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Early Germline BRCA Testing in Breast Cancer: A Review of Value Frameworks and Cost-Effectiveness Analyses

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Objective

- To assess the comprehensiveness of economic analyses of germline BRCA (gBRCA) testing in patients with breast cancer (BC).

Conclusions

- Economic models of gBRCA testing rarely considered societal value elements beyond cascade testing
- No studies assessed the value of early gBRCA testing soon after diagnosis
- Only one study considered the impact of gBRCA testing on both risk-reducing surgery (RRS) uptake and use of targeted adjuvant treatment
- Further studies are needed to comprehensively assess the value of early gBRCA testing strategies in patients with breast cancer

Plain language summary

Why did we perform this research?
To assess how thorough previous economic studies have been in estimating the value of testing patients with BC for inherited mutations in either the BRCA1 or BRCA2 genes (gBRCA mutations), which help repair damaged DNA.

How did we perform this research?
We searched for and reviewed studies about elements of value and frameworks for assessing value relevant to genetic testing. This helped to identify important components of an economic analysis for genetic testing.

Next, we searched for economic studies that estimated the value of gBRCA testing. We assessed each study for thoroughness based on value frameworks.

What were the findings of this research?
Most studies concluded that testing for gBRCA was worth the cost compared to no testing, but many also did not consider important value aspects:

- No studies compared the value of early testing (before surgery) to later testing
- Only one study considered how testing could influence both surgical and treatment choices
- Many studies did not consider the value to society, such as improved work productivity

What are the implications of this research?
More studies are needed to fully understand the value of early gBRCA testing.

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Introduction

- Testing for gBRCA genetic mutations has important consequences for patients with BC. Patients who find out they have a germline BRCA1 or BRCA2 mutation are:
  1. More likely to undergo RRS, such as bilateral mastectomies
  2. Eligible for treatment with poly(adenosine diphosphate [ADP]-ribose) polymerase inhibitor (PARPi) olaparib (for those with human epidermal growth factor receptor 2 [HER2]-negative breast cancer)[1,2]

     Olaparib *is approved in early breast cancer (eBC) due to significant survival benefits*[3]

     Olaparib *and* ***talazoparib*** *are both approved for metastatic breast cancer (mBC) due to significant progression-free survival (PFS) benefits*[3,4]
  3. Able to inform family members to undergo cascade screening and prophylactic interventions[5]
- Early testing (soon after diagnosis and prior to surgery) may impact more treatment decisions and downstream outcomes
- It is important to assess how gBRCA testing impacts value beyond standard cost-effectiveness analysis (CEA) elements

Methods

- Two separate targeted literature reviews (TLRs) were conducted:
  1. Value frameworks or value elements related to genetic testing, inclusive of non-cancer disease states
  2. CEAs of gBRCA testing in BC or ovarian cancer (OC)*

  **Economic models in both BC and OC were included given similar role of gBRCA testing in guiding treatment, resulting in similar model structures*
- MEDLINE was searched for studies published in English from January 1, 2014 to April 24, 2024
  - Timeframe based on expansion of genetic testing, improved technology, and decreasing cost over past 10 years
  - References of included studies were also assessed for relevance
- Exclusions: clinical trial protocols, case reports or case series, letters or editorials, non-human, and non-English studies
- Studies were screened by a single reviewer in two stages: review of title/abstract, followed by full text

Results and interpretation

Value Frameworks Relevant to Genetic Testing

- Of 48 records screened, a total of 6 studies were included, with 2 more included through citation searching:[6-13]
  - Generally not disease or oncology-specific
  - Two studies focused on diagnostic testing for rare diseases[6,10]
  - Four studies focused on next-generation sequencing or comprehensive genomic profiling[6,7,12,13]
- We identified and categorized 22 value elements, shown in **Table 1**
  - Not all value elements were necessarily relevant to gBRCA testing in BC
  - Many societal elements are difficult to quantify due to lack of data or well-established methodology

Table 1. Value Elements of Genetic Testing

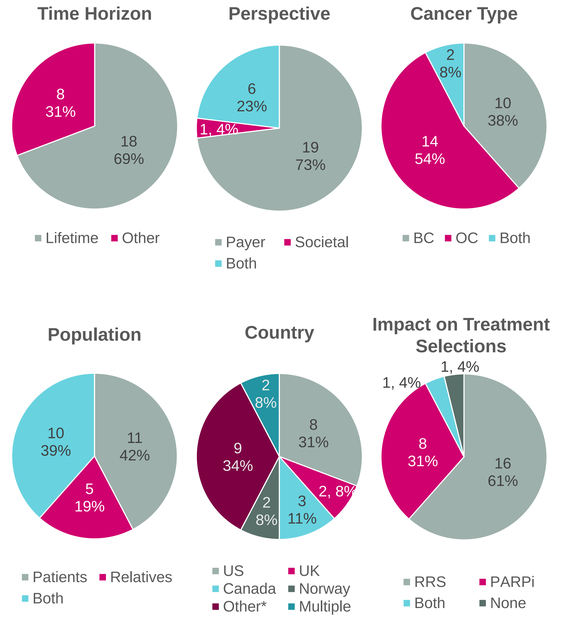
	Likely Relevant to gBRCA Testing	Maybe Relevant to gBRCA Testing	Not Relevant or Unclear
Standard CEA Elements	• Clinical outcomes[6-13] • Medical costs[7,9-13]		
Other Clinical	• Test performance and diagnostic yield[6,7,9-11,13]	• Safety of test[7,8] • Real option value*[7]	
Patient-Related	• Productivity[7,10,11] • Patient time and resources[7,10,11] • Consequences of wrong diagnosis[7]	• Value of knowing[6,8,10,12,13]	• Risk of overutilization[7]
Family-Related	• Access to cascade testing[6,8,10-12] • Caregiver burden[7,11]	• Reproductive planning[6,8,10,11]	
Other Societal	• Public health, population benefit[7,8]	• Scientific spillover[6,7,10,12] • Equity, accessibility[7,8,10] • Broader social impact†[7,10] • Ethical and legal aspects‡[7,8]	• Fear of contagion[7] • Environmental impact[7] • Quality of scientific evidence[7,10]

*Refers to the value of an intervention extending life such that a patient has opportunities to benefit from future technologies.
†Impact on sectors outside of health, such as job creation
‡Impact on societal values and norms, such as eugenics attitudes
gBRCA – germline BRCA.

Economic Evaluations of gBRCA Testing in Breast or Ovarian Cancer

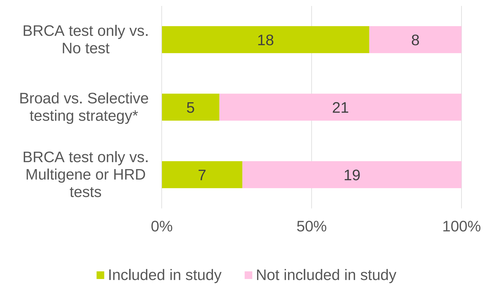
- Of 188 records identified, 26 CEAs were included[5,14-38]
- **Figure 1** provides an overview of included studies
  - **Figure 2** describes the types of comparisons made in included studies
  - **Figure 3** shows inclusion of societal value elements
- Most studies (n=18) included a comparison of gBRCA testing alone vs no testing[15,16,19-21,23-26,28,30,32-37]
  - Of these, 13 concluded that gBRCA testing was cost-effective[16,19-21,23-26,28,32,33,35,36]
  - Three studies in mBC, recurrent OC, and platinum-resistant OC concluded gBRCA testing was not cost-effective, which suggests greater value when testing at earlier stages of disease[30,34,37]
- No CEAs assessed the impact of test timing
- Most studies assumed gBRCA testing would impact either RRS uptake or PARPi use, but only one study considered impacts of both[35]
- Few studies considered broader value elements, which suggests that the societal value of gBRCA testing has been underestimated:
  - Access to cascade testing for family members was modeled in about half of studies
  - Impact to work productivity was explicitly modeled in 5 studies[5,27,31,32,37]
  - Patient costs were included in two ex-US studies, but have not been extensively modeled[24,27]

Figure 1. Overview of CEAs of gBRCA Testing



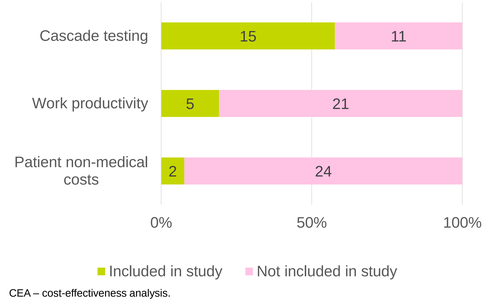
*Other countries include Australia, Brazil, China, Italy, Japan, Korea, Malaysia, Norway, and Spain. Two studies include results for more than 1 country.
BC – breast cancer; CEA – cost-effectiveness analysis; OC – ovarian cancer; PARPi – poly (adenosine diphosphate-ribose) polymerase inhibitor; RRS – risk-reducing surgery; UK – United Kingdom; US – United States.

Figure 2. Types of Comparisons Included in CEAs



*Some studies compared broad testing strategies, such as screening all patients with breast or ovarian cancer, to selective strategies, such as testing only patients with family history of BRCA-related cancers.
CEA – cost-effectiveness analysis; HRD – homologous recombination deficiency.

Figure 3. Societal Value Elements Included in CEAs



CEA – cost-effectiveness analysis.

References

1. Garber J. Poster presented at: SABCS 2024. **2.** Tutt ANJ et al. *N Engl J Med*. 2021;384(25):2394-2405. **3.** Lynparza prescribing information. AstraZeneca, Dec 2023. **4.** Talzenna prescribing information. Pfizer, Feb 2024. **5.** Guzauskas GF, et al. *Ann Intern Med*. 2023;176(5):585-595. **6.** Abbott M, et al. *J Community Genet*. 2022;13(5):487-501. **7.** Augustovski F, et al. *Value Health*. 2024;27(5):670-685. **8.** Botkin JR, et al. *Genet Med*. 2010;12(4)228-35. **9.** Bush WS, et al. *Public Health Genomics*. 2019;22(1-2):16-24. **10.** Fehlberg Z, et al. *Genet Med*. 2024;26(6):101116. **11.** Ferket BS, et al. *Genet Med*. 2022;24(10):2014-2027. **12.** Tarride JE, et al. *Int J Technol Assess Health Care*. 2022;38(1):e57. **13.** Weymann D, et al. *J Community Genet*. 2022;13(5):467-476. **14.** Asphaug L, et al. *MDM Policy Pract*. 2019;4(1):2381468318821103. **15.** Dottino JA, et al. *Obstet Gynecol*. 2019;133(4):795-802. **16.** Eccleston A, et al. *Value Health*. 2017;20(4):567-576. **17.** Foote JR, et a. *J Oncol Pract*. 2017;13(2):e120-e129. **18.** Guzauskas GF, et al. *JAMA Netw Open*. 2020;3(10):e2022874. **19.** Hoskins P, et al. *Gynecol Oncol*. 2019;153(1):87-91. **20.** Hurry M, et al. *Int J Technol Assess Health Care*. 2020;36(2):104-112. **21.** Jang J, et al. *Ann Lab Med*. 2023;43(1):73-81. **22.** Kemp Z, et al. *JAMA Netw Open*. 2019;2(5):e194428. **23.** Kwon JS, et al. *Gynecol Oncol*. 2019;152(3):459-464. **24.** Lertwilaiwittaya P, et al. *Front Public Health*. 2023;11:1257668. **25.** Lim KK, et al. *Appl Health Econ Health Policy*. 2018;16(3):395-406. **26.** Moya-Alarcon C, et al. *Clin Transl Oncol*. 2019;21(8):1076-1084. **27.** Norum J, et al. *ESMO Open*. 2018;3(3):e000328. **28.** Ramos MCA, et al. *Rev Saude Publica*. 2018;52:94. **29.** Rognoni C, et al. *Adv Ther*. 2024;41(4):1385-1400. **30.** Saito S, et al. *Per Med*. 2019;16(6):439-448. **31.** Sun L, et al. *JAMA Oncol*. 2019;5(12):1718-1730. **32.** Sun L, et al. *Cancers (Basel)*. 2022;14(7). **33.** Tuffaha HW, et al. *Genet Med*. 2018;20(9):985-994. **34.** Wallbillich JJ, et al. *Gynecol Oncol*. 2016;142(1):144-149. **35.** Wu HL, et al. *Br J Cancer*. 2023;128(4):638-646. **36.** Elsea D, et al. *Target Oncol*. 2023;18(4):531-541. **37.** Oh M, et al. *Expert Rev Pharmacoecon Outcomes Res*. 2023;23(3):317-325. **38.** Gonzalez R, et al. *Gynecol Oncol*. 2020;159(2):483-490.