An Overview of Methods Employed in Economic Models of Cancer Screening Tests: 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, USA, [2]Genesis Research Group, Newcastle, UK

INTRODUCTION

- Cancer is a leading cause of mortality in the United States, imposing substantial health and economic burdens[1]
- Screening interventions have demonstrated promise in detecting cancer at its early stages, thereby enhancing outcomes and reducing cancer treatment costs[2,3]
- Recognizing the significance of screening, the United States Preventive Services Task Force (USPSTF) recommends screenings for four types of cancers (breast, cervical, lung, and colorectal),[4-7] as well as screening for prostate cancer on an individual basis.[8] However, approximately 70% of cancer deaths are from cancer types without recommended screening[9,10]
- Innovations such as multi-cancer early detection (MCED) tests present novel opportunities for early cancer diagnosis[11-13]
- A thorough assessment of the economic evaluations of cancer screening technologies is needed to inform the value framework and relative value of new cancer screening technologies

OBJECTIVE

- To summarize and evaluate the methods employed in economic models of cancer screening

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

Figure 1. PICOS Selection Criteria

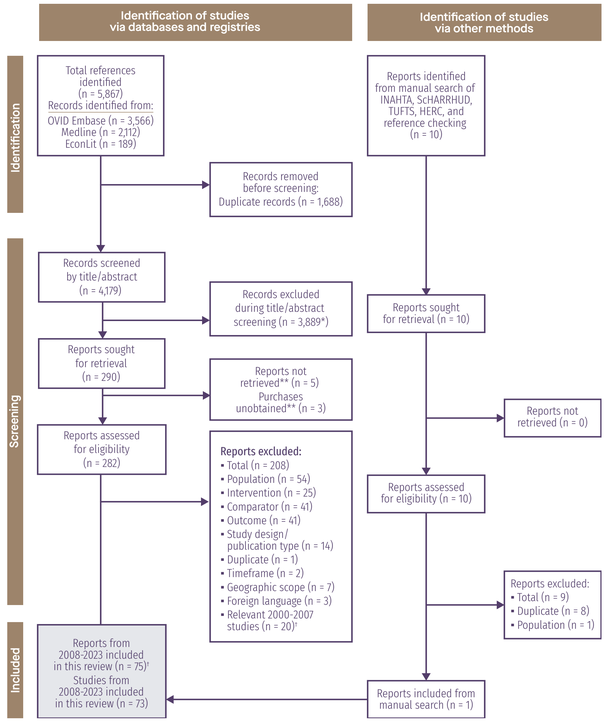
Element	Inclusion/Exclusion Criteria
Population	*Inclusion criteria:* ▪ US adult patients ▪ Average age of sample at least 45 years ▪ Asymptomatic patients *Exclusion criteria:* ▪ Populations who are pregnant, receiving active cancer treatment, <18 years old, or presenting signs and symptoms with a suspicion 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.

KEY RESULTS: ECONOMIC VALUE ASSESSMENTS OF CANCER SCREENINGS IN THE US MAY UNDERESTIMATE THE FULL VALUE AND/OR IMPACT ON SOCIETY

- 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

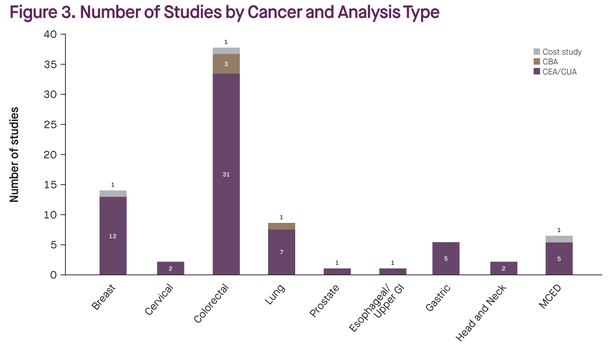


*Note: For speed of screening, records excluded by title/abstract were not excluded in PICO order. Reasons for exclusion were Population (1244), Intervention (402), Comparator (293), Outcome (225), Study design/publication type (519), Geographic scope (1039), Timeframe (146), Language (16), No abstract (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

- Of the 73 studies included, 66 were cost-effectiveness analyses, with a particular emphasis on populations impacted by 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**)
- There are no studies assessing the value/cost implications of screening for anal, bladder, kidney, liver, melanoma, ovarian, pancreatic, or stomach cancer

Figure 3. Number of Studies by Cancer and Analysis Type

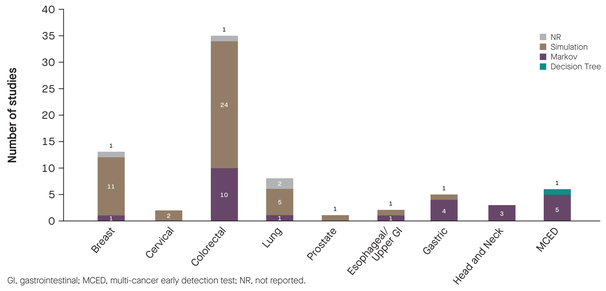


CBA, cost-benefit analysis; CEA, cost-effectiveness analysis; CUA, cost-utility analysis; GI, gastrointestinal; MCED, multi-cancer early detection test.

Modeling Methods by Cancer Type

- **Figure 4** illustrates the various models employed in economic assessment across the different cancer screening categories. Model types were commonly simulation models (n=45) or Markov models (n=25)

Figure 4. Types of Models Used in Economic Evaluations by Cancer Type

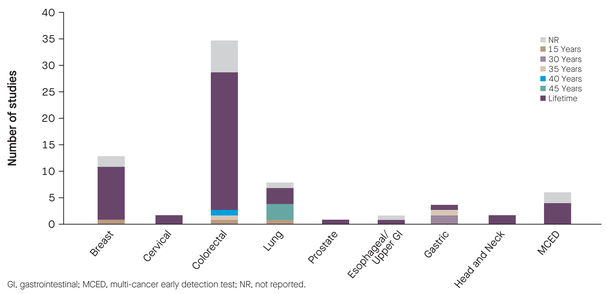


GI, gastrointestinal; MCED, multi-cancer early detection test; NR, not reported.

Time Horizons Across Cancer Types

- Time horizons considered in the models ranged from 15 years to lifetime (**Figure 5**)

Figure 5. Number of Models With Different Time Horizons by Cancer Type



GI, gastrointestinal; MCED, multi-cancer early detection test; NR, not reported.

Economic Evaluation Perspective and Cost Components Considered

- Models were analyzed from the payer (n=34), healthcare system (n=15), or societal (n=14) perspectives
- While 14 studies reported modeling from a societal perspective, only 6 studies included indirect costs in the models. Indirect costs included patient productivity, travel time and costs. Two studies considered time and travel for caregivers as well as participants (**Table 1**)

Table 1. Analyses Reported to Be From Societal Perspective and Considered Cost Components

Cancer Type	Reference	Indirect Cost Components Considered
Breast cancer	Allaire et al. (2019)[14]	NA
	Shih et al. (2021)[15]	Productivity loss
	Tina Shih et al. (2019)[16]	NA
Colorectal cancer	Areia et al. (2022)[17]	NA
	Barzi et al. (2017)[18]	NA
	Dinh et al. (2013)[19]	NA
	Hassan et al. (2008)[20]	NA
	Knudsen et al. (2012)[21]	NA
	Pickhardt et al. (2009)[22]	Time lost from work
	Van Hees et al. (2014)[23]	Patient time costs
GI/gastric cancer	Yeh et al. (2016)[24]	Time lost from work
Head and neck cancer	Dedhia et al. (2011)[25]	NA
Lung cancer	Black et al. (2014)[26]	Time and travel costs for participant and caregiver
	McMahon et al. (2011)[27]	Participant and caregiver time costs

Note: Direct medical costs include costs like screening, diagnosis, treatment/ care, complications, and surveillance costs.
GI, gastrointestinal; NA, not applicable.

Modeled Screened Population Characteristics by Cancer Type and Risk Level

- Populations considered for screening included the US general population with different age categories and insurance status and individuals with other cancer risk factors such as family history of cancer, dense breasts (for breast cancer screening), smoking history, alcohol consumption, and minority race/ethnicity groups (**Table 2**)

Table 2. Modeled Screened Population Characteristics by Cancer Type

Cancer type	Population Assessed
Breast (n=13)	Women eligible for breast screening (n=3) Women without family history (n=2) Women aged ≥40 (n=7) Women without dense breasts (n=2) Medicaid enrollees (n=1) Women aged ≥50 (n=2) Women with dense breasts (n=3) Women with family history of cancer (n=2)
Cervical (n=2)	Hypothetical cohort of 100,000 U.S. women (n=1) African-American women in the Mississippi Delta (n=1)
Colorectal (n=35)	US general population (n=16) Kaiser Permanente North California members (n=1) Commercially insured (n=12) Average risk persons (n=12) Unscreened with no comorbidities (n=1) Not up-to-date with CRC screening (n=1) Unscreened with some comorbidities (n=1) High risk (n=1) Alaskan people (n=1)
Esophageal/Upper G (n=1)	US individuals born in 1950 stratified by sex and race (White or Black) (n=1)
Gastric (n=5)	Non-Hispanic White patients (n=1) Men aged 50 years (n=1) 50-year-old patients undergoing colonoscopy for CRC screening (n=1) Non-Hispanic Black, Hispanic, and Asian patients (n=1) Asymptomatic, 50-year-old, Asian American patient (n=1) 40-year-old who started asymptomatic, then developed gastric cancer (n=1)
Head and neck (n=2)	Males aged >40 years regularly using tobacco and/or alcohol (n=1) Asian American men aged 50 years (n=1)
Lung (n=8)	Never smokers (n=2) ≥20 pack-year smoking history (n=3) ≥30 pack-years of smoking (n=3) Current and former smokers (n=1)
MCED (n=6)	Individuals aged 50 years (n=1) US adults not previously diagnosed with cancer (n=1) US general population aged 50-79 years (n=3) US Medicare population (age 65+)
Prostate (n=1)	A simulated contemporary cohort of US men (n=1)

Note: Some studies included patients from more than one risk category; hence, the total number of studies based on population risk categories might not match the total studies in the cancer category.
CRC, colorectal; GI, gastrointestinal; MCED, multi-cancer early detection test; US, United States.

CONCLUSIONS

- Value assessments of cancer screenings concentrate on USPSTF-recommended screenings
- There was substantial heterogeneity identified in the economic evaluations included in this SLR. Heterogeneity was seen in the populations considered for screening as well as in the methods used for modeling
- Assessments potentially underestimate the full value/impacts on society by only considering direct costs, limited indirect cost components, and/or by truncating the assessments to a short time horizon. Decision-makers should take into account these considerations when allocating resources for early cancer detection

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Disclosures

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