EE211

Economic Evaluations of Cancer Screening Tests in the US: A Systematic Literature Review (SLR)

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Ze Cong,[1] Grace G. Goldsmith-Martin,[2] Angaja Phalguni,[2] Audrey E. Brown[2]
[1]GRAIL, LLC, Menlo Park, CA, [2]Genesis Research Group, Newcastle, UK

INTRODUCTION

- Cancer is a leading cause of death in the US, posing significant health and economic burdens[1]
- The performance and effectiveness of cancer screening interventions have been assessed extensively in trial settings.[2,3] However, the limited time duration of the clinical trials likely will underestimate the overall impact of cancer screening on mortality outcomes
- Cost-effectiveness models of cancer screening provide an alternative to trials for estimating the long-term/lifetime outcomes of screened vs. unscreened populations, employing mathematical modeling/simulation to consider the impact of cancer screening on stage of cancer upon diagnoses (i.e., stage shifting) and mortality

OBJECTIVE

- An SLR was conducted to identify economic evaluations of cancer screening tests conducted in the US in order to systematically summarize economic evaluation results of screenings across multiple cancer types, particularly in terms of life years gained

METHODS

- An SLR was conducted using the Population, Intervention, Comparison, Outcomes, and Study design (PICOS) criteria for economic evaluations comparing cancer screening tests with no screening (**Figure 1**)
- Searches were conducted in Ovid Embase, Medline, Econlit, and Cochrane for US-based economic evaluations published between 2008 and 2023. The gray literature was also searched for relevant studies

CONCLUSIONS

- There was heterogeneity in the included studies both in terms of the models themselves and in the populations considered for screening
- Life years gained results were sensitive to factors such as the screening interval and adherence rates
- Cost-effectiveness was impacted by the age, sex, and race/ethnicity of the populations considered for screening as well as factors such as smoking status or family history
- Cancer screenings improve life expectancy and provide good economic value in the majority of scenarios assessed, with increased value among higher risk groups

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Disclosures

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KEY RESULTS: CANCER SCREENINGS IMPROVE LIFE EXPECTANCY AND PROVIDE GOOD ECONOMIC VALUE IN THE MAJORITY OF SCENARIOS ASSESSED, WITH INCREASED VALUE AMONG HIGHER RISK GROUPS

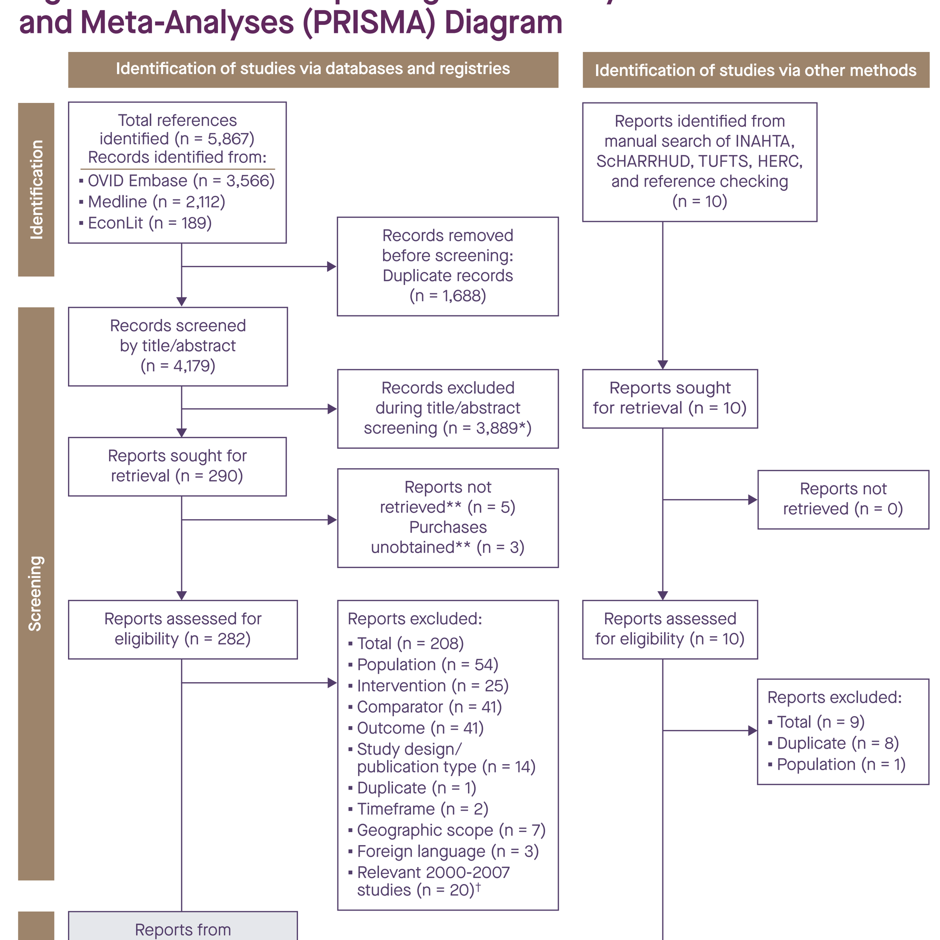
Figure 1: PICOS Selection Criteria

Element	Inclusion/Exclusion Criteria
Population	*Inclusion criteria:* ▪ US adult patients ▪ Average age of sample at least 45 years ▪ Asymptomatic patients *Exclusion criteria:* ▪ Populations who are pregnant, receiving active cancer treatment, <18 years old, or presenting signs and symptoms with a suspicion of cancer
Intervention*	*Cancer screening tests for asymptomatic patients, including:* ▪ Anal: anal cytology, digital ano-rectal examination ▪ Bladder: urinalysis, urine cytology, urine tests for tumor markers (UroVysion, bladder tumor-associated antigen [BTA], ImmunoCyt, nuclear matrix protein 22 [NMP22]) ▪ Breast: mammography, digital breast tomosynthesis (DBT) ▪ Cervical: Pap smear, human papillomavirus (HPV) testing ▪ Colon and rectum: fecal immunochemical test (FIT), fecal occult blood test (FOBT), guaiac and immunochemical, flexible sigmoidoscopy, colonoscopy ▪ Esophageal: endoscopic screening ▪ Head and neck: plasma Epstein Barr virus (EBV) (nasopharyngeal), visual exam (oral cavity) ▪ Kidney: CT, MRI, or Focused renal ultrasound ▪ Liver: alpha-fetoprotein (AFP) blood test, ultrasound ▪ Lung: low-dose computed tomography (LDCT) ▪ Melanoma: visual examination ▪ Ovary: transvaginal ultrasound (TVUS), CA-125 blood test ▪ Pancreatic: endoscopic ultrasound, MRI ▪ Prostate: prostate-specific antigen (PSA) test, digital rectal exam ▪ Stomach: endoscopic screening, microRNA blood test ▪ Multi-cancer early detection (MCED) tests
Comparator	▪ *For studies evaluating screening:* no screening ▪ *For studies evaluating screening + standard of care (SOC):* SOC
Outcomes	*From cost-effectiveness/cost-utility studies:* ▪ Total costs and other cost components ▪ Quality-adjusted life years (QALYs) ▪ Life years (LYs) ▪ Other measures of benefit such as reduction in lifetime risk of cancer by stage ▪ Incremental cost-effectiveness ratios (ICERs) *From BIM/cost minimization/cost-offset/cost-benefits studies:* ▪ Healthcare resource use ▪ Direct costs ▪ Indirect costs ▪ Cost drivers associated with cancer screening ▪ Cost components
Study design	*Economic models and studies including:* ▪ Budget impact models ▪ Cost minimization analysis ▪ Cost-offset analysis ▪ Cost-effectiveness analysis ▪ Cost-utility analysis ▪ Cost-benefit analysis

*Interventions were included based on recommendations for cancer screening according to United States Preventive Services Task Force (USPSTF) and American Cancer Society (ACS) website guidelines/recommendations.
CT, computed tomography; BIM, budget impact models; MRI, magnetic resonance imaging; PICOS, Population, Intervention, Comparison, Outcomes, and Study design; US, United States.

- A total of 73 studies from 75 publications met the PICOS criteria and were included (**Figure 2**)

Figure 2. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Diagram

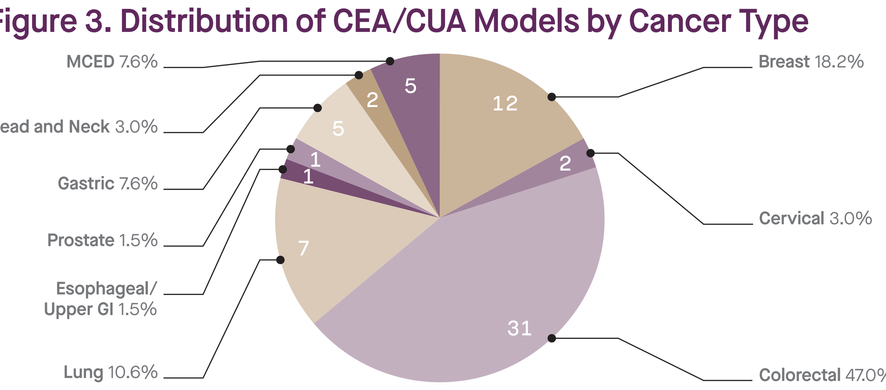


*Note: For speed of screening, records excluded by title/abstract were not excluded in PICO order. Reasons for exclusion were Population (1244), Intervention (402), Comparator (293), Outcome (225), Study design/publication type (519), Geographic scope (1039), Timeframe (146), Language (16), No abstract (4), Duplicate (1).
**3 articles were not obtained as they were pre-2008 studies, behind a paywall and therefore not purchased. 5 articles were unobtainable.
†Only articles from 2008 onwards were included in this systematic literature review.

Study Count and Type of Analysis by Cancer Type

- A total of 66 studies were cost-effectiveness analyses, predominantly focused on screening tests for breast, colorectal, or lung cancer. Data regarding cancer screening tests for cervical, esophageal/upper GI, gastric, head and neck, and prostate cancers were notably scarce (**Figure 3**)

Figure 3. Distribution of CEA/CUA Models by Cancer Type



Numbers within the chart indicate number of studies. CEA, cost-effectiveness analysis; CUA, cost-utility analysis; MCED, multi-cancer early detection test.

Life Years Gained by Cancer Type

- In breast cancer screening, life year (LY) gained per screened individual compared with no screening ranged from 0.0030-0.402 in lifetime models, influenced by mammography type, age, and risk factors such as breast density (**Table 1**)

Table 1. Breast Cancer Screening CEA/CUA Model LY Gained (LYG) Results

Reference	Intervention*	Screening interval	Screened population	LYG per person screened
Allaire et al. (2019)[4]	Mammography	NR	Women aged 40-64	0.065
Lee et al. (2015)[5]	Digital mammography & tomosynthesis vs. digital mammography	Biennial	Women aged 50-74 with dense breasts	0.005
Melnikow et al. (2013)[6]	Film Mammography	Annual	Age 40-64	0.0036
			Age 50-64	0.0060
	Digital mammography	Annual	Age 40-64	0.0064
			Age 50-64	0.0069
	Film mammography	Biennial	Age 40-64	0.0030
			Age 50-64	0.0053
	Digital mammography	Biennial	Age 40-64	0.0045
			Age 50-64	0.0060
Shih et al. (2021)[7]	Mammography	Triennial	Age 50-75	0.0255
		Biennial	Age 50-75	0.029
		Stratified	No dense breasts age 50-75: triennially Dense breasts: annually	0.03078
			Dense breasts: age 50-75 annually No dense breasts: age 50-75 biennially	0.03218
			Dense breasts: age 40-75 annually No dense breasts: age 50-75 triennially	0.04138
			Dense breasts: age 40-75 annually No dense breasts: age 50-75 biennially	0.04411
Sprague et al. (2015)[8]	Mammography alone	Biennial	Age 50-74	0.0333
	Mammography + ultrasound		Age 50-74, extremely dense breasts	0.0339
			Age 40-74, heterogeneously or extremely dense breasts	0.0367
	Mammography alone	Annual	Age 40-74	0.0777
	Mammography + ultrasound		Age 40-74, extremely dense breasts	0.0797
			Age 40-74, heterogeneously or extremely dense breasts	0.0846
Stout et al. (2014)**[9]	Digital mammography	Annual	Age 40-74	0.053
			Age 50-74	0.043
		Biennial	Age 40-74	0.046
			Age 50-74	0.032
	Film mammography	Biennial	Age 50-74	0.039
Trentham-Dietz et al. (2016)[10]	Mammography	Annual	Age 50-74 Range of breast density and risk	0.084 - 0.411
			Age 65-74 Range of breast density and risk	0.026 – 0.109
		Biennial	Age 50-74 Range of breast density and risk	0.064 – 0.294
			Age 65-74 Range of breast density and risk	0.019 – 0.076
		Triennial	Age 50-74 Range of breast density and risk	0.050 – 0.221
			Age 65-74 Range of breast density and risk	0.016 – 0.050

*Comparators are no screening if unspecified. **Results presented from 1 model; 5 models were included in analysis. LY, life years; LYG, life years gained; NR, not reported.

- Colorectal cancer screening tests including colonoscopy, FIT, FOBT, multi-target stool DNA (mt-sDNA), and CT colonography all had positive LY gained compared with no screening (**Table 2**)

Table 2. Colorectal Cancer Screening LY Gained Results

Reference	Intervention*	Screening interval	Screened population	LYG per person screened
Aziz et al. (2023)[11]	Colonoscopy	NR	US general population	0.08
	Colonoscopy + liquid biopsy			0.09
	Liquid biopsy only			0.01
Barzi et al. (2017)[12]	FOBT	Annual	US general population	0.01
	FIT	Annual		0.006
	Annual FOBT and Flex SIG every 5 years			0.012
	Annual FIT and Flex SIG every 5 years			0.009
	Colonoscopy	10 years		0.022
	Flex SIG	5 years		0.016
	FOBT	Biennial		0.013
	FIT	Biennial		0.01
	Biennial FOBT and Flex SIG every 5 years			0.014
	Biennial FIT and Flex SIG every 5 years			0.012
	DNA stool	Annual		0.011
	DNA stool	Biennial		0.014
	CTC	10 years		0.02
Deibel et al. (2021)[13]	Colonoscopy (100%/Real world adherence)	10 years	Age 50-75 US general population	0.0716/0.0433
	FIT	Annual		0.0749/0.0543
	FIT	Biennial		0.0651/0.0451
	ColoGuard®	Triennial		0.0679/0.0530
	Epi proColon®	Annual		0.0748/0.0642
	PolypDx™	Triennial		0.0676/0.0550
Dinh et al. (2012)[14]	Colonoscopy (with/without history of diabetes at age 50)	One time	Stop age 50	0.1282/0.1985
		Twice	Stop age 60	0.1543/0.2549
		3x	Stop age 70	0.1641/0.2832
		4x	Stop age 80	0.1659/0.2905
		10 years	No stop age	0.1661/0.2910
Fisher et al. (2021)[15]	mt-sDNA	Triennial	Medicare population	0.1129-0.1665
	FIT	Annual		0.0566-0.1800
	FOBT	Annual		0.0504-0.1824
Fitch et al. (2015)[16]	Colonoscopy	10 years	Age 50-64	0.011-0.018
Hassan et al. (2008)[17]	CTC	10 years	Age 50-100	0.09835
	Optical colonoscopy			0.10699
	Optical colonoscopy + ultrasound			0.10699
Haug et al. (2015)[18]	gFOBT	Annual	Age 50	0.098
	FIT			0.113
	Hypothetical new test			0.098
Karlitz et al. (2022)[19]	mt-sDNA	Triennial	Medicaid age 50-64	0.2281
Knudsen et al. (2010)[20]	Hemoccult II	Annual	Medicare age 65	0.0599-0.0657
	Hemoccult SENSA	Annual		0.0811-0.0873
	IFOBT	Annual		0.0798-0.0847
	SIGB	5 years		0.0652-0.0758
	SIG	5 years		0.0691-0.0804
	Hemoccult II annually + SIGB 5 yearly			0.0849-0.0929
	Hemoccult II annually + SIG 5 yearly			0.0854-0.0945
	Hemoccult SENSA annually + SIGB 5 yearly			0.0880-0.0999
	Hemoccult SENSA annually + SIG 5 yearly			0.0879–0.1005
	IFOBT annually + SIGB 5 yearly			0.0881-0.0992
	IFOBT annually + SIG 5 yearly			0.0881-0.0999
	Colonoscopy	10 years		0.0867-0.1055
	CTC (DoD/NCTC)	5 years		0.013-0.1012
Knudsen et al. (2012)[21]	Colonoscopy	10 years	Negative colonoscopy at age 50	0.046 (imperfect adherence)/0.0081 (perfect adherence)
	FOBT	Annual		0.048/0.074
	FIT	Annual		0.044/0.072
	CTC	5 years		0.047/0.078
Lansdorp-Vogelaar et al. (2009)[22]	Colonoscopy	10 years	Age 50-80	0.0411
	Colonoscopy	8 years	Age 51-75	0.0433
	Colonoscopy	7 years	Individualized across gender and race	0.0434
Meester et al. (2015)[23]	Colonoscopy	10 years	General population Quintiles of ADR (15.32%)	0.0773
			Quintiles of ADR (21.27%)	0.0895
			Quintiles of ADR (25.61%)	0.0968
			Quintiles of ADR (30.89%)	0.1048
			Quintiles of ADR (38.66%)	0.1117
Meester et al. (2016)[24]	Colonoscopy after positive FIT	NR	2-week average time from FIT	0.0937
			1 month	0.0937
			2 months	0.0937
			3 months	0.0915
			6 months	0.0891
			12 months	0.0848
Meester et al. (2022)[25]	mt-sDNA	Triennial	General population	0.192
	FIT	Annual		0.193
	Colonoscopy	10 years		0.193

*Comparators are no screening if unspecified. **Results from 3 different models considering 2 adherence scenarios (100% and 50%).
ADR, adenoma detection rate; CTC, computed tomography colonography; DoD, Department of Defense study; F-DNA, fecal DNA; FIT, fecal immunochemical test; FOBT, fecal occult blood test; gFOBT, guaiac-based FOBT; IFOBT, immunochemical fecal occult blood test; LYG, life year gained; mt-sDNA, multi-target stool DNA; NCTC, National CT Colonography Trial; NR, not reported; SIG, sigmoidoscopy; SIGB, sigmoidoscopy with biopsy; US, United States.

Table 2 *(Continued)*. Colorectal Cancer Screening LY Gained Results

Reference	Intervention*	Screening interval	Screened population	LYG per person screened
Naber et al. (2019)[26]	gFOBT	Annual	Medicare age 65	0.0866-0.0916
	FIT	Annual		0.0872-0.0919
	SIG	5 years		0.0708-0.0889
	gFOBT annually & SIG 10 years			0.0987-0.0991
	FIT annually & SIG 10 years			0.0985-0.0993
	Colonoscopy	10 years		0.1016-0.1074
	mt-sDNA	Triennial		0.0793-0.0879
Omidvari et al. (2021)[27]	Colonoscopy	15 years	Start-stop age 55-75	0.0647
		15 years	Age 55-85	0.0650
		10 years	Age 55-75	0.0681
		10 years	Age 55-85	0.0683
		5 years	Age 55-75	0.0718
		5 years	Age 55-85	0.0722
		15 years	Age 50-75	0.0714
		15 years	Age 50-80	0.0727
		10 years	Age 50-75	0.0773
		10 years	Age 50-80	0.0781
		5 years	Age 50-75	0.0826
		5 years	Age 50-80	0.0829
		15 years	Age 45-75	0.0830
		15 years	Age 45-75	0.0774
		10 years	Age 45-75	0.0836
		10 years	Age 45-85	0.0838
		5 years	Age 45-75	0.0901
		5 years	Age 45-80	0.0904
		5 years	Age 45-85	0.0904
Parekh et al. (2008)[28]	F-DNA version 1	Triennial	Average risk from age 50	0.045
	F-DNA version 1.1	Triennial		0.053
	FOBT	Annual		0.056
	F-DNA version 2	Triennial		0.058
	Colonoscopy	10 years		0.062
	FIT	Annual		0.065
Pickhardt et al. (2009)[29]	Optical colonoscopy	10 years	Age 65-80	0.0603
	CTC	5 years		0.0779
	CTC	10 years		0.0703
Vanness et al. (2011)**[30]	Annual FOBT + 5-year Flex SIG		General population	0.085-0.138
	CTC	10 years		0.045-0.115
	Colonoscopy	10 years		0.06-0.137
	Annual FIT + 5-year Flex SIG			0.084-0.138
	CTC	5 years		0.063-0.129
Zauber et al. (2010)[31]	Hemoccult II	Annual	Age 50	0.0853
	Hemoccult Sensa	Annual		0.1002
	FIT	Annual		0.0997
	SIGB	5 years		0.0892
	SIG	5 years		0.0922
	Annual Hemoccult II and 5-year SIGB			0.103
	Annual Hemoccult II and 5-year SIG			0.1029
	Annual Hemoccult Sensa and 5-year SIGB			0.1048
	Annual Hemoccult Sensa and 5-year SIG			0.1044
	Annual FIT and 5-year SIGB			0.1056
	Annual FIT and 5-year SIG			0.105
	Colonoscopy	10 years		0.1018
	CTC (DoD/NCTC)	5 years		0.0961/0.1006

*Comparators are no screening if unspecified. **Results from 3 different models considering 2 adherence scenarios (100% and 50%).
ADR, adenoma detection rate; CTC, computed tomography colonography; DoD, Department of Defense study; F-DNA, fecal DNA; FIT, fecal immunochemical test; FOBT, fecal occult blood test; gFOBT, guaiac-based FOBT; IFOBT, immunochemical fecal occult blood test; LYG, life year gained; mt-sDNA, multi-target stool DNA; NCTC, National CT Colonography Trial; NR, not reported; SIG, sigmoidoscopy; SIGB, sigmoidoscopy with biopsy; US, United States.

- Low-dose computed tomography for lung cancer had positive LY gained (0.0036-0.045) with values varying by population risk status (**Table 3**)

Table 3. Lung Cancer Screening LY Gained Results

Reference	Intervention*	Screening interval	Screened population	LYG per person screened
Black et al. (2014)[32]	LDCT	Annual	Aged 55-74 years with smoking history ≥30 pack years	0.0315
Criss et al. (2019)[33]	LDCT	Annual up to age 74	Current, former, and never smokers aged 45 years from 1960 US birth cohort	0.0265
Kowada et al. (2022)[34]	LDCT	Annual	Males aged 60 years never smokers	0.0052
	Chest x-ray			0.0036
	LDCT	Annual	Females aged 60 years never smokers	0.0096
	Chest x-ray			0.007
McMahon et al. (2011)[35]	LDCT	Annual	White, aged 50, 60, or 70 years with smoking history ≥20 pack years	0.018-0.045

*Comparators are no screening if unspecified. LDCT, low-dose computed tomography; LYG, life years gained; US, United States.

Table 4. Cost-Effectiveness Results*

Cancer Type	Cost-Effectiveness Results Summary vs. No Screening
Breast	Mammography is cost effective in all scenarios/group tested other than low risk group such as no family history of cancer and no abnormality in previous mammography
Cervical	Cost effective
Colorectal	All screening technologies were cost effective other than patients with diabetes with colonoscopy screening discontinuing after age 80 or no stopping age
Lung	LDCT is cost effective in all groups and scenarios tested, other than starting late such as at 70 years old
Prostate	Varying cost-effectiveness results (LYG 0.027-0.105)
Gastric	Repeated endoscopy or H. pylori screening are not cost effective
Head and Neck	One-time nasophargeal screening is cost effective
MCED	Cost effective (LYG 0.10-0.18)

*Screenings are determined to be cost effective vs. no screening if cost per quality-adjusted life years gained is below $150,000. LDCT, low-dose computed tomography; LY, life years; LYG, life years gained; MCED, multi-cancer early detection test.