

Cost-Effectiveness of Screening Older Adult Smokers for Lung Cancer with an Autoantibody Test (AABT)

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BACKGROUND

- Lung cancer (LC) is most common cause of cancer death in US, in part because it typically is not diagnosed until advanced stages
- Trials suggest screening with computed tomography (CT) may yield favorable shift in LC stage at diagnosis, although a survival benefit has not been convincingly demonstrated
- AABT—EarlyCDT-Lung (Oncimmune Ltd)—to aid in LC detection recently developed:
 - AABT comprises 6 tumor-related antigens produced by LC cells and detectable several years before tumor large enough to appear on CT
- While less sensitive than CT, AABT can detect smaller, less-advanced cancers; it also has greater specificity than CT
- Patients who are positive on both AABT and CT are 3-4 times more likely to have LC; aggressive evaluation and treatment may yield tangible (eg, survival) benefits

STUDY OBJECTIVE

- To estimate cost-effectiveness of screening older adult smokers for LC with AABT, using techniques of decision-analytic modeling

STUDY METHODS

Model Description

- Model depicts clinical and economic consequences of alternative strategies for LC screening in cohort of 100,000 screening-naïve older adult smokers

- Model considers a single “prevalence-round” screening exam

- Strategies include:

- AABT followed by CT if positive (AABT→CT)
- AABT plus CT (AABT+CT)
- CT alone
- No Screening

- Patients assumed to be 60 years of age and at high-risk of having previously undetected LC due to current smoking:

- NSCLC stratified based on nature of disease—aggressive vs. indolent; all SCLC considered to be aggressive

- Patients classified into one of four groups—true-positive, true-negative, false-positive, false-negative—based on LC+ vs LC- and screening+ vs screening-

- True-positives undergo further diagnostic evaluation followed by LC treatment:

- Diagnostic tests employed, and their scheduling, depend on whether AABT and/or CT are positive, and nodule size
- Detection of aggressive NSCLC/SCLC by CT screening yields earlier stage and smaller tumor (NSCLC stage 1), which confer survival benefits (vs no screening):
- LC detected with AABT assumed, on average, to be smaller and less advanced, which results in stage, size, and survival benefits

- Detection of indolent NSCLC by screening (“overdiagnosis bias”) generates additional costs but confers no survival benefit

Model Description (Cont.)

- True-negatives undergo no further diagnostic evaluation
- False-positives undergo additional evaluation that ultimately rules out diagnosis
- False-negatives with aggressive NSCLC/SCLC are correctly diagnosed, on average, 12 months following screening and subsequently undergo LC treatment:
 - Cancer assumed to have same size/stage as that detected in clinical practice, and thus to be more advanced than that for true-positives
 - Vast majority of patients with false-negative indolent NSCLC never diagnosed
- Costs include: initial screening (all patients); follow-up diagnostic evaluation (true-positives and false-positives); LC treatment (true-positives and false-negatives)
- Study perspective is US healthcare system ; future benefits and costs (2008US\$) discounted at 3% per year

Model Estimation

- LC prevalence estimated assuming a three-year “look-forward period”:
 - AABT+ could result from tumor detectable by CT at time of screening or from one so small it would not be detectable by CT for up to three years
- CT sensitivity/specificity calculated from “prevalence-screen” perspective based on results of Mayo Clinic study¹⁻³; for AABT, estimates based on published data^{4,5}

Table 1. Estimated values of selected model parameters

Model Parameter	Value		Reference
	NSCLC	SCLC	
Disease Characteristics			
Prevalence of Lung Cancer, %	4.10%	0.72%	1-3, 6, 7
Type of Lung Cancer, %	85%	15%	7
Screening Test Characteristics			
CT			
Sensitivity	47%	47%	
Specificity	49%	49%	
AABT			
Sensitivity	40%	40%	4, 5
Specificity	93%	93%	
Stage Shift vs No Screening, %			
CT	50%	25%	8 (NSCLC), Expert Opinion (SCLC)
AABT→CT	80%	40%	Expert Opinion
AABT+CT	62.6%	31.3%	Derived
Size Shift (Stage 1) vs No Screening, mm			
CT	16.0	---	2
AABT→CT	18.0	---	Expert Opinion
AABT+CT	17.2	---	Derived
Overdiagnosis Bias, %			
	27%	---	9
Costs			
Initial Screen			
CT	\$301	\$301	10
AABT	\$300	\$300	Assumed
LC Treatment			
11			
Initial Year (Stage 1 - 4)	\$35,871 - \$50,346	\$50,346	
Continuing Years (Annual)	\$4,576	\$4,576	
Last Year of Life (Stage 1 - 4)	\$46,295 - \$78,623	\$78,623	

*Stage shift defined as reclassification of given percentage of stage III and IV tumors to stages I and II in same proportion as these stages occur absent screening

Analyses

- Cost-effectiveness calculated as ratio of difference in expected costs to difference in expected quality-adjusted life-years (QALYs) between:
 - AABT→CT vs No Screening and CT alone, respectively
 - AABT+CT vs No Screening and CT alone, respectively
 - CT vs No Screening

RESULTS

Outcomes

- Of 3,720 cases of aggressive NSCLC/SCLC, 1,488 (true-positives) would be detected with AABT→CT, 2,537 with AABT+CT, and 1,748 with CT alone; false-positives would total 6,662 (AABT→CT), 51,802 (AABT+CT), and 48,538 (CT alone)

Table 2. Classification from screening for lung cancer in a hypothetical population of 100,000 older adult smokers

	No Screening	CT	AABT→CT	AABT+CT
True Negatives	96,123	46,634	88,510	43,370
False Positives	---	48,538	6,662	51,802
True Positives	---	2,269	1,931	3,293
NSCLC	---	1,929	1,641	2,799
Aggressive	---	1,408	1,198	2,043
Indolent	---	521	443	756
SCLC	---	340	290	494
False Negatives	3,877	2,559	2,897	1,535
NSCLC	3,153	2,175	2,463	1,305
Aggressive	2,996	1,588	1,798	953
Indolent	157	587	665	352
Detected	157	0	0	0
Undetected	0	587	665	352
SCLC	724	384	434	230

- Compared with no screening, screening would increase costs by \$403 (AABT→CT), \$1198 (AABT+CT), and \$791 (CT alone) per patient, and yield an additional 0.04 (AABT→CT), 0.06 (AABT+CT), and 0.03 (CT alone) QALYs per patient

Table 3. Outcomes from screening for lung cancer in a hypothetical population of 100,000 older adult smokers*

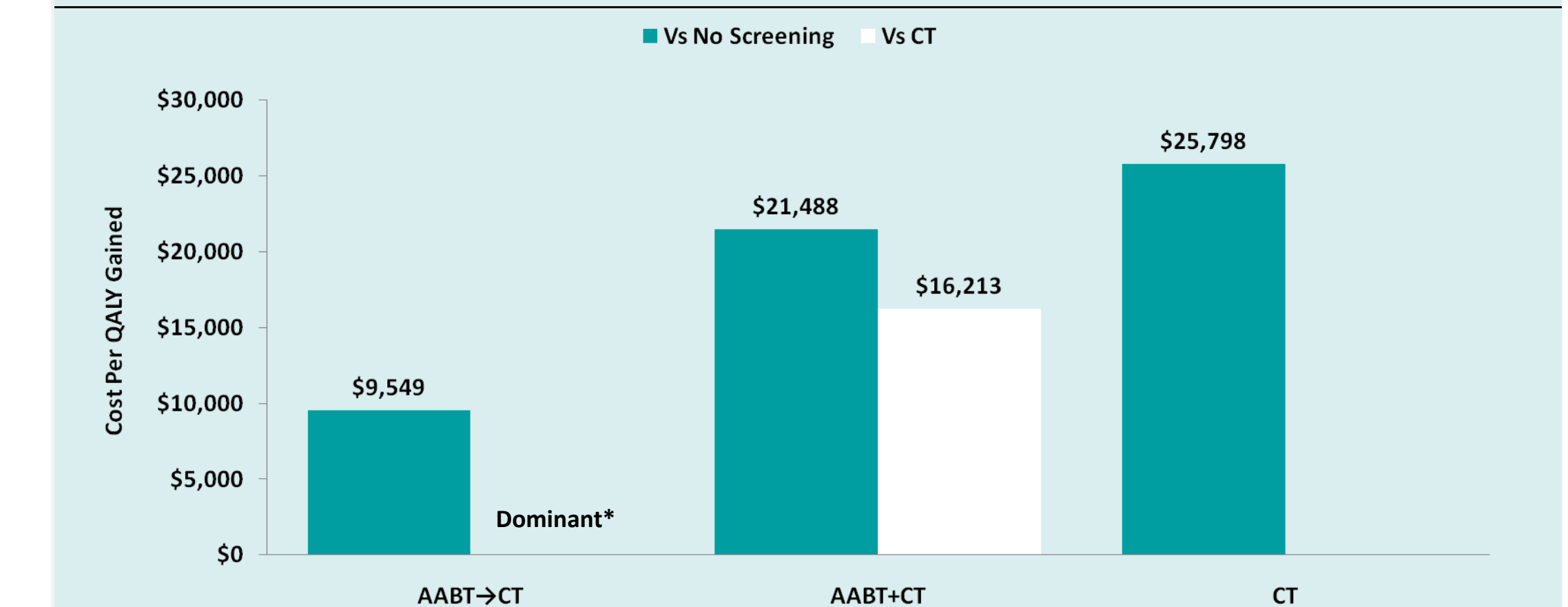
	No Screening	CT	AABT→CT	AABT+CT
Life-Years	1,360	1,365	1,366	1,368
Quality-Adjusted Life-Years	1,145	1,148	1,149	1,151
Cost	\$316,356	\$395,497	\$356,700	\$436,141
Screening	\$0	\$30,051	\$32,582	\$60,051
Diagnostic Follow-up	\$13,437	\$52,694	\$20,845	\$59,183
Treatment	\$302,920	\$312,752	\$303,272	\$316,907

*Discounted values, in 000s

RESULTS (CONT.)

Cost-Effectiveness

Figure. Cost-effectiveness of screening for lung cancer with AABT→CT and AABT+CT versus no screening and versus screening with CT alone, respectively



*Less costly, more effective

Sensitivity Analyses

Table 4. Sensitivity analyses on cost per QALY gained

Base-case	AABT→CT vs		AABT+CT vs	
	No Screening	CT	No Screening	CT
Base-case	\$9,549	Dominant	\$21,488	\$16,213
Prevalence				
Age 50 (1.37%)	\$24,134	Dominant	\$49,453	\$36,782
Age 70 (10.11%)	\$7,040	Dominant	\$18,308	\$14,036
Cost of AABT screening				
\$0	\$2,448	Dominant	\$16,106	\$4,246
\$100	\$4,815	Dominant	\$17,900	\$8,235
\$200	\$7,182	Dominant	\$19,694	\$12,224
\$500	\$14,283	Dominant	\$25,075	\$24,191
Sensitivity - AABT				
20%	\$16,835	\$46,692 (CT)	\$24,755	\$22,796
30%	\$11,987	Dominant	\$22,992	\$18,829
60%	\$7,074	Dominant	\$19,088	\$13,004
Specificity - AABT				
80%	\$14,902	Dominant	\$23,856	\$21,479
95%	\$8,726	Dominant	\$21,123	\$15,403
Stage Shift - AABT→CT				
NSCLC 65%, SCLC 40%	\$12,411	---	---	---
NSCLC 50%, SCLC 40%	\$16,803	---	---	---
NSCLC 25%, SCLC 40%	\$33,365	---	---	---
NSCLC 80%, SCLC 0%	\$10,564	---	---	---
Stage Shift - AABT→CT vs CT				
NSCLC 65% vs 50%, SCLC 40% vs 25%	---	Dominant	---	---
NSCLC 50% vs 50%, SCLC 40% vs 25%	---	\$99,599 (CT)	---	---
NSCLC 25% vs 25%, SCLC 40% vs 25%	---	\$261,520 (CT)	---	---
NSCLC 80% vs 50%, SCLC 0% vs 0%	---	Dominant	---	---
Stage Shift - AABT+CT				
NSCLC 50%, SCLC 31.3%	---	---	\$27,407	---
NSCLC 25%, SCLC 31.3%	---	---	\$53,744	---
Stage Shift - AABT+CT vs CT				
NSCLC 50% vs 50%, SCLC 31.3% vs 25%	---	---	---	\$30,811
NSCLC 25% vs 25%, SCLC 31.3% vs 25%	---	---	---	\$58,581

CONCLUSION AND CLINICAL IMPLICATION

- Screening older adult smokers for LC using AABT, in conjunction with CT, is likely to be cost-effective by current standards versus CT screening or no screening
- Use of AABT in early detection of lung cancer is supported by clinical as well as economic evidence

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