercial), and 118,089 (Medicare), while the total spending (allowed) in this population was \$2,281,981,711 (commercial) and \$2,619,153,436 (Medicare), so the per-patient spending in 2004 was \$35,692 (commercial) and \$22,179 (Medicare), and the corresponding Medicare-to-commercial ratio was about 62%. According to this source, in 2014 the cancer population was 264,204 (commercial), and 133,225 (Medicare), while the total spending (allowed) in this population was \$13,908,337,950 (commercial) and \$3,672,799,298 (Medicare), so the per-patient spending in 2014 was \$52,642 (commercial) and \$27,568 (Medicare), and the corresponding Medicare-to-commercial ratio was about 52%. Therefore, the rough ratio for breast cancer we obtained above from the [14,18] data is in the ballpark of those based on the [28] data (for all cancers).¹⁰

5. Melanoma

[19] provides malignant melanoma costs by stage at diagnosis based on 2008 data.¹¹ Based on [19], we compile the costs in the first year after diagnosis and incidence rates by stage at diagnosis in Table 9. As in the previous section, we can estimate the following quantities: C_{12-mo} (average per-patient cost in the first 12 months after diagnosis based on stages I-IV) using Equation (3); S_{12-mo} (average per-patient cost-savings from early diagnosis in the first 12 months from diagnosis) using Equation (1); and E_{12-mo} (the relative cost-savings) using Equation (7). In Equations (1) and (3) the quantity (the stage I/II cost) $X_{I,II}$ is given by Equation (11). Using the data for stages I-IV in Table 9, we have $C_{12-mo} = \$12,541$, $S_{12-mo} = \$5085$ and $E_{12-mo} = 40.55\%$. Such a dramatic cost reduction from early diagnosis is due to more than a 3-fold increase in melanoma treatment costs between stages II and III. Using the melanoma incidence rates from Table 3, we would get a higher $E_{12-mo} = 41.41\%$.

⁷ To wit, \$35,264 for breast cancer, \$28,213 for prostate cancer, \$78,444 for lung cancer, and \$69,687 for colorectal cancer. [18] cites “CCR-Medicare, 2014 data linkage, Healthcare Delivery Research Program, National Cancer Institute” as the source for these average spending figures.

⁸ The \$35,264 figure from [18] (see fn.7 hereof), divided by $\tilde{C}_{12-mo} = \$84,598$ (see Section 2.3) gives 41.7%.

⁹ Based on Milliman analysis of the 2004–2014 Truven Health MarketScan® data and Medicare 5% sample data.

¹⁰ The aforesaid Medicare (based on [18]) and commercial (based on [14]) data are not necessarily uniformly normalized. On the other hand, we expect that the Medicare and commercial figures from Appendix D of [28] are uniformly normalized and can be meaningfully compared with each other.

¹¹ There is a variability in costs reported in various studies [29]. Also see [30].

Table 9. Average costs in the first year after diagnosis (second column) and incidence rates by stage at diagnosis (third column) for malignant melanoma based on 2008 data as reported in [19]. The incidence rates are given for stages I-IV and add up to 100%.

Stage	Average Costs, \$	Incidence Rate, %
0	984	NA
I	4259	52.1
II	12,566	32.6
III	39,761	9.7
IV	42,303	5.6
IV (recurrent)	39,281	NA

6. Extrapolating to Other Cancers

6.1. Relative Cost-Savings

Using the definitions in Equations (1), (3) and (7), we can rewrite the relative cost-savings E_{12-mo} as follows:

$$E_{12-mo} = F / (1 + F) \tag{12}$$

$$F = R_{Late} \times G \tag{13}$$

where $R_{Late} = R_{III,IV} = R_{III} + R_{IV}$ is the incidence rate of late-stage (stages III and IV) diagnosis, and

$$G = X_{Late} / X_{Early} - 1 \tag{14}$$

We define $X_{Late} = X_{III,IV} = (X_{III} \times R_{III} + X_{IV} \times R_{IV}) / R_{Late}$, and $X_{Early} = X_{I,II}$ is defined in Equation (11). Therefore, the relative-cost savings are controlled by two parameters, R_{Late} and G .

We summarize these quantities in Table 10 for breast cancer (based on the commercial claims data from [14] and the Medicare data from [18]), prostate, lung and colorectal cancers (based on the Medicare data from [18]), and melanoma (based on the data from [19]). There is a substantial heterogeneity in both R_{Late} and G , including in commercial vs. Medicare data. Lung cancer has higher $E_{12-mo} = 25.08\%$ largely due to it mostly being diagnosed late ($R_{Late} = 74\%$). On the other hand, melanoma has a very high $E_{12-mo} = 40.55\%$, mainly due to a large jump in the treatment costs between early ($X_{Early} = \$7,456$) and late ($X_{Late} = \$40,641$) diagnoses. In contrast, for prostate cancer, we have low $E_{12-mo} = 6.26\%$ due to the low $R_{Late} = 16\%$ as well as low $G = 0.42$.

Table 10. The quantities in columns 2–9 are defined in Subsection 6.1. Row two corresponds to the commercial claims data of [14]. Rows 3–6 correspond to the Medicare data of [18]. Row seven corresponds to the data reported in [19].

Cancer	C_{12-mo} \$	S_{12-mo} \$	E_{12-mo} %	X_{Early} \$	X_{Late} \$	G	R_{Late} %	F
Breast*	90,610	8489	9.37	82,121	130,909	0.5941	17.4	0.1034
Breast	38,130	4330	11.35	33,801	60,861	0.8006	16	0.1281
Prostate	28,275	1770	6.26	26,505	37,566	0.4173	16	0.0668
Lung	82,897	20,787	25.08	62,110	90,201	0.4523	74	0.3347
Colorectal	75,170	16,623	22.11	58,546	94,684	0.6172	46	0.2839
Melanoma	12,541	5085	40.55	7456	40691	4.4573	15.3	0.682

Table 3 contains incidence rates by stage at diagnosis for 19 cancer sites. We will use this data for cancer sites (for which cost data is available—see below)¹² beyond the five cancers we discuss above.

¹² E.g., cost data are available for colorectal cancer, not for colon cancer or rectum carcinoma separately; etc.

For such cancer sites, we will use the mean value of R_{Late} based on the last two columns of Table 3. This mean value is $\bar{R}_{Late} = 39.94\%$ with a standard deviation¹³ = 21.04%.

To estimate F via Equation (13), we also need the values of G . For breast, prostate, lung and colorectal cancers and melanoma, we will take these values from Table 10. Conservatively, for breast cancer we will take the lower value from row 2 of Table 10. For cancer sites beyond these five, we must estimate G . We exclude row three (the higher value of G for breast cancer) and row seven (melanoma, which is an outlier). The remaining four values of G (rows two and 4–6 in Table 10) have the mean of 0.5202 and the median of 0.5232. We will set $G = 0.5202$ for the other sites.

6.2. Estimated National Expenditures

Estimated national expenditures between 2010 and 2020 are provided in [2]¹⁴ for 17 cancer sites (which are not the same as those in Table 3). Detailed data can be downloaded from the webpage referenced in [2]. For each year, including 2017 which we focus on, this data contains six numbers for the estimated national expenditures based on six different assumptions, to wit: (i) both incidence and survival are constant; (ii) incidence follows recent trends, survival is constant; (iii) survival follows recent trends, incidence is constant; (iv) both incidence and survival follow recent trends; (v) both incidence and survival follow recent trends, annual costs increase at 2% (applied to initial and last phases);¹⁵ (vi) both incidence and survival follow recent trends, annual costs increase at 5% (applied to initial and last phases). In (i)–(iv) above annual costs are assumed to be constant. For estimated national costs for 2017 we take the mean of these six figures, and the so-averaged figures are in column two of Table 11, while the corresponding standard deviations (in %) are in column three thereof. These standard deviations are reasonably small. For the cancer sites in column one of Table 11, we also give the expected 2017 new incidence rates (as reported in [3,27]) in column four. Dividing column two by column four produces column five, the per-new-incidence estimated costs.¹⁶ Columns 6–8 list the values of G , R_{Late} and E_{12-mo} as set forth above (also see the caption to Table 11). We then *roughly* estimate national cost-savings S_{nat} from early diagnosis via

$$S_{nat} = C_{nat} \times E_{12-mo} \times H \quad (15)$$

$$H = \tilde{E}_{12-mo} / E_{12-mo} = 1 / (1 + X_0 \tilde{R}_0 / C_{12-mo} (1 - \tilde{R}_0)) \quad (16)$$

here the factor H corrects for the stage 0 contributions (see Section 2.3). For breast cancer, we take $H = 85.59\%$ (see Section 2.3). For melanoma, using $\tilde{R}_0 = 40.08\%$ from Table 3, $X_0 = \$984$ from Table 9, and $C_{12-mo} = \$12,541$ from Section 5, we get $H = 95.01\%$, so the reduction due to stage 0 is small despite a large \tilde{R}_0 as the stage 0 cost X_0 is small. For other cancer sites \tilde{R}_0 is sub-10% (or NA) and assuming that X_0 is sizably smaller than C_{12-mo} (see Section 2.3), for these cancer sites H is expected to be close to 1. The results for estimated national costs-savings S_{nat} are in column nine of Table 11 (and the national cost estimates C_{nat} are taken from column two thereof). The factor H is set to 85.59% for breast cancer, and to 1 for other cancer sites. The all-sites national cost-savings estimate is \$26B.

¹³ For the same data in Table 3, median = 42.4% and MAD = 28.9% (MAD = mean absolute deviation). Below we will use the lower mean value $\bar{R}_{Late} = 39.94\%$ and not the higher median value for our conservative estimate.

¹⁴ Also see [4].

¹⁵ Initial phase = initial year after diagnosis; last phase = last year of life; continuing phase = in-between period. For detailed information about the methods, data sources and assumptions in [2], see [31].

¹⁶ Which are not the same as the per-patient costs. We give column five in Table 11 for orientation purposes.

Table 11. Cancer site abbreviations in column one are the same as in Table 3. Column two = mean estimated spending based on [2] (which uses the “head-and-neck” nomenclature for Oral = oral cavity and pharynx cancer), and column three = standard deviation (see Subsection 6.2). Column four = number of estimated new incidences as reported in [3,27]. Column five = estimated per-new-incidence spending. The factors G (column 6) and rate R_{Late} (column seven) are taken from Table 10 for breast, colorectal, lung and prostate cancers and melanoma (bold green font). For other cancer sites, the factor G is extrapolated from the values in Table 10 (italicized red font) and rate R_{Late} is taken from Table 3 (regular font) or extrapolated therefrom (italicized blue font). See Subsection 6.1. The relative cost-savings E_{12-mo} (column 8) are obtained via Equations (12) and (13), and cost-savings from early diagnosis (column nine) via Equation (15), where the factor H is set to 1 for all cancer sites except breast cancer, for which $H = 85.59\%$.

Cancer	Estimated National Spending in 2017, \$M	SD, %	Estimated New Cases in 2017, #	Estimated Per-new-incidence Spending in 2017, \$	G	R_{Late} %	E_{12-mo} %	Estimated National Cost-Savings, \$M
All Sites	152,901.1	8.49	1,688,780	90,539	—	—	—	25,902
Bladder	4543.33	6.41	79,030	57,489	<i>0.5202</i>	12.42	6.07	276
Brain	5604.18	11.58	23,800	235,470	<i>0.5232</i>	<i>39.94</i>	17.28	968
Breast	19,478.58	7.81	252,710	77,079	0.5941	17.4	9.37	1562
Cervix	1441.05	10.69	12,820	112,406	<i>0.5232</i>	34.71	15.37	221
Colorectal	15,727.4	9.29	135,430	116,129	0.6172	46	22.11	3477
Esophagus	1857.85	15.09	16,940	109,672	<i>0.5232</i>	60.99	24.19	449
Oral	4101.55	9.34	49,670	82,576	<i>0.5232</i>	62.41	24.62	1010
Kidney	5487.4	13.12	63,990	85,754	<i>0.5232</i>	33.36	14.86	815
Leukemia	6772.22	8.72	62,130	109,001	<i>0.5232</i>	<i>39.94</i>	17.28	1170
Lung	13,693.22	11.31	222,500	61,543	0.4523	74	25.08	3434
Lymphoma	15,096.07	8.76	80,500	187,529	<i>0.5232</i>	<i>39.94</i>	17.28	2609
Melanoma	3308.32	10.28	87,110	37,979	4.4573	15.3	40.55	1342
Ovary	5338.73	11.32	22,440	237,911	<i>0.5232</i>	61.89	24.46	1306
Pancreas	3040.12	16.06	53,670	56,645	<i>0.5232</i>	66.45	25.8	784
Prostate	14,873.72	5.47	161,360	92,177	0.4173	16	6.26	931
Stomach	2074.28	11.88	28,000	74,081	<i>0.5232</i>	60.56	24.06	499
Uterus	2947.42	9.08	61,380	48,019	<i>0.5232</i>	21.14	9.96	294
Other	27,515.67	10.11	275,300	99,948	<i>0.5232</i>	<i>39.94</i>	17.28	4755

6.3. Caveats

Our estimates are clearly far from being “precise” for a variety of reasons, including extrapolating G and R_{Late} to various cancer sites based on data available for four and 19 cancer sites, respectively. However, we have taken a conservative approach to thus extrapolating G . Nonetheless, e.g., for certain cancers, cost-savings from early diagnosis may be less attainable than from others.¹⁷ Also, in Equation (15) we simply use E_{12-mo} (estimated relative cost-savings for the first year after diagnosis).¹⁸ The last phase (the last year of life) costs are skewed toward higher figures (see, e.g., [4]) due to added expenses at this phase. However, with early diagnosis the survival rate would also go up thereby decreasing the contribution of the last phase to the overall costs. Another caveat is that commercial insurance vs. Medicare vs. other payer costs are heterogeneous (and the corresponding data is not readily available), the costs have strong temporal dependence as new treatments become available continuously (and most available data is at least some years out-of-date), etc., so cost-estimates are uneven (see, e.g., [29]). However, the \$26B figure above is likely correct within a factor of 2.

¹⁷ Let us note a minor caveat that for bladder cancer the stage 0 and stage I figures in Table 3 are combined.

¹⁸ Albeit adjusted for stage 0 contributions via the factor H (see above). Also, note that the rates E_{12-mo} and E_{24-mo} are consistent with each other (see the discussion after Equation (10) in Section 2.3), so using the E_{12-mo} rates in our extrapolated estimations is reasonable. A more important caveat is related to the last year of life costs, which are skewed, and which we discuss below in this Section.

7. Conclusions

The above rough estimate for cost-savings from early cancer diagnosis, \$26B, is only about 17% of the total estimated expenditures (see Table 11) and appears to be reasonable despite various built-in (conservative) extrapolations. If we take breast, lung, prostate and colorectal cancers and melanoma, which are top five cancers by incidence with the total 859,110 estimated new cases in 2017, which amounts to 50.87% of all 1,688,780 estimated new cases across all cancer sites,¹⁹ the estimated costs add up to over \$67B (or about 43.87% of costs for all sites), and the corresponding estimated cost-savings from early diagnosis add up to over \$10.7B (or about 41.49% of cost-savings for all sites). Again, these figures should be considered keeping in mind the caveats we discuss above. Even assuming only 50%, the cost-savings are staggering.²⁰

Above, we focus on the U.S. cost-savings from early cancer diagnosis; some other regions of the world have been addressed in the literature. We will not attempt an exhaustive review here. Instead, keeping in mind that, generally, healthcare costs in other countries are in many cases lower than in the U.S., let us mention a U.K. study [32]²¹ and a shorter summary thereof [33], according to which the fractions of the costs for stage I vs. stage IV at diagnosis for colon, rectal, ovarian and lung cancers are approximately 27.2%, 37.3%, 35.1% and 61.1%, respectively. Again, cost-savings from early diagnosis are staggering.

It is precisely these economic considerations that underlie recent high fund-raising figures by companies such as Grail, Inc., which raised close to \$1B in its recent series B funding round [12], and Guardant Health, which recently raised \$360M from investors (bringing its total raised to \$550M) [13]. These figures may appear inflated at first, but are not unreasonable based on the estimated annual cost-savings we discuss here. Early cancer diagnosis does not only save lives but will also save billions of dollars in costs.

In this regard, we can estimate a rough upper bound on the cost of a routine early cancer screening test. We have estimated \$26B/yr in savings from early cancer diagnosis. According to [34], there were about 44.4M adults annually who received preventive health examinations during 2002–2004. Let us take this figure as a rough estimate for the number of annual early cancer screening tests. Then, on a cost-neutral basis, an approximate upper bound for the cost of such a test is \$600. Let us note that this estimate could actually be lower or higher, depending on various details. First, our \$26B/yr estimate is conservative and the actual cost-savings could be higher. Second, this estimate is extrapolated to all cancer sites. Early screening tests may apply to a limited number of cancer sites, and the available cost-savings would be lower. However, if so, then the number of patients screened may also be limited to those at risk, which would decrease the number of tests administered. Third, as mentioned above, we are not including indirect costs of cancer or considerations stemming from the quality-adjusted life-years (QALY), etc., which may also increase said upper bound.²²

Let us emphasize that our goal here is *not* to determine cost-savings from any particular early cancer screening (be it blood-based or any other such) test. Realistically, all such tests are expected to have false negatives and false positives. Clearly, false negatives would decrease any cost-savings associated with early cancer detection. However, if the rate of false negatives is too high to begin with, such a test may not be viable in the first instance. On the other hand, false positives could increase costs as they may cause unnecessary additional testing and/or treatment, not to mention all the anxiety and stress to the patients misdiagnosed with cancer by such false positives. Again, if the rate of

¹⁹ These figures relate to invasive cancer incidences. Thus, in addition, e.g., about 63,410 cases of female breast cancer in situ and 74,680 cases of melanoma in situ are expected to be diagnosed in 2017 [27].

²⁰ Also, as mentioned above, we are not including here the indirect costs of cancer or considerations stemming from the quality-adjusted life-years (QALY), etc. Again, our goal here is to arrive at a reasonable conservative estimate.

²¹ Also, see, e.g., [35].

²² Our aforesaid estimate \$600 per test is consistent with Grail, Inc.'s projections of \$1000 per test, as reported in [36].

false positives is too high to begin with, such a test may not be viable in the first instance. Without specific and reliable data (which does not exist yet) from, say, blood tests, it is virtually impossible to intelligently estimate the effects of false positives or negatives and such an estimate would at best be highly speculative and likely uninformative. Thus, currently it is unknown what the rates of false positives or negatives will be for new cancer screening technologies such as ctDNA (circulating tumor DNA) based blood tests—these technologies are still in nascent stages [7]. Instead, our goal here is to *conservatively estimate* the size of cost-savings from early detection (which is roughly the size of the “market”, which affects the pricing of early detection tests as discussed above). Our estimate is only rough for the multitude of reasons discussed in detail above and our \$26B/yr figure likely is accurate within a factor of 2. However, this figure is reasonable, and there is value in knowing the order of magnitude of the available cost-savings. Thus, from our analysis, it is clear that these cost-savings should be much larger than, say, \$1-2B/yr, but at the same time they are unlikely to lead to a 50% overall cost reduction (this, among other things, is due to high-incidence-level cancers such as prostate and breast cancers already being diagnosed early in many cases based on currently available screenings such as mammograms and prostate exams). However, by piecing together scattered (and not-so-readily available) data and being conservative, our estimates appear to be reasonable and in line with others (see fn.22).

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