Gene expression profile testing of cancer tissue

Clinical Expert

Nancy E. Davidson, MD

Senior Vice President and Director, Clinical Research Division
Fred Hutchinson Cancer Research Center

President and Executive Director, Seattle Cancer Care Alliance

Head, Department of Medicine, Division of Medical Oncology
University of Washington School of Medicine
1. Business Activities

(a) If you or a member of your household was an officer or director of a business during the immediately preceding calendar year and the current year to date, provide the following:

<table>
<thead>
<tr>
<th>Title</th>
<th>Business Name &amp; Address</th>
<th>Business Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(b) If you or a member of your household did business under an assumed business name during the immediately preceding calendar year or the current year to date, provide the following information:

<table>
<thead>
<tr>
<th>Business Name</th>
<th>Business Address</th>
<th>Business Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Honorarium

If you received an honorarium of more than $100 during the immediately preceding calendar year and the current year to date, list all such honoraria:

<table>
<thead>
<tr>
<th>Received From</th>
<th>Organization Address</th>
<th>Service Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Damon Runyon</td>
<td>New York, NY</td>
<td>exec. reviewer/adv.</td>
</tr>
<tr>
<td>Sidney Kimmel</td>
<td>Philadelphia, PA</td>
<td>exec. reviewer/adv.</td>
</tr>
<tr>
<td>Harvard University</td>
<td>Cambridge, MA</td>
<td>exec. reviewer/adv.</td>
</tr>
<tr>
<td>(see add'l sheet: ZA or Y)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

3. Sources of Income

(a) Identify income source(s) that contributed 10% or more of the combined total gross household income received by you or a member of your household during the immediately preceding calendar year and the current year to date.

<table>
<thead>
<tr>
<th>Source Name &amp; Address</th>
<th>Received By</th>
<th>Source Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fred Hutchinson</td>
<td>Nancy E. Davidson</td>
<td>Salary</td>
</tr>
<tr>
<td>University of Pittsburgh</td>
<td>Thomas Kessler (spouse)</td>
<td>Salary</td>
</tr>
<tr>
<td>Johns Hopkins University</td>
<td></td>
<td>Salary</td>
</tr>
</tbody>
</table>
WA – Health Technology Assessment

Continuation - #2: Honorarium

<table>
<thead>
<tr>
<th>Received From</th>
<th>Organization Address</th>
<th>Services Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memorial Sloan Kettering</td>
<td>New York, NY</td>
<td>Reviewer/Advisor</td>
</tr>
<tr>
<td>George Washington University</td>
<td>Washington, DC</td>
<td>Reviewer/Advisor</td>
</tr>
<tr>
<td>University of Michigan</td>
<td>Ann Arbor, MI</td>
<td>Reviewer/Advisor</td>
</tr>
<tr>
<td>MD Anderson Cancer Center</td>
<td>Houston, TX</td>
<td>Reviewer/Advisor</td>
</tr>
<tr>
<td>University of Chicago</td>
<td>Chicago, IL</td>
<td>Reviewer/Advisor</td>
</tr>
<tr>
<td>University of Chapel Hill</td>
<td>Chapel Hill, NC</td>
<td>Reviewer/Advisor</td>
</tr>
<tr>
<td>University of WA</td>
<td>Seattle, WA</td>
<td>Reviewer/Advisor</td>
</tr>
<tr>
<td>University of Pennsylvania</td>
<td>Philadelphia, PA</td>
<td>Reviewer/Advisor</td>
</tr>
<tr>
<td>UBM, LLC</td>
<td>San Francisco, CA</td>
<td>Journal Co-editor</td>
</tr>
</tbody>
</table>
(b) Does any income source listed above relate to, or could it reasonably be expected to relate to, business that has, or may, come before the Committee?

☐ Yes ☒ No

If “yes”, describe:  Click here to enter text.

(c) Does an income source listed above have a legislative or administrative interest in the business of the Committee?

☐ Yes ☒ No

If “yes”, describe:  Click here to enter text.

4. Business Shared With a Lobbyist

If you or a member of your household shared a partnership, joint venture, or similar substantial economic relationship with a paid lobbyist, were employed by, or employed, a paid lobbyist during please list the following:

(Owning stock in a publicly traded company in which the lobbyist also owns stock is not a relationship which requires disclosure.)

<table>
<thead>
<tr>
<th>Lobbyist Name</th>
<th>Business Name</th>
<th>Type Business Shared</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Provide the information requested in items 5, 6, and 7 below only if:

(a) Your response involves an individual or business if you or a member of your household did business with, or reasonably could be expected to relate to business that has or may come before the Health Technology Clinical Committee.

(b) The information requested involves an individual or business with a legislative or administrative interest in the Committee.

5. Income of More Than $1,000

List each source (not amounts) of income over $1,000, other than a source listed under question 3 above, which you or a member of your household received during the immediately preceding calendar year and the current year to date:

<table>
<thead>
<tr>
<th>Income Source</th>
<th>Address</th>
<th>Description of Income Source</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>See item 2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6. Business Investments of More Than $1,000

(Do not list the amount of the investment or include individual items held in a mutual fund or blind trust, a time or demand deposit in a financial institution, shares in a credit union, or the cash surrender value of life insurance.)

If you or a member of your household had a personal, beneficial interest or investment in a business during the immediate preceding calendar year of more than $1,000, list the following:

<table>
<thead>
<tr>
<th>Business Name</th>
<th>Business Address</th>
<th>Description of Business</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

7. Service Fee of More Than $1,000

(Do not list fees if you are prohibited from doing so by law or professional ethics.)

List each person for whom you performed a service for a fee of more than $1,000 in the immediate preceding calendar year or the current year to date.

<table>
<thead>
<tr>
<th>Name</th>
<th>Description of Service</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I certify that I have read and understand this Conflict of Interest Form and the information I have provided is true and correct as of this date.

Print Name: Nancy E. Davidson

Check One: ☑ Committee Member ☐ Subgroup Member ☐ Contractor

Signature: ____________________________ Date: 3/6/18
1. **Personal Data:**

   Birth Place: Denver, Colorado

   Business Address: Fred Hutchinson Cancer Research Center  
       1100 Fairview Avenue North  
       Thomas Bldg., M/S D5-310  
       Seattle, Washington 98109

   Business Phone: 206-667-6363

   Business Fax: 206-667-6936

   Email Address: ndavidson@fredhutch.org

2. **Education:**

   9/1971 – 6/1975  Wellesley College; Wellesley, Massachusetts; BA, Molecular Biology

   9/1975 – 6/1979  Harvard Medical School; Boston, Massachusetts; MD, Medicine

3. **Postgraduate Training:** Internship, residencies, fellowships  
   (dates and places, oldest to newest).

       Intern, Internal Medicine

   7/1980 – 6/1982  The Johns Hopkins Hospital; Baltimore, Maryland;  
       Resident, Internal Medicine

   7/1982 – 7/1985  National Cancer Institute, National Institutes of Health; Bethesda, Maryland  
       Medical Staff Fellow

4. **Faculty Positions Held:**

   1985-1987  Medical Breast Cancer Section,  
       Guest Worker  
       Medicine Branch, National Cancer Institute  
       Bethesda, Maryland

   1985-1986  Uniformed Services  
       Research Assistant  
       University of Health Sciences  
       Professor of Pharmacology  
       Bethesda, Maryland

   1986-1992  The Johns Hopkins University  
       Assistant Professor of Oncology  
       Baltimore, Maryland  
       Associate Professor of Oncology

   1995-2009  The Johns Hopkins University  
       Breast Cancer Research  
       Baltimore, Maryland  
       Chair of Oncology

   1999-2009  The Johns Hopkins University  
       Professor of Oncology  
       Baltimore, Maryland

   1986-2009  Johns Hopkins Hospital  
       Active Staff
1994-2009  The Johns Hopkins Oncology Center  Director, Breast Cancer Program
          Baltimore, Maryland
1997-2009  The Johns Hopkins Bloomberg School of Public Health  Joint Appointment in Department of Biochemistry and Molecular Biology
          Baltimore, Maryland
2009-Present The Johns Hopkins University Adjunct Professor of Oncology
          Baltimore, Maryland
2009-2010  University of Pittsburgh  Chief, Division of Hematology/Oncology
          Pittsburgh, PA
2009-2016  University of Pittsburgh  Director, University of Pittsburgh Cancer Institute Professor of Medicine and Pharmacology and Chemical Biology Associate Vice Chancellor for Cancer Research Hillman Professor of Oncology
          Pittsburgh, PA
2010-2016  University of Pittsburgh  Professor, Clinical and Translational Science Institute
          Pittsburgh, PA
2013-2016  University of Pittsburgh  Distinguished Professor of Medicine
          Pittsburgh, PA
2016 – Present  Seattle Cancer Care Alliance  President & Executive Director
          Seattle, WA
2016 – Present  Fred Hutchinson Cancer Research Center, Clinical Research Division Senior Vice President & Full Member
          Seattle, WA
2016 - Present  University of Washington Division Head, Medical Oncology
          Department of Medicine
          Seattle, WA
2016- Present  University of Pittsburgh Adjunct Professor of Medicine
          School of Medicine
          Pittsburgh, PA

5.  Hospital Positions Held:

12/2016 – Present  University of Washington Medical Center 1959 NE Pacific Street Seattle, WA 98195
7/2009 - 11/2016 Magee Women’s Hospital of UPMC 300 Halket Street Pittsburgh, PA  15213
7/2009 -  UPMC Shadyside Hospital
6. **Honors:**

- Phi Beta Kappa 1974
- Sigma X 1975
- American Society of Clinical Oncology Young Investigator Award 1986-1987
- Susan Komen Foundation Award 1987-1988
- American Cancer Society Clinical Oncology Career Development Award 1988-1991
- Merck Clinician Scientist Award 1989-1990
- Breast Cancer Research Chair in Oncology, Johns Hopkins 1995-2009
- ACS Research Award, American Cancer Society - Maryland Division 1998
- Brinker International Award for Breast Cancer Research 1999
- Wellesley College Alumnae Achievement Award 2000
- Avon Foundation Medical Advancement Award 2003
- President, American Society of Clinical Oncology 2007-2008
- 7th Rosalind E. Franklin Award for Women in Science, National Cancer Institute 2008
- 11th American Association for Cancer Research-Women in Cancer Research Charlotte Friend Award 2008
- Johns Hopkins University Alumni Association Distinguished Alumna Award 2009
- American Society of Clinical Oncology Gianni Bonadonna Breast Cancer Award 2010
- Association of American Physicians 2010
- National Academy of Medicine (formerly the Institute of Medicine) 2011
- Pennsylvania Breast Cancer Coalition Potamkin Award 2012
- Distinguished Professor of Medicine, University of Pittsburgh 2013
- Thomson Reuters Highly Cited Researchers 2014, 2015
- The Johns Hopkins Women’s Medical Alumnae Assoc. Hall of Fame 2015
- Johns Hopkins University Society of Scholars 2016
- Fellow, American College of Physicians 2016
- Distinguished Daughters of Pennsylvania 2016
- Fellow of the AACR Academy 2017
- Jill Rose Award, Breast Cancer Research Foundation 2017
7. **Board Certification:**

National Board of Medical Examiners 1980
American Board of Internal Medicine 1982
Medical Oncology 1985

8. **Current License(s) to Practice:**

State of Maryland 1982
Commonwealth of Pennsylvania 2009
State of Washington Dept. of Health #MD.60721914 2017

9. **Professional Organizations:**

**American Society of Clinical Oncology** *1985-present*
- Member, Public Issues Committee 1992-1996
- Member, Award Selection Committee 1992-1996
- Chair, Award Selection Committee 1994-1995
- Member, Ad hoc Technology Assessment Committee 1993-1994
- Co-Chair, Breast Cancer Follow-up Testing Guidelines Expert Panel 1996- present
- Member, Membership Committee 1997-1999
- Member, Board of Directors 1996-1999
- Member, Grants Selection Committee 1999-2002
- Member, Task Force on Quality of Cancer Care 1999-2004
- Member, Publications Committee 2004-2007
- Chair, Publications Committee 2005-2006
- Member, Translational Research Task Force 2005-2006
- President-Elect, President, and Immediate Past President 2006-2009
- Member, Value in Cancer Care Task Force 2007-present
- Chair, Special Awards Selection Committee 2008-2009
- Member, Translational Research Professorship Selection Committee 2008-2009
- Government Relations Committee 2013-2016
- By-laws Committee 2010-2014
- Chair, 2012-2014

**American Association for Cancer Research** *1988- present*
- Member, Maryland Legislative Committee 1993-1997
- Member, Program Committee 2000-2001, 2002-2003
- Co-Chair, Program Committee 2003-2004
- Member, Clinical Cancer Research Committee 2001
Member, AACR-Richard and Hinda Rosenthal Foundation Award Selection Committee 1998-1999, 2001-2003
Member, Board of Directors 2002-2005
Chair, Education Committee 2003-2004
Member, Grants Selection Committee 2004-2005
Member, Lifetime Achievement Award Selection Committee 2004-2005
Member, Landon Award Selection Committee 2005-2006
Chair, AACR-Breast Cancer Research Foundation Grants Selection Committee 2008-2009
Member, Landon Translational Award Selection Committee 2008-2009
Co-Chair, Program Committee, 7th Annual Frontiers in Cancer Prevention Research Conference 2008
Member and Chair (2010-11), AACR Nominating Committee 2010-2012
Member, Continuing Medical Education Committee, Chair 2015-2016
Member, AACR-San Antonio Breast Cancer Symposium, Education Committee 2012-2013
Program Committee 2011-2014
President-Elect, President, and Immediate Past President 2015-2018

**Eastern Cooperative Oncology Group ECOG ACRIN** 1987-present

Member, Breast Cancer Core Committee 1987-present
Chair, Breast Cancer Biology Committee 1992-1996
Co-Chair, Breast Cancer Committee 1992-1996
Chair - Breast Cancer Committee 1997-2002

**American College of Physicians** 2009-present

Member, National Surgical Adjuvant Bowel and Breast Project 2010-present

**Board of Directors, Association of American Cancer Institutes** 2010-2013

Member, Association of American Physicians Council 2015-present

10. **Teaching Responsibilities at Johns Hopkins and University of Pittsburgh**

1988-2005 Lecturer, Pathophysiology Course for 2nd Year Medical Students
1991 Medical Student Advisor
1996-2009 Lecturer, Fundamentals of Clinical Oncology for Public Health Practitioners
1997-2009 Lecturer, Topics in Molecular Endocrinology, School of Public Health
2004-2009 Lecturer, Pathophysiology of Disease, Cellular and Molecular Medicine
2010-2016 Lecturer, Cancer Biology and Therapy
2013-2016 ILS Neoplasia & Neoplastic Diseases

**Mentoring:**

<table>
<thead>
<tr>
<th>Postdoctoral Fellows – Laboratory</th>
<th>Current Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988-1990 M. John Kennedy, MD</td>
<td>Consultant, St. James Hospital, Dublin, Ireland</td>
</tr>
<tr>
<td>1989-1992 Deborah K. Armstrong, MD</td>
<td>Professor of Oncology, Johns Hopkins</td>
</tr>
</tbody>
</table>
1991-1993 Yvonne L. Ottaviano, MD  Private Practice, Baltimore, MD
1993-1996 Diane McCloskey, PhD  Associate Professor of Cellular & Molecular Physiology, Penn State, Hershey, PA
1993-1997 Rena Lapidus, PhD  Director, Translational Core Laboratory
1993-1998 Anne Ferguson, PhD  Associate Professor, University of Maryland
1994-1995 Christian Jackisch, MD  Non-profits, San Francisco, CA
1996-1999 Hillary Hahm, MD, PhD  Director of Translational Core Laboratory
1997-1999 Sharyl Nass, PhD  Private Practice, Atlanta, GA
1993-1997 Diane McCloskey, PhD  Associate Professor of Cellular & Molecular Physiology, Penn State, Hershey, PA
1993-1997 Rena Lapidus, PhD  Director, Translational Core Laboratory
1993-1998 Anne Ferguson, PhD  Associate Professor, University of Maryland
1994-1995 Christian Jackisch, MD  Chief, Clinic for Gynecology and Obstetrics, Klinikum Offenbach, Offenbach, Germany
1996-1999 Hillary Hahm, MD, PhD  Private Practice, Atlanta, GA
1997-1999 Sharyl Nass, PhD  Director of the National Cancer Policy Forum
1998-2001 Xiaowei Yang, MD, PhD  Institute of Medicine, National Academy of Medicine, Washington, DC
1998-2001 Xiaowei Yang, MD, PhD  Staff Scientist, National Cancer Institute
1999-2001 Valerie Dunn, MD  Private Practice, Rochester, NY
2000-2001 Lan Yan, MD, PhD  Staff Scientist, Amgen, Thousand Oaks, CA
2001-2006 Yi Huang, MD, PhD  Assistant Professor, University of Pittsburgh, Pittsburgh, PA
2001-2004 Judith C. Keen, PhD  Director of Scientific Affairs at the American Society for Radiation Oncology (ASTRO)
2002-2003 Dipali Sharma, PhD  Associate Professor of Oncology, Johns Hopkins University School of Medicine, Baltimore, MD
2004-2008 Qun Zhou, MD, PhD  Associate Professor of Biochemistry and Molecular Biology, University of Maryland Medical School
2005-2006 Allison Tracy, PhD  Lecturer of Chemistry and Biochemistry, UMBC
2006-2009 Qingsong Zhu, PhD  Chief Operating Officer, InSilico Medicine, Inc., Baltimore, MD
2006-2009 Madhavi Billam, PhD  Senior Toxicologist, L’Oreal USA & RI
2011-2013 Tiffany Katz, PhD  Instructor, Baylor College of Medicine, Center for Precision Environmental Health
2014-2016 Nilgun Tasdemir, PhD  Department of Molecular and Cellular Biology
2015-2017 Lin Chen  Postdoctoral Fellow, University of Pittsburgh
2000-2005 Julie Blum, PhD  Clinical Content Manager, MED-IQ
2001-2005 Allison Pledgie, PhD  Senior Lecturer in Chemistry and Biochemistry at University of Maryland Baltimore County (UMBC)
2004-2010 Abigail Witt, PhD  Postdoctoral Fellow, University of Miami School of Medicine
2005-2010 Talmesha Richards, PhD  Chief Academic and Diversity Officer at STEMconnector
2006-2010 Patrick Shaw, PhD  Chief, Pathogen Detection Lab. USA Public Health Command Region-Pacific Camp Zama, Japan

Doctoral Students

<table>
<thead>
<tr>
<th>Years</th>
<th>Name</th>
<th>Current Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000-2005</td>
<td>Julie Blum, PhD</td>
<td>Clinical Content Manager, MED-IQ</td>
</tr>
<tr>
<td>2001-2005</td>
<td>Allison Pledgie, PhD</td>
<td>Senior Lecturer in Chemistry and Biochemistry at University of Maryland Baltimore County (UMBC)</td>
</tr>
<tr>
<td>2004-2010</td>
<td>Abigail Witt, PhD</td>
<td>Postdoctoral Fellow, University of Miami School of Medicine</td>
</tr>
<tr>
<td>2005-2010</td>
<td>Talmesha Richards, PhD</td>
<td>Chief Academic and Diversity Officer at STEMconnector</td>
</tr>
<tr>
<td>2006-2010</td>
<td>Patrick Shaw, PhD</td>
<td>Chief, Pathogen Detection Lab. USA Public Health Command Region-Pacific Camp Zama, Japan</td>
</tr>
</tbody>
</table>

Graduate Training Programs
1997-2011 Biochemistry and Molecular Biology, Hopkins Bloomberg School of Public Health (adjunct 2009-2011)
1999-2013 Cellular and Molecular Medicine, Hopkins School of Medicine (adjunct 2009-2013)

11. Editorial Board Responsibilities:

1995-2005 Cancer Research
1995-2009 The Breast Journal
1996-2011 The Breast
1997-2005 American Journal of Medicine
1999-2005 Clinical Cancer Research
2007-2014 Hem/Onc Today
2008-present Oncology
2008-present Cancer Prevention Research
2012-present Journal of the National Cancer Institute
2012-present Breast Cancer Research and Treatment

12. Special National Responsibilities:

Study Section Memberships:

1988 Member, Ad Hoc Technical Review Section, National Cancer Institute, Bethesda, MD
1990, 1991, 1992 Ad Hoc Member, Reproductive Endocrinology Study Section, National Institutes of Health, Bethesda, MD
1992-1993 Member, Awards Committee, Susan G. Komen Foundation, Dallas, TX
1993-1997 Member, Reproductive Endocrinology Study Section, National Institutes of Health, Bethesda, MD
1994 Member, Walt Disney – American Cancer Society Breast Cancer Professorship Selection Committee, Atlanta, GA
1997-1998 Co-Chair, Progress Review Group for Breast Cancer Research, National Cancer Institute, Bethesda, MD
1996-1998 Chair, Pre-clinical and Clinical Studies Study Section, California Breast Cancer Research Program, San Francisco, CA
1999-Present Medical Advisory Board, Breast Cancer Research Foundation, New York City, NY
2001 Member, Breast and Prostate SPORE Review Group, National Cancer Institute
2002 Co-chair, Breast Cancer SPORE Review Group, National Cancer Institute
2003-2008 Vice-Chair, National Cancer Institute Breast Cancer Intergroup Correlative Science Committee
2002-2005 Member, Charles Kettering Prize Selection Committee, General Motors Cancer Research Foundation, Chair, 2005
2003 Chair, Innovator Award Review Committee, Department of Defense Breast Cancer Program
2005 Member, Lung and Bladder Cancer SPORE Review Group, National Cancer Institute
2005-2006 Ad hoc member, Kimmel Scholars Award Committee
2006-2017 Member, Kimmel Scholars Award Committee
2006-2010 Member, Subcommittee A – Cancer Centers, National Cancer Institute
2008 Co-chair, Lung Cancer and Lymphoma SPORE Review Group, National Cancer Institute
2008-Present  Member, Scientific Advisory Board, V Foundation for Cancer Research
2008  Chair, Therapeutic Targets I Review Committee, Susan G Komen for the Cure
2012-Present  Member, Damon Runyon Cancer Research Foundation Clinical Investigator Award Committee
2012-2013  Chair of the Cancer Program Review, Helmholtz Senate Commission, Helmholtz Association of German Research Centers, Berlin, Germany
2014  Member, Scientific Advisory Committee, Breakthrough Breast Cancer, London, UK
2014  Chair, CTAC SPORE Program Evaluation Working Group, NCI
2015  Chair, Stand Up To Cancer Canada-Canadian Breast Cancer Foundation Breast Cancer Dream Review Team Committee

**Extra-mural Grant Reviewing:**
Ad hoc grant reviewer for: National Institutes of Health, American Cancer Society, Veterans Administration, Manitoba (Canada) Health Council, Health Research Council of New Zealand, National Cancer Institute - Canada, Medical Research Council - Canada, Department of Defense Breast Cancer Program, many others

**Advisory Board Memberships:**
2000-present  Member, External Advisory Board, Vanderbilt-Ingram Cancer Center, Nashville, TN
2001-2006  Member, External Advisory Board, Fox Chase Cancer Center, Philadelphia, PA
2001-2011  Member, External Advisory Board, Bay Area UCSF Breast Cancer SPORE, San Francisco, SF
2003-2016  Member, External Advisory Board, Karmanos Cancer Center, Detroit, MI
2003-2008  Member, External Advisory Board, Indiana University Cancer Center, Indianapolis, IN
2005-2016  Member, External Advisory Board, University of Maryland Cancer Center, Baltimore, MD
2008-Present  Member, Board of Scientific Consultants, Memorial Sloan Kettering Cancer Center, Baltimore, MD
2008-Present  Member, External Advisory Board, Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, Chair 2014-
2009-Present  Member, External Advisory Board, MD Anderson Cancer Center, Houston, TX, Chair 2014-
2010-Present  Member, External Advisory Board, University of Michigan Comprehensive Cancer Center
2010-Present  Member, External Advisory Board, Washington University Siteman Cancer Center, St. Louis, MO
2010-Present  Member, External Advisory Board Breast Cancer SPORE, Mayo Clinic, Rochester, MN
2010-Present  Member, External Advisory Board, Institut National du Cancer, Paris, France
2011-2016  Member, External Advisory Board, Fred Hutchinson Cancer Research Center University of Washington Cancer Consortium, Seattle, Washington
2011-2016  Member, Scientific Advisory Board, CTSA, Case Western Reserve University School of Medicine, Cleveland, Ohio
2012-Present  Member, Scientific Advisory Board, Cologne Center for Integrated Oncology, Cologne, Germany
2013-Present  Member, External Advisory Board, Baylor College of Medicine Breast Cancer SPORE
2014-Present  Member, External Advisory Board, University of Chicago Comprehensive Cancer Center, Chicago, IL
2014-2015  Member, Scientific Advisory Board, A. Alfred Taubman Medical Research Institute, University of Michigan, Ann Arbor, MI

**External Organizations:**
1993-1995  Member, Medical Advisory Committee, Maryland Cancer Consortium  
1994-1996  Executive Committee, American Cancer Society – Maryland Division Chair, Research Committee  
1995-1998  Member, Medical Knowledge Self-Assessment Program 11-Oncology, American College of Physicians  
1999-2000  Planning Committee, National Institutes of Health Consensus Development Conference on Adjuvant Therapy for Breast Cancer, Bethesda, MD  
1998-2001  Data Monitoring Committee, Southwest Oncology Group  
1999-2006  Data Monitoring Committee, RUTH Trial, Lilly  
2000-2006  Data Monitoring Committee, Breast Cancer International Research Group (BCIRG)  
2006-2011  Member, Data and Safety Monitoring Committee, TEACH Trial, Glaxo Smith Kline  
2009-2012  NMR Center Advisory Committee, Carnegie Mellon University  
2010-2016  Co-Chair, Breast Cancer Steering Committee, National Cancer Institute  
2011-Present  Member, Clinical Trials and Translational Research Advisory Committee (CTAC), National Cancer Institute, Chair 2015-present  
2013-2016  Board of Trustees, Phipps Conservatory, Pittsburgh, PA  
2015  Member, Search Committee for the Scientific Director (SD), Center for Cancer Research (CCR), National Cancer Institute  
2015-2017  Member, Breast Cancer Now’s Science Strategy Committee, United Kingdom  
2017-Present  Member, Board of Scientific Counselors-Clinical Sciences and Epidemiology, NCI  

13. **Special Local Responsibilities:**

**Committees - Johns Hopkins**

1987  Co-Director, Oncology Multidisciplinary Conference  
1987-1997  Member, Oncology Fellowship Selection Committee  
1993-1995  Department Representative, Medical School Council  
1999-2003  Departmental Appointments and Promotions Committee  
2000-2005  Member, School of Medicine Professorial Promotion Committee  
2001-2009  Member, MD-PhD Admissions Committee  
2003-2005  Member, Search Committee for Director of Biophysics and Biophysical Chemistry  

**Committees – University of Pittsburgh, University of Pittsburgh Physicians (UPP), UPMC**

2009-2016  Member, Chair Management Committee  
2009-2016  Member, UPP Clinical Chairs Committee  
2009-2016  Member, Breast Cancer Steering Committee  
2009-2016  Member, Clinical Research Oversight Committee  
2009-2012  Member, ReSet Steering Committee  
2009-2016  Member, Adolescent and Young Adult Cancer Committee  
2010-2011  Member, Search Committee for Department of Medicine Chairman  
2011-2012  Member, Search Committee for the Institute of Personalized Medicine  
2012-2016  Member, UPMC Presbyterian Shadyside Hillman Cancer Committee
2012-2016 Member, School of Medicine Financial Oversight Committee
2012-2016 Member, Internal Advisory Board Skin SPORE
2014-2016 Member, Internal Advisory Board Gynecologic SPORE
2015-2016 Member, Internal Advisory Board for the Center for Causal Discovery
2015-2016 Member, Internal Advisory Board of the Center for Medical Counter Measures Against Radiation (CMCR)

14. Research Funding:

Current Research Funding

<table>
<thead>
<tr>
<th>Grant ID</th>
<th>Description</th>
<th>PI</th>
<th>Percentage</th>
<th>Years</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>NIH P30CA015704</td>
<td>Cancer Center Support Grant</td>
<td>Davidson co-deputy director</td>
<td>15%</td>
<td>2017-2019</td>
<td>$5,408,473</td>
</tr>
<tr>
<td>NIH T32 CA009515</td>
<td>Training in Cancer Biology and Transplantation</td>
<td>Davidson</td>
<td>5%</td>
<td>2017-2020</td>
<td>$593,274</td>
</tr>
<tr>
<td>BCRF Davidson, PI</td>
<td>Identifying kinase vulnerabilities of dormant disseminated breast tumor cells and micrometastases using cutting edge models</td>
<td>Davidson</td>
<td>1%</td>
<td>1998-2018</td>
<td>$208,334</td>
</tr>
</tbody>
</table>

Past Research Funding

Grants Awarded as Principal Investigator

1986-1987 American Society of Clinical Oncology Young Investigator Award, "Isolation of estrogen-induced genes from human breast cancer."
1989-1990 Merck Clinician Scientist Award, Johns Hopkins University School of Medicine.
1990-1991 Johns Hopkins University School of Medicine Institutional Research Grant, "Elimination of breast cancer cells from human bone marrow by counter flow centrifugal elutriation".
1994-1998 NIH Grant R21 CA/ES 66204 "Development of a breast cancer program at Johns Hopkins".

1995-1999 NIH Grant 1 U01 CA66084. "New therapeutic approaches for breast cancer".


1998-2004 NIH Grant R01 CA78352 “DNA methylation as a determinant of hormone resistant breast cancer.”


2001-2009 Avon Foundation

2001-2005 Susan G. Komen Foundation Postdoctoral Fellowship

2003-2005 Susan G. Komen Foundation Predoctoral Fellowship

2000-2009 American Breast Cancer Foundation

2006-2008 Susan G. Komen Foundation, BCTR 65706, “Polyamine analogues as novel anti-estrogen receptor alpha agents


2008-2011 Susan G. Komen for the Cure, KG080923, Inhibition of lysine specific demethylase 1 (LSD1) as a strategy for re-expression of epigenetically silenced genes in breast cancer; Robert Casero, Jr. and Nancy E. Davidson , Co-PIs

2000-2013 NIH P50 CA88843. SPORE in Breast Cancer

Nancy E. Davidson co-PI of University of Pittsburgh site 2009-2012

2011-2013 Gynecologic Center of Excellence. Henry M. Jackson Foundation

2009-2013 Stand up to Cancer (AACR). Bringing epigenetic therapy to the forefront of cancer. Dream Team Principal, with Stephen Baylin and Peter Jones

2009-2016 P30CA047904 Cancer Center Support Grant-- National Cancer Institute. To support senior leadership, shared resources, and developmental funds for the University of Pittsburgh Cancer Institute

2009-2016 Translational Breast Cancer Research Consortium and the Komen Foundation

2009-2016 Translational Breast Cancer Research Consortium and the Avon Foundation


2014-2016 U10 CA180844, NCI NCTN-Network, Lead Academic Site at University of Pittsburgh

15. Bibliography

a) Publications in Refereed Journals


2. Kensler TW, Busby WF, Davidson NE, and Wogan GN. Effect of hepatocarcinogens on the binding of glucocorticoid-receptor complex in rat liver nuclei. Cancer Res. 36:4647-51, 1976. PMID 1000507


22. Rowley SD, Piantadosi S, Marcellus DC, Jones RJ, Davidson NE, Davis JM, Kennedy J, Wiley JM, Wingard J, Yeager AM and Santos GW. Analysis of factors predicting speed of hematologic recovery after transplantation with 4 hydroperoxycyclophosphamide-purged autologous bone marrow grafts. Bone Marrow Trans. 7:183-91, 1991. PMID 2059755


37. Davidson NE and Abeloff MD. Menstrual effects on surgical treatment for breast cancer, Cancer Treat Rev. 19:105-12, 1993. PMID 8481925


61. Issa J-P, Zehnbauer BA, Civin CI, Collector M, Sharkis SJ, Davidson NE, Kaufmann SH and Baylin SB. The estrogen receptor CpG island is methylated in most hematopoietic neoplasms. Cancer Res. 56:973-77, 1996. PMID 8640788


75. Ferguson AT, Lapidus RG and Davidson NE. Demethylation of the progesterone receptor CpG island is not required for progesterone receptor gene expression. Oncogene. 17:577-83, 1998. PMID 9704923
78. Hahm HA and Davidson NE. Apoptosis in the mammary gland and breast cancer. Endocrine-Related Cancer. 5:199-211, 1998.
102. Dees EC and Davidson NE. Ovarian ablation as adjuvant therapy for breast cancer. Seminars in Oncology. 28:322-33, 2001. PMID 11498826


120. Emens LA and Davidson NE. The follow-up of breast cancer. Semin Oncol. 338-348, 2003. PMID 12870135


130. Prowell TM and Davidson NE. What is the role of ovarian ablation in the management of primary and metastatic breast cancer today? The Oncologist. 9:507-17, 2004. PMID 15477635


137. Huang Y, Pledgie A, Casero RA and Davidson NE. Molecular mechanisms of polyamine analogues in cancer cells, Anti-Cancer Drugs. 16: 229-41, 2005. PMID 15711175


175. Bao T, Davidson NE. How we maintain bone health in early stage breast cancer patients on aromatase inhibitors, J Oncology Practice. 3:323-5, 2007. PMC2793755


205. Emens LA, **Davidson NE.** Post operative endocrine therapy for invasive breast cancer. Cancer Treat Res. 151:139-61, 2009. PMC3086398


208. Yao Y, Li H, Gu Y, **Davidson NE,** Zhou Q. Inhibition of SIRT1 deacetylase suppresses estrogen receptor signaling. Carcinogenesis. 31:382-387, 2010: PMC2832546


217. Davidson, NE. HER2-targeted therapies: how far we’ve come—and where we’re headed. Oncology. 25(5):425-6, 2011. PMID 21710840

218. Davidson, NE. Retrospective on the last quarter-century in medical oncology. Oncology. 25(5):396, 2011. PMID 21710831


254. Davidson NE. Fifteen years of anti-HER2 therapy. Oncology. 27(3):151, 2013. PMID 23687781


265. Jankowitz RC, Davidson NE. Adjuvant endocrine therapy for breast cancer: how long is long enough? Oncology. 27(12):1210-6, 2013. PMID 24624537


b) Book Chapters.


Book Reviews:

Books Edited:

c) Published Books, Videos, Software, etc.

d) Other Publications (e.g., in non-refereed journals, letters to the editor). Indicate type of publication* in brackets at end of reference (e.g., [invited review], [editorial], etc.)

Editorials:
22. Davidson NE. The maturation of medical oncology. Lancet Oncol. 8:457-8, 2007
40. Bhargava R, Brufsky AM, Davidson NE. “Take two”? the role of second opinions for breast biopsy specimens. BMJ 353:i3256. Doi:10.1136/bmj.i3256. PMID 27339037
42. Bhargava R, Brufsky AM, Davidson NE. “Take two”? the role of second opinions for breast biopsy specimens. BMJ 353:i3256. Doi:10.1136/bmj.i3256. PMID 27339037
44. Bhargava R, Brufsky AM, Davidson NE. “Take two”? the role of second opinions for breast biopsy specimens. BMJ 353:i3256. Doi:10.1136/bmj.i3256. PMID 27339037
2. Davidson NE. Hormone replacement therapy in perspective; Medical and Health Annual, Encyclopedia Britannica, Inc., Chicago, IL pp. 361-6, 1997.

e) Manuscripts Submitted.

None

f) Abstracts.

Not recorded

16. Other:

Invited Seminars

1985 Grand Rounds, Washington Veterans Administration Hospital, Washington, DC

1986 Medical Grand Rounds, Johns Hopkins Medical Institutions, Baltimore, MD
Symposium on Breast Cancer, Millville Hospital, Vineland, NJ
Department of Hematology-Oncology, University of Missouri, Kansas City, MO
Kansas City Round Table of Hematology/Oncology, Kansas City, MO
American Association of Osteopathic Internists, Washington, DC
Cincinnati Cancer Conference V, Cincinnati, OH
Advances in Oncology, Cherry Hill, NJ

1987 13th Annual Symposium on Diagnosis and Treatment of Neoplastic Disorders Course, Johns Hopkins Medical Institutions, MD
Breast Cancer Session, Eastern Cooperative Oncology Group, Clearwater, FL

1988 Early Breast Cancer Conference, Memorial Hospital, Colorado Springs, CO
Grand Rounds, Liberty Medical Center, Baltimore, MD
Medical Grand Rounds, Johns Hopkins Medical Institutions, Baltimore, MD
Annual Hematology/Oncology Conference, The Medical Center of Delaware, Wilmington, DE
Department of Medicine Professors Rounds, Johns Hopkins Medical Institutions, Baltimore, MD
Medical Residents Journal Club, Johns Hopkins Medical Institutions, Baltimore, MD
Plastic Surgery Grand Rounds, Johns Hopkins Medical Institutions, Baltimore, MD

1989 Department of Medicine Bench to Bedside, Johns Hopkins Medical Institutions, Baltimore, MD
Twelfth Annual Symposium on Current Concepts in Medicine and Surgery, Peninsula General Hospital, Salisbury, MD
Topics in Internal Medicine Course, Johns Hopkins Medical Institutions, Baltimore, MD
15th Annual Symposium on Diagnosis and Treatment of Neoplastic Disorders, Johns Hopkins Medical Institutions, Baltimore, MD
Eleventh Annual Cancer Symposium Selected Topics in Oncology, Raleigh, NC
Plastic Surgery Grand Rounds, Johns Hopkins Medical Institutions, Baltimore, MD
St. George's Society, Johns Hopkins Medical Institutions, Baltimore, MD
Hematology-Oncology Division Seminar, Indiana University School of Medicine, Indianapolis, IN

1990 Grand Rounds, St. Agnes Hospital, Baltimore, MD
Department of Medicine Bench to Bedside, Johns Hopkins Medical Institutions, Baltimore, MD
American Cancer Society, Maryland Division, Baltimore, MD
Medical Grand Rounds, Johns Hopkins Medical Institutions, Baltimore, MD
16th Annual Symposium on Diagnosis and Treatment of Neoplastic Disorders, Johns Hopkins Medical Institutions, Baltimore, MD
NCI Strategy Meeting on High Dose Chemotherapy in Breast Cancer, National Cancer Institute, Bethesda, MD
Hematology-Oncology Division Seminar, University of Maryland School of Medicine, Baltimore, MD

1991
Hematology-Oncology Conference, Chester Hospital, West Chester, PA
Department of Medicine Professors Rounds, Johns Hopkins Medical Institutions, Baltimore, MD
Symposium on Early Breast Cancer, Montgomery General Hospital, Olney, MD
Hematology-Oncology Division Seminar, Northwestern University School of Medicine, Chicago, IL
Pennsylvania Oncology Society, Gettysburg, PA
Susan G. Komen Foundation Scientific Symposium, University of Texas - Southwestern Medical School, Dallas, TX

1992
Breast Cancer Symposium, Crozer-Chester Hospital, Upland, PA
Hematology-Oncology Grand Rounds, University of Maryland School of Medicine, Baltimore, MD
Department of Medicine Ambulatory Care Rounds, Johns Hopkins Medical Institutes, Baltimore, MD
Staff Conference, Roswell Park Cancer Institute, Buffalo, NY
Tumor Board, Anne Arundel Hospital, Annapolis, MD
18th Annual Symposium on the Diagnosis and Treatment of Neoplastic Disorders, Johns Hopkins Medical Institutions, Baltimore, MD
American Cancer Society, Teaneck, NJ
Australia - New Zealand Breast Cancer Trials Group, Surfers Paradise, Australia
Laboratory of Biologic Chemistry, National Cancer Institute, Bethesda, MD
Lederle Advisory Board, New York City, NY
Gordon Conference on Cancer, Newport, RI
American Society of Clinical Pathologists, Las Vegas, NV
The Cancer Center at Fairfax Hospital, Fairfax, VA
American Fertility Society, New Orleans, LA
Visiting Professor, Department of Medicine, Hahnemann University School of Medicine, Philadelphia, PA

1993
NCI Strategy Meeting on Breast Cancer in Young Women, National Institutes of Health, Bethesda, MD
St. Georges Society, University of Maryland School of Medicine, Baltimore, MD
US-Japanese Joint Scientific Meeting on New Breast Cancer Therapies, Oakland, CA
Isaac Lewin Symposium, Baystate Medical Center, Springfield MA
Discussant, Adjuvant Breast Cancer Session, American Society of Clinical Oncology, Orlando, FL
Educational Session, National Cancer Institute Phase I Meeting, Bethesda, MD
Working Group on the Pulmonary Complications Associated with Breast Cancer Therapy, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD
Shanghai Cancer Institute, Shanghai, Peoples Republic of China
Ethics and Politics in Clinical Trials, Johns Hopkins Medical Institutions, Baltimore, MD
NCI Workshop on Prognostic and Predictive Factors in Breast Cancer, Bethesda, MD

1994
Hematology/Oncology Grand Rounds, Wayne State University School of Medicine, Detroit, MI
Clinical Oncology Program Grand Rounds, National Cancer Institute, Bethesda, MD
NCI Strategy Meeting on High Dose Chemotherapy for Breast Cancer, Bethesda, MD
11th Annual Advances in Cancer Treatment Research, Albert Einstein College of Medicine, New York City, NY
Recent Advances in the Biology of Breast, Colon, and Lung Cancer, American Society of Clinical Oncology, Dallas, TX
Discussant, Plenary Session, American Society of Clinical Oncology, Dallas, TX
Women’s Health Seminar Series, Breast Cancer, National Institutes of Health, Bethesda, MD
Chemotherapy Symposium, Berlex Oncology Foundation, Leesburg, VA
The State of Breast Cancer 1994: An Interactive Symposium, University of California at San Francisco, San Francisco, CA
Grand Rounds, Washington County Hospital, Hagerstown, MD
Y-ME of the Cumberland Valley, Hagerstown, MD

1995
Department of Pharmacology and Toxicology, Robert C. Byrd Health Sciences Center of West Virginia University, Morgantown, WV
12th Annual International Breast Cancer Conference, Miami, FL
Controversy Session, American Association for Cancer Research, Toronto, Canada
Department of Pharmacology, Mayo Clinic, Rochester, MN
Susan G. Komen Foundation Congressional Breakfast, Washington, DC
Commonwealth of Massachusetts Course on Breast Cancer, Boston, MA
Law and Health Care Program, University of Maryland and Baltimore School of Law, Baltimore, MD
Discussant, Breast Cancer Session, American Society of Clinical Oncology, Los Angeles, CA
Topics in Clinical Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
Gordon Research Conference on Mammary Gland Biology, New London, NH
The Endocrine Society’s 51st Conference on Recent Progress in Hormone Research, Stevenson, WA
Eighteenth Thomas W. Green Memorial Lecture, East Tennessee State University James H. Quillen College of Medicine, Bristol, TN
Fifth International Congress on Hormones and Cancer, Quebec City, Canada
Cancer Medicine, Harvard Medical School, Boston, MA
Medical Oncology Board Review, George Washington University School of Medicine, Washington, DC
The First Annual Kimmel-Slavin Memorial Lecture, George Washington University School of Medicine, Washington, DC
Chemotherapy Symposium, Berlex Oncology Foundation, Leesburg, VA
Meet the Professor, American Society of Clinical Oncology Fall Educational Conference, Washington, DC
Grand Rounds, Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
Division of Hematology/Oncology, Washington Hospital Center, Washington, DC
18th Annual San Antonio Breast Cancer Symposium, San Antonio, TX
Department of Medicine, St. Joseph Hospital, Baltimore, MD
Dana-Farber Cancer Institute, Boston, MA
22nd Annual Symposium on the Diagnosis and Treatment of Neoplastic Disorders, Johns Hopkins

1996
Department of Embryology, Carnegie Institute of Washington, Baltimore, MD
Mayo Clinic Cancer Center, Rochester, MN
New Approaches to Cancer Therapy, The Johns Hopkins Oncology Center, Baltimore, MD
Topics in Clinical Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
University of Maryland Cancer Center, Baltimore, MD
Discussant, Breast Cancer Session, American Society of Clinical Oncology, Philadelphia, PA
Bowman Gray Comprehensive Cancer Center, Wake Forest University, Winston-Salem, NC
American College of Surgeons, San Francisco, CA
Session Chair, Gordon Conference on Cancer Chemotherapy, Oxford, UK
Chemotherapy Symposium, Berlex Oncology Foundation, Leesburg, VA
City of Hope National Medical Center, Duarte, CA
Upstate New York Cancer Research and Education Foundation, Syracuse, NY
Wendy and Emery Reeves International Breast Cancer Symposium, University of Texas Southwestern Medical Center, Dallas, TX 30th Anniversary Symposium, National Institute of Environmental Health Sciences, Research Triangle, NC
Meet the Professor, American Society of Clinical Oncology Fall Educational Conference, Phoenix, AZ
Maryland Cancer Control Symposium, Baltimore, MD
Lombardi Cancer Center, Georgetown University Medical Center, Washington, DC
Department of Biochemistry, Johns Hopkins School of Hygiene and Public Health, Baltimore, MD

1997
Breast Cancer Think Tank 7, St. Lucia
4th Annual Breast Cancer Symposium of the New York Metropolitan Breast Cancer Group, New York City, NY
2nd Annual Multidisciplinary Symposium on Breast Disease, Amelia Island, FL
University of Colorado Cancer Center, Denver, CO
Cambridge Symposium, Genetic Approaches to Breast and Prostate Cancer, Lake Tahoe, CA
St. George’s Society, University of Maryland Medical School, Baltimore, MD
Issues in the Treatment of Breast Cancer, Greater Baltimore Medical Center, Baltimore, MD
University of Chicago Cancer Center, Chicago, IL
Conjoint Clinic, Johns Hopkins University School of Medicine, Baltimore, MD
Breast Cancer Tumor Panel, American Society ofClinical Oncology, Denver, CO
Pittsburgh Cancer Institute, University of Pittsburgh Medical School, Pittsburgh, PA
International Cancer Alliance, Washington, DC
Perspectives in Breast Cancer, Emory University, Atlanta, GA
US Public Health Services Office on Women’s Health Healthy Women 2000, Washington, DC
Chemotherapy Symposium, Berlex Oncology Foundation, Leesburg, VA
American College of Surgeons, Chicago, IL
Susan G. Komen Foundation Breast Cancer Symposium, Dallas, TX
Medical Oncology Board Review, George Washington University School of Medicine, Washington, DC
Case Western Reserve University/Ireland Cancer Center, Cleveland, OH
Holy Cross Hospital, Silver Spring, MD
Department of Medicine and Cancer Center, University of California at San Francisco, San Francisco, CA
American Society of Clinical Oncology Fall Education Conference, Orlando, FL
14th Annual American College of Physicians/Army Regional Meeting, Reston, VA Fallston Hospital, Fallston, MD

1998
Breast Cancer Think Tank 8, Tobago
Session Co-Chair, 6th International Conference on Adjuvant Therapy of Primary Breast Cancer, St. Gallen, Switzerland
Controversy Session Chair, American Association for Cancer Research, New Orleans, LA
24th Annual Symposium on Diagnosis and Treatment of Neoplastic Diseases, Johns Hopkins Medical Institutions, Baltimore, MD
Breast Cancer Symposium, Inova Fairfax Hospital, Fairfax, VA
Discussant, Plenary Session, American Society of Clinical Oncology, Los Angeles, CA
Department of Pathology, Vanderbilt School of Medicine, Nashville, TN
Suburban Hospital, Bethesda, MD
Department of Medicine, Columbia-Presbyterian Medical Center, New York City, NY
Gordon Conference on Cancer, Newport, RI
Chemotherapy Symposium, Berlex Oncology Foundation, Leesburg, VA
2nd Annual Advances in Cancer Therapy, VCU/MCV, Richmond, VA
Kent and Queen Anne’s Hospital, Chestertown, MD
Breast Cancer Awareness Month, The White House Washington, DC
Medical Oncology Board Review, George Washington University School of Medicine, Washington, DC
21st Annual San Antonio Breast Cancer Symposium, San Antonio, TX
1999

Breast Cancer Think Tank 9, St. Thomas, Virgin Islands
Joint Cancer Conference of the Florida Universities, Orlando, FL
Grand Rounds, Department of Medicine, Johns Hopkins Medical Institutions, Baltimore, MD
Congressionally Directed Medical Research Programs, Frederick, MD
Topics in Internal Medicine, Department of Medicine, Johns Hopkins, Baltimore, MD
American Society of Clinical Oncology, Atlanta, GA
1st Milan Breast Cancer Conference, Milan, Italy
Johns Hopkins Singapore, Singapore
Grand Rounds, Department of Surgery, Northwest Hospital, Baltimore, MD
6th Nottingham International Breast Cancer Conference, Nottingham, England
Seeking Excellence in Breast Cancer Care: Best Practices in Diagnosis and Treatment, Johns Hopkins University School of Medicine, Baltimore, MD
First Annual Lynn Sage Breast Cancer Symposium, Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, IL
Chemotherapy Symposium, Berlex Oncology Foundation, Leesburg, VA
Cancer Medicine, Harvard Medical School, Boston, MA
41st Annual Meeting of the American Society of Therapeutic and Radiation Oncology, San Antonio, TX
SERMs - Implication for Prevention and Treatment of Cancer, Philadelphia, PA
American Society of Clinical Oncology Fall Education Conference, San Francisco, CA
Genetics Program, University of Missouri, Columbia, MO
22nd Annual San Antonio Breast Cancer Symposium, San Antonio, TX

2000

Sibley Hospital, Washington, DC
Franklin Square Hospital, Baltimore, MD
Molecular Biology of Breast Cancer, Lillehammer, Norway
Keystone Symposium in Advances in Human Breast and Prostate Cancer, Lake Tahoe, NV
NIH Workshop on Selective Estrogen Receptor Modulators (SERMs), Bethesda, MD
Topics in Internal Medicine, Johns Hopkins University School of Medicine, Baltimore, MD
National Breast Cancer Coalition Eighteenth Annual Advocacy Training Conference
2nd Milan Breast Cancer Conference, Milan, Italy
Australia - New Zealand Breast Cancer Trials Group, Queenstown, New Zealand
Suburban Hospital, Bethesda, MD
15th Annual Excalibur Round Table, American Cancer Society, Baltimore, MD
Susan G. Komen Breast Cancer Foundation National Symposium - Reaching for the Cure..... Making a Difference, Washington, DC
WellStar Kennestone Hospital, Marietta, GA
WellStar Cobb Hospital, Marietta, GA
Hematology-Oncology Board Review, George Washington University School of Medicine, Arlington, VA
Berlex Oncology Foundation Clinical Pharmacology of Anticancer Drugs, Leesburg, VA
42nd Annual Meeting of the American Society of Therapeutic and Radiation Oncology, Boston, MA
National Institutes of Health Consensus Development Conference on Adjuvant Therapy of Breast Cancer, Bethesda, MD
Seeking Excellence in Breast Cancer Care, Johns Hopkins University School of Nursing and School of Medicine, Baltimore, MD

2001

Breast Cancer Think Tank 11, Punta Cana, Dominican Republic Potential Clinical Applications for GnRH Agonists, National Institutes of Health, Bethesda, MD
7th International Conference on Adjuvant Therapy of Primary Breast Cancer, St. Gallen, Switzerland
8th Annual Miami Breast Cancer Conference, Miami, FL
Central Pennsylvania Oncology Group, Harrisburg, PA
Mary E. Humphreys Biology Lecture, Mary Baldwin College, Staunton, VA
Department of Medicine Grand Rounds, Johns Hopkins Bayview, Baltimore, MD
Discussant, American Society of Clinical Oncology, San Francisco, CA
Anne Arundel Medical Center, Annapolis, MD
Lombardi Comprehensive Cancer Center, Georgetown University, Washington, DC
Women’s Malignancy Group, MD Anderson Cancer Center, Houston, TX
3rd Milan Breast Conference, Milan, Italy
Gordon Conference on Polyamines, New London, CT
Australian Society for Breast Diseases, Surfers Paradise, Australia (by video conference)
White House/Komen Breast Cancer Summit, Washington, DC
3rd Annual Lynn Sage Breast Cancer Symposium, Northwestern University, Chicago, IL
Hematology-Oncology Board Review, George Washington University School of Medicine, Arlington, VA
Berlex Oncology Foundation Clinical Pharmacology of Anticancer Drugs, Leesburg, VA
Tumor Board, Greater Baltimore Medical Center, Baltimore, MD
Hematology Grand Rounds, Johns Hopkins, Baltimore, MD
William L. McGuire Memorial Lecture, 24th Annual San Antonio Breast Cancer Symposium, San Antonio, TX

2002
Breast Cancer Symposium Think Tank 12, St. Maarten, The Netherlands Antilles
Grand Rounds Department of Medicine, Johns Hopkins University, Baltimore, MD
Current Trends in Breast Cancer, Philadelphia, PA
3rd European Breast Cancer Conference, Barcelona, Spain
The Third North American Symposium on Skeletal Complications of Malignancy, National Institutes of Health, Bethesda, MD
Educational Symposium, American Society for Clinical Oncology, Orlando, FL
4th Milan Breast Cancer Conference, Milan, Italy
Second International Conference on Recent Advances and Future Directions in Endocrine Manipulation of Breast Cancer, Cambridge, MA
Breast Cancer: Current Controversies and New Horizons, Dana Farber Cancer Institute, Boston, MA
Center for Cancer Research Grand Rounds, National Cancer Institute, Bethesda, MD
2nd Annual Karmanos Cancer Institute Breast Cancer Symposium, Detroit, MI
Era of Hope, Department of Defense Breast Cancer Research Program, Orlando, FL
Fox Chase Cancer Center, Philadelphia, PA
IX Congresso Nacional de Oncologia, Lisbon, Portugal

2003
NCI – Hopkins Workshop on Clinical Translation of Gene Re-expression in Cancer, Baltimore, MD
Breast Cancer Think Tank 13, Aruba
20th Annual Miami Breast Cancer Conference, Miami, FL
8th International Conference on Primary Therapy of Early Breast Cancer, St. Gallen, Switzerland
American Society for Breast Disease, Dallas, TX
Upper Chesapeake Medical Center, Fallston, MD
American Society of Clinical Oncology, Chicago, IL
Gordon Conference on Cancer Chemotherapy, Oxford, UK
National Cancer Institute Workshop on Ductal Lavage, Bethesda, MD
9th Annual Perspectives in Breast Cancer, Boston, MA
Cancer Education Consortium Clinical Pharmacology of Anticancer Agents, Leesburg, VA
Indiana University Cancer Center, Indianapolis, IN
4th Annual Hampton Roads Fall Cancer Conference, Portsmouth, VA
Friends of Cancer Research, Woodrow Wilson International Center for Scholars, Washington, DC
Astrazeneca Breast Cancer Symposium, Waltham, MA

2004
Breast Cancer Think Tank 14, St Kitts
Translational Conference, Johns Hopkins Oncology Center, Baltimore, MD
Breast Cancer—Bench to Bedside, Loyola University, Chicago, IL
Massachusetts General Hospital, Boston, MA
4th European Breast Cancer Conference, Hamburg, Germany
American Association for Cancer Research, Orlando, FL
The Philip A. Tumulty Topics in Clinical Medicine at Johns Hopkins, Baltimore, MD
Medical Grand Rounds, University of Florida—Shands Medical School, Gainesville, FL
Henry Lemon Memorial Lecture, University of Nebraska—Eppley Cancer Center, Omaha, NE
Discussant, Best of Oncology Symposium, American Society of Clinical Oncology, New Orleans, LA
6th Milan Breast Cancer Symposium, Milan, Italy
Gordon Conference on Molecular Therapeutics of Cancer, New London, NH
7th Annual Mission Conference of the Susan G. Komen Breast Cancer Foundation, Washington, DC
George Washington University Hematology-Oncology Board Review Course, Alexandria, VA
Cancer Education Consortium Clinical Pharmacology of Anticancer Agents, Leesburg, VA
6th Lynn Sage Breast Cancer Symposium of Northwestern University, Chicago, IL
Alta Bates Summit Medical Center, Berkeley, CA
Association of Northern California Oncologists, San Francisco, CA
4th American Association for Cancer Research Prevention Meeting, Seattle, WA
Project LEAD, National Breast Cancer Coalition, Washington, DC
Mayo Clinic Oncology Society, Rochester, MN
Department of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic, Rochester, MN
Career Day, Baltimore Polytechnic Institute, Baltimore, MD
2nd Breast Cancer Inter-SPORE Meeting, Chapel Hill, NC
27th Annual San Antonio Breast Cancer Symposium, San Antonio, TX

2005
Greenebaum Cancer Center, University of Maryland Medical School, Baltimore, MD
Breast Cancer Think Tank 15, Curacao
22nd Miami Breast Cancer Symposium, Miami, FL
Lorne Cancer Conference, Phillip Island, Australia
Delaware Oncology Society, Wilmington, DE
New Strategies in Breast Cancer Conference, Philadelphia, PA
Educational Symposium, American Society of Clinical Oncology, Orlando, FL
Highlights of the Day Symposium, American Society of Clinical Oncology, Orlando, FL
National Breast Cancer Coalition Fund Annual Advocacy Conference, Washington, DC
Third International Symposium on the Molecular Biology of Breast Cancer, Molde, Norway
Breast Cancer: Current Controversies and New Horizons, Harvard Medical School, Boston, MA
New England Journal of Medicine Clinical Pathologic Conference, Harvard Medical School, Boston, MA
Hematology-Oncology Board Review, George Washington University Medical Center, Washington, DC
Frances Bull Lecture, University of Michigan, Ann Arbor, MI
University of Minnesota Cancer Center, Minneapolis, MN
50th Anniversary Avon Foundation Symposium, New York City, NY
Cancer Education Consortium Clinical Pharmacology of Anticancer Agents, Leesburg, VA
100 Women Professors Symposium, Johns Hopkins, Baltimore, MD
Working Group on Translational Epigenetics in Cancer, National Cancer Institute, Bethesda, MD

2006
Mayo Clinic, Rochester, MD
Helen Padykula Lecture, Wellesley College, Wellesley, MA
Lynne Abraham Symposium, Susan G. Komen Foundation, New York City, NY
Third Current Concepts in the Multidisciplinary Management of Breast Cancer, Johns Hopkins, Baltimore, DC
5th Santiago Breast Cancer Symposium, Santiago, Chile
8th Milan Breast Cancer Symposium, Milan, Italy
International Union Against Cancer (UICC) World Cancer Congress, Washington, DC
8th Lynn Sage Breast Cancer Symposium, Chicago, IL
Hematology-Oncology Board Review, George Washington University Medical Center, Washington, DC
Cancer Education Consortium Clinical Pharmacology of Anti-Cancer Agents, Leesburg, VA
44th Meeting of the Japan Society of Clinical Oncology, Tokyo, Japan
National Comprehensive Cancer Network Adjuvant Therapy in Breast Cancer Symposium, Baltimore, MD
Women’s Board, Johns Hopkins Hospital, Baltimore, MD
National Cancer Institute-Ft. Detrick Distinguished Scientist Seminar, Frederick, MD
Science Lecture Series 2006-7 Radcliffe Institute for Advanced Study, Cambridge, MA

2007
Johns Hopkins Workshop on Clinical Targeting of Epigenetic Changes in Cancer Treatment, Phoenix, AZ
24th Annual Miami Breast Cancer Conference, Miami, FL
6th Annual Mid-Atlantic Oncology Update, St Agnes Hospital, Baltimore, MD
10th International Conference on Primary Therapy of Early Breast Cancer, St. Gallen, Switzerland
Breast Cancer Think Tank 17, Playa del Carmen, Mexico
Annual Advances in Basic Science Symposium, Northwestern University Cancer Center, Chicago, IL
American Society of Clinical Oncology Education Symposium, Chicago, IL
10th Komen Mission Conference, Washington, DC
St Joseph’s Hospital, Baltimore, MD
Australia-New Zealand Breast Cancer Clinical Trials Annual Meeting, Alice Springs, Australia
National Cancer Advisory Board, Bethesda, MD
Hematology-Oncology Board Review, George Washington University Medical Center, Washington, DC
CR-UK Cambridge Research Institute Plenary Lecture, 3rd National Cancer Research Institute Conference, Birmingham, UK
President’s Cancer Panel, San Diego, CA
Scientific Symposium, Breast Cancer Research Foundation, New York City, NY
Florida Oncology Society, Orlando, FL
Collaborative Summit on Breast Cancer Research, Foundation for the NIH, Lansdowne, VA
American Association of Cancer Research Prevention Symposium, Philadelphia, PA

2008
7th Rosalind E. Franklin Award for Women in Science, National Cancer Institute, Bethesda, MD
Breast Cancer Think Tank 18, Waikaloa, HI
Cancer Institute of New Jersey, New Brunswick, NJ
5th Early Detection Research Network Scientific Workshop, National Cancer Institute, Bethesda, MD
Vanderbilt-Ingram Comprehensive Cancer Center, Nashville, TN
11th American Association for Cancer Research-Women in Cancer Research Charlotte Friend Award, San Diego, CA
14th Annual Educational Symposium, Susan G. Komen for the Cure Maryland, Baltimore, MD
4th Current Concepts in the Multidisciplinary Management of Breast Cancer, Johns Hopkins University, Baltimore, MD
Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA
Best of ASCO, Boston, MA
Annual Meeting of the American Association for Clinical Chemistry, Washington, DC
Seventh International Congress on the Future of Breast Cancer, Kauai, HI
Nuclear Hormone Receptors, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY
Hematology-Oncology Board Review, George Washington University, Washington, DC
Fourth Annual Oncology Congress, San Francisco, CA
Oberstar Lecture, George Washington University, Washington, DC

2009
Breast Cancer Think Tank 19, Costa Rica
Bernard Fisher Lecture, University of Pittsburgh, Pittsburgh PA
11th International Congress Oncology Conference on Primary Therapy of Early Breast Cancer, Saint Gallen, Switzerland
Grand Rounds, MD Anderson Cancer Center – Houston TX
Women Leading the Way, MD Anderson Cancer Center, Houston, TX
Jean Sindab Lecture, Emory Winship Cancer Institute, Atlanta, GA
Oncology Grand Rounds, Ohio State University, Columbus, OH
16th Annual Pennsylvania Bar Association Women in the Profession, Pittsburgh, PA
American Society of Clinical Oncology Educational Symposium, Orlando, FL
24th Annual Aspen Cancer Conference, Aspen, CO
Harvard Breast Cancer Conference, Boston, MA
Medical Grand Rounds, UPMC Shadyside Hospital, Pittsburgh, PA
University of Pittsburgh Postdoctoral Association Data and Dine Lecture, Pittsburgh, PA
Women's Studies and the Provost's Advisory Committee on Women's Concerns New Faculty Lecture, University of Pittsburgh, Pittsburgh, PA
Pancreasfest 2009, University of Pittsburgh, Pittsburgh, PA
AACR Advances in Breast Cancer Research, San Diego, CA
Cincinnati Cancer Symposium, Jensen Symposium on Nuclear Receptors, Cincinnati, OH
Translating Scientific Advances into Clinical Care Cancer, Lineberger Comprehensive Cancer Center, Chapel Hill, NC
New Options in Breast Cancer Treatment, UPMC Cancer Centers, Johnstown, PA

2010
University of Pittsburgh Winter Academy, Naples, FL
Achievement Rewards for College Scientists, Pittsburgh, PA
Medical Grand Rounds, UPMC Montefiore University Hospital, Pittsburgh, PA
Katz Lecture, Magee Womens Hospital of Pittsburgh, Pittsburgh, PA
NYU Cancer Institute Seminar Series, New York, NY
The Regional Cancer Center, Erie, PA
Lesses Visiting Professor, Medical Grand Rounds, Beth Israel Deaconess Medical Center, Boston, MA
Hematology-Oncology Grand Rounds, Beth Israel Deaconess Medical Center, Boston, MA
University of Maryland Marlene and Stewart Greenebaum Cancer Center, Hormone Responsive Cancer Program Retreat, Baltimore, MD
Lois O'Grady Breast Cancer Lecture, University of California Davis Cancer Center, Sacramento, CA
11th Annual Advances in Oncology, University of California Davis Cancer Center, Sacramento, CA
American Society of Clinical Oncology Breast Cancer Symposium - Gianni Bonadonna Award, Washington, DC
Advances in Oncology, Keynote speaker, UPMC Beacon Hospital, Ireland
Oncology Grand Rounds, Thomas Jefferson University Kimmel Cancer Center, Philadelphia, PA

2011
Dept of Environmental & Occupational Health, University of Pittsburgh, Pittsburgh, PA
Department of Pharmaceutical Sciences, University of Pittsburgh, Pittsburgh, PA
Breast Cancer Program Retreat, UCSF Cancer Center, San Francisco, CA
Lineberger Cancer Center, UNC Chapel Hill, Chapel Hill, NC
XI Michelangelo Foundation Seminar, Milan Italy
Georgetown University, Undergraduate Research Conference Keynote Speaker, Washington, DC
City of Hope Cancer Center Grand Rounds, Duarte, CA
Cleveland Clinic Grand Rounds, Taussig Cancer Center, Cleveland, Ohio
McArdle Laboratory Seminar, University of Wisconsin, Madison, WI
13th Milan Breast Cancer Conference, Milan, Italy
Annual Meeting, American Society of Clinical Oncology, Chicago, IL
International Cancer Conference, Trinity Medical School, Dublin, Ireland
Fifth Annual R.MED Scientific Symposium, Palermo, Italy
Medical Oncology Board Review, George Washington University, Washington, DC
Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA
Department of Pharmacology and Chemical Biology, University of Pittsburgh, Pgh, PA
San Antonio Breast Cancer Symposium, San Antonio, TX

2012
Breast Cancer Think Tank 22, Mexico
Siteman Cancer Center at Washington University, Saint Louis, MO
Miami Breast Cancer Conference, Miami, FL
University of Pittsburgh Department of Pathology, Pittsburgh, PA
American Society of Preventive Oncology, Washington, DC
Tsinghua University, Beijing, China
University of Pittsburgh, Chancellors Inaugural Lecture - Hillman Professor of Oncology, Pittsburgh, PA
University of Chicago Cancer Biology Seminar Series, Chicago, IL
Johns Hopkins University School of Medicine, Baltimore, MD
American Society of Clinical Oncology, Chicago, IL
34th Annual Scientific Meeting, Australia-New Zealand Breast Cancer Trials Group, Hobart, Australia
Medical Oncology Board Review, George Washington University, Washington, DC
University of Texas Southwestern, Pamela Hearn Isom Lecture, Medicine Grand Rounds, Dallas Texas
Potamkin Lecture, PA Breast Cancer Coalition Conference, Harrisburg, PA
Northwestern University Feinberg School of Medicine's 16th Annual Department of Pathology Joseph C. Calandra Lecture, Chicago, IL
The Shanghai Breast Cancer Symposium, Shanghai, China

2013
Bay City Capital Scientific Advisory Board Meeting
13th International Congress Oncology Conference on Primary Therapy of Early Breast Cancer, St. Gallen, Switzerland
Annual Meeting, American Association of Cancer Research, Washington, DC
Case Western Reserve Comprehensive Cancer Center, Cleveland, Ohio
Medical Oncology Board Review, George Washington University, Washington, DC
The Hong Kong University of Science and Technology, Tetralateral Symposium, Hong Kong
PA Cancer Planning Summit, Pittsburgh, PA
Breast Cancer Symposium, San Francisco, CA
Cancer Caucus, House of Representatives, Harrisburg, PA
Science 2013, Pittsburgh, PA
Global Breast Cancer Conference, Seoul, South Korea

2014
Annual Meeting, American Association for Cancer Research, San Diego, CA
American Society of Clinical Oncology, Chicago, IL
German Cancer Research Center (DKFZ), Heidelberg, Germany
Medical Oncology Board Review, George Washington University, Washington, DC
National Cancer Advisory Board, Bethesda, MD
International Oncology Symposium, Astana, Kazakhstan
University of Chicago Simon M. Shubitz Lecture, Chicago, IL
Congressional Briefing, Alliance for Health Reform, Washington, DC
San Antonio Breast Cancer Conference, San Antonio, TX

2015
14th St. Gallen International Breast Cancer Conference, Primary Therapy of Early Breast Cancer, Vienna, Austria
Pediatric Hematology/Oncology Pediatric Hematology/Oncology BMT & CT Conference, Childrens Hospital of Pittsburgh, Pittsburgh, PA
University of Pittsburgh, Winter Academy, Palm Beach, Florida
The Wistar Institute, Distinguished Lecture, Philadelphia, PA
Annual Meeting, American Association for Cancer Research, Philadelphia, PA
Inaugural Lecture as Distinguished Professor of Medicine, University of Pittsburgh, Pittsburgh PA
Stephen D Williams, MD Lectureship, Indiana University Simon Cancer Center, Indianapolis, IN
Medical Oncology Board Review, George Washington University, Washington, DC
ASCO 2015 Breast Cancer Symposium, San Francisco, CA
Taipei Medical University, Taipei, Taiwan
Eighth Annual Robert B. Dickson Memorial Lectureship, Georgetown University Lombardi Cancer Center, Washington DC
First Gabriel Hortobagyi Lecture, MD Anderson Cancer Center, Houston, TX
Lynn Sage Distinguished Lecture, Robert H. Curie Comprehensive Cancer Center of Northwestern University, Chicago, IL

2016
University of Pittsburgh, Winter Academy, Palm Beach, Florida
American Association for Cancer Research (AACR), 2016 Annual Meeting, New Orleans, LA
American Society of Clinical Oncology (ASCO), 2016 Annual Meeting, Chicago, IL
Maryland Breast Cancer Consortium, Baltimore, MD
AACR High Tech Strategic Business Meeting, Sunnyvale, CA
Medical Oncology Board Review, George Washington University, Washington, DC
Great Lakes Breast Cancer Symposium, University of Pittsburgh, Pittsburgh, PA
Seattle Cancer Care Alliance, Dutch Harbor, Alaska
2016 Cooper Lecture, University of Pittsburgh, Pittsburgh, PA

2017
AACR New Frontiers in Cancer Research, Cape Town, South Africa
The David & Lyn Silfen University Forum, A Formidable Foe: Cancer in the 21st Century, Philadelphia, PA
American Association of Cancer Research (AACR), 2017 Annual Meeting, Washington, DC
Fred Hutchinson Cancer Research Center, HICOR Value in Cancer Care Summit, Seattle, WA
American Society of Clinical Oncology (ASCO) 2017 Annual Meeting
Fred Hutchinson Cancer Research Center Breast Cancer Program
Medical Oncology Board Review, George Washington University, Washington, DC
Cambridge Cancer Institute, University of Cambridge, Cambridge, UK
Breast Cancer Research Foundation Symposium, New York City, NY
University of Washington Thoracic and Breast Malignancies Symposium, Seattle, WA
Gene expression profile testing of cancer tissue

Emily Transue, MD, MHA
Associate Medical Director, WA Health Care Authority

March 16, 2017

Background

- 40% of Americans will receive a cancer diagnosis over a lifetime
- 20% of Americans will die from cancer
- Increasing number of patients are being detected at early stages, where risk for progression and need for aggressive treatment is unclear
- Gene expression profile testing (GEP) identifies groups of genes in cancer tissue that predict risk of progression and metastasis
- Clearer prognostic information can strongly influence a patient’s choices about chemotherapy and other treatment
Gene expression profile testing: use case

• Assesses expression of genes in cancer tissue to clarify risk of progression/metastasis
  NOT:
  – Screening of individual’s genome to determine risk of developing cancer
  – Testing for sensitivity to specific chemo agents

• Typical use is to determine whether adjuvant therapy* is needed to reduce recurrence risk

* Therapy beyond the initial cancer treatment; i.e., chemo or hormone therapy after surgical resection.

Stages of care

• Diagnosis (biopsy)
• Risk assessment: Staging, etc.
• Treatment decision
• Outcome (short term)
• Outcome (long term)
Stages of care

- Diagnosis (biopsy)
- Risk assessment: staging, etc.
  - Size, grade, tumor markers, GEP
- Treatment:
  - Preference-sensitive decisions informed by prognosis, weighing pros and cons of treatment
- Outcome
  - Short term: side effects, work loss, etc.
  - Long-term: recurrence risk, side effects, survival

Adjuvant therapy: Risks and side effects

- Chemotherapy (varies by agent):
  - Neuropathy (may be permanent)
  - Cardiotoxicity (may be permanent)
  - Fatigue, nausea, malaise, hair loss
  - Work loss

- Endocrine therapy (varies by agent):
  - Elevated risk of blood clots/DVT/PE
  - Sexual dysfunction
  - Menopausal symptoms in women
  - Impact on bone density and fracture risk

For the purposes of this presentation:
- “Chemotherapy” refers to cytotoxic therapy
- “Endocrine therapy” refers to hormonal modulation therapy
**Treatment decisions**

**Active Surveillance (AS):**
- Avoid risks and side effects of treatment
- No decrease in recurrence risk

**Adjuvant Therapy:**
- Risks vary by aggressiveness of therapy
- Decreased recurrence risk proportional to baseline risk (i.e., benefit depends on prognosis)

---

**Treatment decisions: Hypothetical example**

**Chemotherapy regimen X:**
- Reduces relative recurrence risk by 50%
- Nausea, fatigue and work loss for 3 months are typical
- Permanent neuropathy occurs in 15%

**Patient A:**
- 30% recurrence risk
- Chemotherapy X reduces absolute recurrence risk by 15%, balanced against above side effects/risks

**Patient B:**
- 6% recurrence risk
- Chemotherapy X reduces absolute recurrence risk by 3%, balanced against above side effects/risks
Sample report (Oncotype Dx)

Gene expression profile: theory of impact

- GEP result predicts prognosis/recurrence risk (enhances existing staging data)
- Altered baseline risk impacts treatment recommendations
- Recommendations impact treatment selected
- Treatment selection impacts patient experience/outcomes
  - Short term (side effects, etc.)
  - Long term (recurrence, survival)
Gene expression profile: testing impact

Question 1: • Does GEP predict prognosis/recurrence risk?
Question 2: • Does GEP impact treatment recommendation?
Question 3: • Does GEP impact treatment selection?
Question 4: • Does GEP impact patient experience/outcomes?
   4a — Short term (side effects, etc.)
   4b — Long term

Clinical validity vs. Clinical utility

• Clinical validity: Does the test do what it says it does?
  — Is it correct?
  — In this case, does the GEP add prognostic information beyond existing data? (Question 1)

• Clinical utility: Does the test impact treatment decisions and/or outcomes?
  — Does it matter?
    1. Does testing impact treatment selection? (Questions 2, 3)
    2. Does it impact risks and outcomes (includes therapy and disease)? (Questions 4a, 4b)
Tests

Gene expression profile testing of cancer tissue to inform treatment decisions:

**Breast Cancer** —
- Oncotype DX Breast Cancer Assay, EndoPredict, MammaPrint,
- Prosigna Breast Cancer Prognostic Gene Signature Assay (PAM50), Mammostrat, Breast Cancer Index (BCI)

**Prostate Cancer** —
- Prolaris, Decipher, Oncotype DX Prostate Cancer Assay

**Colon Cancer** —
- Oncotype DX Colon Cancer Assay, ColoPrint

**Multiple Myeloma** —
- Myeloma Prognostic Risk Signature (MyPRS), SKY92-signature (formerly EMC92)

Current state agency policy

- **PEBB** PreAuth
- **HCA/MCO Medicaid:** PreAuth; Expedited Pre-Auth for Oncotype Dx and Mammaprint
- **Labor and Industries** No policy
Agency Medical Director Concerns

Safety = Medium
Efficacy = Medium High
Cost = High

2015 – 2017 Claims for gene expression profile

PEBB/UMP (No Medicare)

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<td>Colon Cancer</td>
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<tr>
<td>Multiple Myeloma</td>
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Medicaid HCA and Medicaid MCO

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<tr>
<td>Prostate</td>
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2015 - 2017 Medicaid MCO and Medicaid HCA Utilization CPT Code 81519

Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score

2015-2017 PEBB/UMP Utilization CPT Code 81519

Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin-embedded tissue, algorithm reported as recurrence score
Breast cancer
Gene expression profile tests

Oncotype Dx data (Breast, 21 gene)

- Population: LN- or 1-3 LN+; ER+; HER-
- Clinical validity: High (per Blok et al)
- Impact on treatment recommendation: High
  - 21-74% of patients had change in recommendation
  - Roughly 3:1 ratio of reduced intensity to increased intensity of rx
- Impact on patient choice: High
  - Cohort studies showed pts with test had less chemo than those w no test
- Impact on long term recurrence: No data
- Subsets: Pts w int. score did better with hormone rx than chemo
- Data quality: 64 studies; bias risk ranged from low to high; all directionally similar
Treatment intensity recommendation impact

Clinical recurrence risk assessment (before testing)

Recurrence risk assessment after testing

% recurrence risk

Typically recommend no chemo
Typically recommend chemo

Mammaprint (Breast, 70 gene)

- Population: LN- or 1-3 LN+; ER+; HER-
- Clinical validity: High (per Blok et al)
- Impact on treatment recommendation: High
  - 10-51% of patients had change in recommendation
  - ~3:1 ratio of reduced intensity to increased intensity; 10% less chemo
- Impact on patient choice: High
  - 90-91% followed recommendation
- Impact on long term recurrence:
  - For women with low clinical and high genomic risk or vice versa, 5 year met-free survival similar with or without chemo
- Misc: Increased MD confidence in rec 78.6% of the time
- Data quality: 8 studies; bias risk high
Prosigna PAM 50 (Breast, 50 gene)

- Population: Early stage breast cancer
- Clinical validity: High (per Blok et al)
- Impact on treatment recommendation: High
  - 18% of patients had change in recommendation
  - ~3:1 ratio of reduced intensity to increased intensity
- Impact on long term recurrence: No data
- Data quality: 3 studies, 608 pts, mod bias risk

Endopredict (Breast, 12 gene)

- Population: Early stage breast cancer
- Clinical validity: High (per Blok et al)
- Impact on treatment recommendation: High
  - 37.7% of patients had change in recommendation
  - ~2:1 ratio of reduced intensity to increased intensity
- Impact on long term recurrence: No data
- Data quality: 1 study, 167 pts, mod bias risk
Breast Cancer Impact (BCI) (Breast, 7 gene)

- Population: Women who have had 3.5+ years of adjuvant hormone rx, deciding about additional hormone rx
- Impact on treatment recommendation: High
  - 27% of patients had change in recommendation
  - ~3:1 ratio of less aggressive rx to more aggressive rx
- Impact on long term recurrence: No data
- Data quality: 1 study, 26 pts

Mammostrat (Breast, 5 protein immunoassay)

- Population: Women with early stage cancer randomized to adjuvant Tamoxifen therapy
- Evaluated benefit of tamoxifen relative to Mammostrat score range (high, medium, or low risk)
  - Low risk patients had a 5% absolute improvement in recurrence free survival with Tamoxifen
  - Mod risks patients had no benefit (unexpected result)
  - High risk patients had a 21% absolute improvement
- 1 study, 711 women
Cost impact estimates: Breast GEP (con’t)

• Wide variation in estimates including net positive and net negative impact on costs
• Cost/QALY generally within acceptable ranges
• Quality of evidence low to very low

Guidelines

• 5/5 support Oncotype Dx
• 3/5 support Mammaprint, Endopredict, Prosigna
• 2/5 support BCI in LN-
• None support Mammastrat
• Typically require:
  — Early stage CA (stage 1 or 2)
    • ER positive (sometimes also PR positive)
    • HER2-NEU negative
    • LN negative or 1-3 positive
  — Test results will impact treatment decisions
Payer Policies: Breast GEP

- No Medicare National Coverage Determinations (NCD)
- Local Coverage Decisions (LCD) for WA
  - Provide coverage for Endopredict, Prosigna, and BCI
  - No LCDs for Oncotype x, Mammaprint, or Mammostrat
- Aetna, Cigna, and Regence:
  - All cover Oncotype Dx
  - Two cover Mammaprint, Endopredict, Prosigna, and BCI
  - None cover Mammostrat

Prostate cancer
Gene expression profile tests
Oncotype Dx (Prostate, 17 gene)

- Population: Men with positive bx or surgery deciding about further therapy
- Clinical validity: High significance (Canfield et al), but not a large impact (Brand et al)
- Impact on treatment recommendation: High
  - Range: 11-59% of patients had change in recommendation
  - ~2:1 ratio of reduced intensity to increased intensity
- Impact on patient choice: AS increased 24% with test
- Impact on long term recurrence: No data
- Data quality: 4 studies, high risk of bias


Prolaris (Prostate, 46 gene)

- Population: Men with positive bx deciding about further therapy
- Clinical validity: High (Canfield et al)
- Impact on treatment recommendation: High
  - 37-48% of patients had change in recommendation
  - ~3:1 ratio of reduced intensity to increased intensity
- Impact on long term recurrence: Unknown
- Data quality: 2 studies
Decipher (Prostate, 22 gene)

• Population: Men considering adjuvant treatment after radical prostatectomy
• Clinical validity: High (Canfield, Spratt)
• Impact on treatment recommendation: High
  – Range: 18-42% of patients had change in recommendation
  – Roughly equal ratio of less aggressive rx to more aggressive rx
• Impact on long term recurrence: No data
• Misc: Decreased decisional conflict
• Data quality: 2 studies

Prostate GEP: Cost impact

• Polaris: Ontario HTA estimated test increased costs for province (mod bias risk)
• Decipher (Lubo et al): Increased cost $5,453 per pt, QALY 0.066, cost/QALY $90K (high bias risk)
• Oncotype (Abala et al): Decreased cost $2,286 relative to historical costs (high bias risk)
Prostate Guidelines

• American Urological Association, American Society for Radiation Oncology, and Society of Urologic Oncology, 2017
  – “...Have not shown a clear role in active surveillance for localized prostate cancer.”

• National Comprehensive Cancer Network, 2017
  – Recommend Decipher after prostatectomy with specific criteria
  – Recommend Prolaris and Oncotype Dx for low risk patients...who are candidates for AS or definitive rx

Payer Policies: Prostate GEP

• No Medicare National Coverage Determinations (NCD)
• Local Coverage Decisions (LCD) for WA
  – Coverage with conditions for Decipher, Prolaris, and Oncotype Dx
  – Decipher: Radical prostatectomy w/in 5 yrs, PSA nadir after surgery, no meds or neoadjuvant rx, adverse surgical pathology
  – Prolaris and Oncotype Dx: localized, under 5 mm, low or very low risk stage OR favorable intermediate risk (Prolaris only); used to determine treatment, etc.

• Aetna, Cigna, and Regence:
  – No coverage, or not included on list of medically necessary tests
Colon cancer
Gene expression profile tests

- Population: Stage 2 disease, considering adjuvant rx
- Clinical validity: Unestablished (per NCCN guideline)
- Impact on treatment recommendation: High
  - Increased intensity for 11.4%
  - Decreased intensity for 32.9%
- Impact on patient choice:
  - Increased intensity for 9.7%
  - Decreased intensity for 28.3%
- Impact on long term recurrence: Unknown
- Data: 2 studies
Colon: Cost impact

- Alberts et al (mod bias risk)
- Pts with stage 2 colon CA
- Slightly lower lifetime costs with testing than without ($103,775 with, $104,767 without; $991 savings)

Colon policies and guidelines

- No clinical practice guidelines with recommendations
- NCCN guideline (fair quality):
  - “There is no evidence of predictive value...”
Guidelines and Policies: Colon GEP

• No Medicare National Coverage Determinations (NCD)
• No Local Coverage Decisions (LCD) for WA
• Aetna, Cigna, and Regence:
  – No coverage

Multiple Myeloma
Gene expression profile tests
Multiple Myeloma GEP

- Clinical validity: Unclear whether test adds prognostic information beyond clinical prediction
- Clinical utility: No studies available
- NCCN guidelines: No recommendations
  - “Could be helpful in selected patients”
- European Society for Medical Oncology:
  - “More research is needed”
- Payer policies: Medicare, Aetna, Cigna, Regence
  - Either not covered or not mentioned

Gene Expression Profile: Testing Impact

**Question 1:**
- Does GEP predict prognosis/recurrence risk?

**Question 2:**
- Does GEP impact treatment recommendation?

**Question 3:**
- Does GEP impact treatment selection?

**Question 4:**
- Does GEP impact patient experience/outcomes?
  - 4a — Short term (side effects, etc.)
  - 4b — Long term
Question 1: Do GEP results add significant information about prognosis/recurrence risk?

- Varies by test
- Strongest data is for breast GEPs including Oncotype Dx breast, Endopredict, Prosigna, and Mammaprint
- Multiple studies in prostate
- Not well supported for colon or multiple myeloma

Question 2: Does GEP impact treatment recommendations?

- Strong evidence for high impact on treatment recommendations for breast and prostate testing
- Only one study in colon cancer, also appears to have high impact on treatment recommendation
- No data for multiple myeloma
Question 3: Does GEP impact treatment selection?

- Limited data shows high correlation between treatment recommended and treatment selected

Question 4: Does GEP impact patient experience/outcomes?

- Question 4A: Short term (side effects, etc).
- Question 4B: Long term

- 4A: Extensive evidence that many patients choose to forego adjuvant chemo or hormone therapy with associated risks and side effects based on testing. A smaller number choose more aggressive treatment based on testing.

- 4B: Only evidence available is one trial showing patients with high clinical risk and low Mammaprint score can safely forego chemotherapy
Recurrence risk assessment (before testing)

% recurrence risk

0  5  10  15  20  25  30  35

Typically recommend no chemo

Typically recommend chemo

Gene Expression Profile: Testing Impact

Variable:
• GEP result predicts prognosis/recurrence risk
• GEP impacts treatment recommendations
• GEP impacts treatment selection
• GEP impacts patient experience/outcomes

YES
• Short term (side effects, etc.)

UNKNOWN
• Long term

Cost impact: High variability of estimates including directionality of impact (cost savings or increase)
Treatment decisions

Active Surveillance (AS):
- Avoid risks and side effects of treatment
- No decrease in recurrence risk

Adjuvant Therapy:
- Risks vary by aggressiveness of therapy
- Decreased recurrence risk proportional to baseline risk (i.e., benefit depends on prognosis)

Proposed decision rubric

- Value of testing to patients and providers as an aid to informed decision making about the relative benefits of adjuvant therapy is high.
  - Demonstrated by high impact on treatment recommendations and decisions in nearly all studies
  - Adjuvant rx carries significant short-term and long-term impact on symptoms and quality of life
- Definitive impact on long-term outcomes is unlikely to be available given time frames and barriers to study
- Given the high value to patients and providers in the setting of preference-sensitive decisions, deferring coverage until/unless this level of evidence becomes available is unreasonable
- Tests should be covered if there is high evidence of clinical validity and of impact on decision making
AMDG Recommendation: Breast GEPs

- **Oncotype DX, Endopredict, Prosigna and Mammaprint:**
  - Cover with conditions
  - Early stage CA (stage 1 or 2)
    - ER positive, HER2-NEU negative
    - LN negative or 1-3 LN positive
  - Test results will impact treatment decisions

- **Mammostrat and BCI:** Cover with conditions
  - Only for women with stage 1-2 deciding about hormone rx

- **Other breast cancer tests/indications:**
  - Covered at agency discretion in the future if developers can show prognostic equivalence or superiority to the above tests

AMDG Recommendation: Prostate GEPs

- Cover with conditions
- **Oncotype DX, Prolaris:** Cover with conditions
  - Early stage disease
  - Test results will impact treatment decisions
- **Decipher:** Cover with conditions
  - Men deciding between active surveillance and adjuvant or salvage radiotherapy after radical prostatectomy
  - Test results will impact treatment decisions
AMDG Recommendation: Other GEPs

- Colon GEPs:
  - Recommend non-coverage
  - Evidence is insufficient to support coverage
- Multiple Myeloma GEPs:
  - Recommend non-coverage
  - Evidence is insufficient to support coverage

Questions?

More information:
Emily.Transue@hca.wa.gov
Order of scheduled presentations:

Gene expression profile testing of cancer tissue

<table>
<thead>
<tr>
<th></th>
<th>Name</th>
<th>Myriad Genetic Laboratories</th>
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<tbody>
<tr>
<td>1</td>
<td>Devki Saraiya MS, CGC,</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Karen Heller, MS, CGC,</td>
<td></td>
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Disclosure

Any unmarked topic will be considered a “Yes”

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<td>2. Equity interests such as stocks, stock options or other ownership interests.</td>
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<td>3. Status or position as an officer, board member, trustee, owner.</td>
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<td>5. Research funding.</td>
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If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

Myriad Genetic Laboratories employee

#6: travel arrangements

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<tr>
<td>funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).</td>
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If yes to #7, provide name and funding Sources: representing Myriad Genetic Laboratories

If you believe that you do not have a conflict, but are concerned that it may appear that you do, you may attach additional sheets explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest form and that the information I have provided is true, complete, and correct as of this date.

X [Signature] 2/22/18 [Print Name]

So we may contact you regarding your presentation, please provide the following:

Email Address: dsaraiya@myriad.com

Phone Number: 206-240-4340
Prostate Cancer Gene Expression Profile Tests

Devki Saraiya, MS, CGC
Certified Genetic Counselor
Myriad Genetic Laboratories
### Levels of evidence in the Simon et al. evidentiary framework

<table>
<thead>
<tr>
<th>LOE</th>
<th>DESCRIPTION</th>
<th>REQUIREMENTS</th>
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| I   | Practice-changing. The biomarker reliably influences clinical treatment decisions. | **One “Category A“ study:** PRCT that tests the biomarker’s prognostic or predictive value.  
-or-  
**At least two “Category B“ studies with consistent results:**  
- Utilizes archived samples from a prospective clinical trial not specifically designed to test the biomarker.  
- Both studies must be designed, conducted, and analyzed in a similar manner. |
| II  | Category C studies meeting LOE II could be sufficient to change practice under “particularly compelling circumstances.” | **One “Category B“ study**  
-or-  
**Three* or more independent “Category C“ studies that provide consistent results**  
- Utilizes archived samples from patients enrolled in a prospective observational registry with specimen collection, treatment, and follow-up dictated by standard of care.  
- Requires careful assessment to rule out confounding or selection bias.  
- At least two validation studies must be designed, conducted, and analyzed in a similar manner. |

*One development study + two validation studies
Simon et al. Applied to Prostate Cancer

- Two “compelling circumstances” qualify PCa as a condition warranting practice change using a validated LOE II prognostic biomarker

**Over-treatment:** In the United States, providers lack trust in current clinicopathologic measures to guide selection between active surveillance (AS) and interventional treatment, i.e., radical prostatectomy or radiation therapy. This often results in interventional treatment for patients who do not need it (Andriole et al., 2009; Chou et al., 2011; Welch et al., 2009)

**Long natural history of PCa:** The indolent, slow-growing nature of most prostate tumors presents challenges to completing prospective, randomized biomarker trials in a time-efficient, cost-efficient, and ethical manner. LOE I is not achievable for PCa prognostics within the current paradigm. Based on an 80% power to detect a statistically significant 25% difference in PCa death, it is estimated that a 5-year study would require between 33,000 and 43,000 subjects with low-risk PCa (Myriad internal analysis).


Treatment Outcomes from Two Landmark Trials

Treatment of Localized Prostate Cancer Does NOT Improve Mortality Outcomes\(^1,\(^3\)

---

**Death from Prostate Cancer**
\[ n = 731 \]

**Prostate-Cancer-Specific Survival**
\[ n = 1643 \]

---

“...studies suggest that all of the major management options produce very similar rates of survival.”

---

“...death from prostate cancer [...] remained low at a median of 10 years of follow-up, at approximately 1%, irrespective of the treatment assigned...”

---


Chain-of-Evidence for Prolaris
Improving Outcomes by Reducing Morbidities

01

Localize
don prostate cancer
is overtreated

02

Prolaris is better predictor of
oncologic endpoints &
decreases overtreatment

03

Reduced
intervention
reduces
associated
morbidities

04

Without
increasing
mortality

05

Driving cost
and medical
resource savings


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<tr>
<td>1. Salary or payments such as consulting fees or honoraria in excess of $10,000.</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>2. Equity interests such as stocks, stock options or other ownership interests.</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>3. Status or position as an officer, board member, trustee, owner.</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>4. Loan or intellectual property rights.</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>5. Research funding.</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>6. Any other relationship, including travel arrangements.</td>
<td>✓</td>
<td></td>
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</tbody>
</table>

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

**Myriad Genetic Laboratories**

**#6 = travel arrangements**

<table>
<thead>
<tr>
<th>Potential Conflict Type</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>7. Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government).</td>
<td>✓</td>
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</tbody>
</table>

If yes to #7, provide name and funding sources:

**Myriad Genetics - commercial products**

If you believe that you do not have a conflict, but are concerned that it may appear that you do, you may attach additional sheets explaining why you believe that you should not be excluded.

I certify that I have read and understand this Conflict of Interest form and that the information I have provided is true, complete, and correct as of this date.

**X**

2/13/18

Karen Heller

Date

Print Name

So we may contact you regarding this information, please provide the following:

Email Address: karenheller@myriad.com

Phone Number: 214-789-5014
**EndoPredict: Gene Expression Test for Breast Cancer**

Karen Heller, MS, CGC  
Certified Genetic Counselor  
Medical Policy Manager  
Myriad Genetic Laboratories

**Targeted patients**  
- ER+, HER2-  
- Node -, Node +  
- Early-stage disease

**Proven outcomes**  
- 10-year risk of DR  
- Low risk, high risk categories

**Proven prognostic power**  
- Combines molecular and clinical information
EPclin discriminates breast cancer recurrence risk better than Oncotype DX

Comparison of the Performance of 6 Prognostic Signatures for Estrogen Receptor–Positive Breast Cancer. A Secondary Analysis of a Randomized Clinical Trial. Sestak et al. JAMA Oncol 2018

Table 1. Univariate Hr’s and C Indexes for All Prognostic Signatures According to Nodal Status During Years 0 to 10

Table 2. Univariate Hr’s and C Indexes for All Prognostic Signatures According to Nodal Status During Years 5 to 10

Table 1. Requirements for a Marker-Based Test to Reach Level IB Evidence of Clinical Utility on the Basis of Prospective-Retrospective Studies

<table>
<thead>
<tr>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Adequate amounts of archived specimen must be available from enough</td>
</tr>
<tr>
<td>patients from a prospective trial (which for predictive factors should</td>
</tr>
<tr>
<td>generally be a randomized design) for analyses to have adequate statistical</td>
</tr>
<tr>
<td>power and for the patients included in the evaluation to be clearly</td>
</tr>
<tr>
<td>representative of the patients in the trial.</td>
</tr>
<tr>
<td>2. The marker-based test should be analytically and preanalytically</td>
</tr>
<tr>
<td>validated for use with archived specimens.</td>
</tr>
<tr>
<td>3. The plan for marker evaluation should be completely specified in writing</td>
</tr>
<tr>
<td>before the performance of marker assays on archived specimens and should</td>
</tr>
<tr>
<td>be focused on the evaluation of a completely defined marker-based test.</td>
</tr>
<tr>
<td>4. The results from archived specimens should be validated by using</td>
</tr>
<tr>
<td>specimens from one or more similar, but separate studies.</td>
</tr>
</tbody>
</table>

NOTE: Adapted from Simon et al.²³

EndoPredict Joins Well-Established Breast Prognostic Assays

- Inclusion in 2016 ASCO Guidelines¹

- Equivalent 1B Evidence as proposed by Simon et al.²³

- Positive recommendation from Blue Cross Blue Shield Association⁴

- Favorable Local Coverage Determination⁵

“...the panel found sufficient evidence of clinical utility for the biomarker assays Oncotype DX, EndoPredict, PAM50, Breast Cancer Index, and urokinase plasminogen activator...in specific subgroups of breast cancer.”

“...the EndoPredict assay has been assigned the level of evidence 1 according to Simon et al., this level of evidence is identical e.g. to the Oncotype DX recurrence score.”

“[Regarding EndoPredict] The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.”

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EndoPredict Joins Well-Established Breast Prognostic Assays

- Favorable Local Coverage Determination⁵

N0 or (1-3 positive nodes)

“...the panel found sufficient evidence of clinical utility for the biomarker assays Oncotype DX, EndoPredict, PAM50, Breast Cancer Index, and urokinase plasminogen activator...in specific subgroups of breast cancer.”

“...the EndoPredict assay has been assigned the level of evidence 1 according to Simon et al., this level of evidence is identical e.g. to the Oncotype DX recurrence score.”

“[Regarding EndoPredict] The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.”

“[Regarding EndoPredict] The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.”

“[Regarding EndoPredict] The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.”

MASCO has stated that healthcare providers may consider utilizing the listed tests for node-negative patients


EndoPredict®
Gene Expression Profile Testing of Cancer Tissue

Washington State Health Care Authority
Health Technology Clinical Committee
March 16, 2018

Valerie J. King, MD, MPH

Outline

- Background
- Methods and search results
- Order of presentation:
  - Evidence review by test
  - GRADE summary
  - Clinical practice guidelines
  - Payer policies
- Conditions under consideration:
  - Breast cancer tests
  - Prostate cancer tests
  - Colon cancer tests
  - Multiple myeloma tests
Background

- Lifetime risk of developing cancer is about 40%
- 1 in 5 Americans will die from cancer
- Strategies to reduce the burden of cancer include prevention, early diagnosis, improving treatment
- Common treatments for cancer are surgery, radiation therapy, chemotherapy, hormone therapy, and immunotherapy
  - Most appropriate treatments for a particular cancer depend on the cancer’s characteristics (e.g., cancer stage and grade), the patient’s age and health status, response to previous treatments, and other factors

Background

- There are a growing number of gene expression profile (GEP) tests for cancers designed to help inform treatment decisions after a cancer diagnosis
- Theoretical benefits of GEP testing:
  - More appropriate treatment decisions
  - Improved patient outcomes, including improved survival and avoidance of treatment-related side effects by forgoing unnecessary treatments
- Purpose of this evidence report is to review the clinical utility and cost-effectiveness of selected GEP tests for breast, prostate, and colon cancers and multiple myeloma
**Background**

- GEP testing identifies genes in cancer tissue making messenger RNA, which carries the genetic information that cancer cells need to make proteins
- GEP tests are designed to provide additional information for patients and clinicians
  - If a test predicts that a cancer is slow growing or unlikely to metastasize, then active surveillance could be the most appropriate course
  - If a test predicts that a cancer is likely to progress and metastasize, then more aggressive or different treatments could be warranted

**FDA Regulation**

- Molecular diagnostic tests are regulated by the U.S. Food and Drug Administration (FDA)
- FDA has exercised discretion in its requirements for approval of in vitro diagnostic assays
  - In vitro tests developed, validated, and performed in-house by a specific reference laboratory are required to abide by Clinical Laboratory Improvement Amendments (CLIA)
  - FDA clearance and approval is currently not required for these laboratory-developed tests (LDTs)
- MammaPrint and Prosigna have received FDA premarket approval
- All the other tests discussed are regulated as LDTs
Scope: PICO

- **Population**
  - Adults with breast, prostate, or colon cancers or multiple myeloma

- **Interventions**
  - Gene expression profile testing of cancer tissue to inform treatment decisions (specific tests listed on next slides)

- **Comparators**
  - Usual care without gene expression profile testing of cancer tissue, alternate gene expression profile tests (i.e., 1 test intervention listed above vs. another)

Gene Expression Profile Tests

- **Breast Cancer**
  - Oncotype DX breast (21-gene test)
  - MammaPrint (70 gene test)
  - EndoPredict (12-gene test)
  - Prosigna: PAM50 (50-gene test)
  - Breast Cancer Index (BCI)
  - Mammostrat

- **Prostate Cancer**
  - Decipher (22-gene test)
  - Prolaris (46-gene test)
  - Oncotype DX prostate (17-gene test)
Gene Expression Profile Tests

- Colon Cancer
  - ColoPrint (18-gene test)
  - Oncotype DX colon (12-gene test)

- Multiple Myeloma
  - Myeloma Prognostic Risk Signature, MyPRS (70-gene or GEP70 test)
  - SKY92, EMC92 (92-gene test)

Scope: PICO

- Outcomes
  - Clinical outcomes (e.g., morbidity, mortality, quality of life)
  - Patient management decisions (including selection of active surveillance rather than active treatment)
  - Harms, such as consequences of false-positive or false-negative test results
  - Cost-effectiveness and other economic outcomes
Scope: Key Questions

1. **Effectiveness**: What is the clinical utility of gene expression profile testing of cancer tissue to inform treatment decisions?
   a. Is there evidence that test results affect treatment decisions?
   b. Do treatment decisions guided by gene expression profile testing result in clinically meaningful improvements in patient outcomes?

2. **Harms**: What harms are associated with conducting gene expression profile testing?

3. **Special populations**: Compared with usual care, do treatment decisions, patient outcomes, or harms after gene expression profile testing of cancer tissue vary by:
   a. Patient demographics (e.g., age, sex, race/ethnicity)?
   b. Clinical history (e.g., means of diagnosis, stage or grade of cancer, results of other testing, previous treatments, chronicity)?
   c. Medical comorbidities?
   d. Provider type or care setting?

4. **What are the cost-effectiveness and other economic outcomes** of gene expression profile testing used to inform treatment management decisions?
Prognostic vs. Predictive Biomarkers
Clinical Validity vs. Clinical Utility

- A biomarker used to identify likelihood of a clinical event or disease recurrence or progression in patients who have the disease or medical condition of interest.

- A biomarker used to identify individuals who are more likely than similar individuals without the biomarker to experience a favorable or unfavorable effect from exposure to a medical product or an environmental agent.


Hierarchy of Genetic Test Evidence Development
### Clinical Utility Outcomes

- Mortality, morbidity, quality of life
- Actual treatment received
- Treatment recommendations

### Eligible Studies

- **Key Questions 1, 2, and 3:**
  - Randomized controlled trials and nonrandomized comparative studies (prospective or retrospective)
  - Systematic reviews (with and without meta-analysis) of these two types of studies

- **Key Question 4:**
  - Cost-effectiveness studies and other comparative economic evaluations
  - Systematic reviews (with and without meta-analysis) of these types of studies
Evidence Sources

- Search of multiple databases:
  - Ovid MEDLINE
  - Cochrane Database of Systematic Reviews
  - Cochrane Central Register of Controlled Trials
- Additional evidence sources included:
  - Agency for Healthcare Research and Quality (AHRQ)
  - U.K. National Institute for Health and Care Excellence (NICE)
  - Veterans Administration Evidence-based Synthesis Program
  - Reference lists of included studies, test manufacturer websites, and a dossier submitted to the Washington State Agency Medical Directors’ Group in December 2016

Evidence Sources

- ClinicalTrials.gov database for ongoing and recently completed registered trials
- For clinical practice guidelines:
  - Evidence sources (e.g., MEDLINE)
  - AHRQ National Guideline Clearinghouse
  - American Society of Clinical Oncology (ASCO)
  - National Comprehensive Cancer Network (NCCN)
- For payer policies:
  - Centers for Medicare & Medicaid Services (CMS) Medicare Coverage Database for National and Local Coverage Determinations applicable to Washington State
  - Private payers: Aetna, Cigna, and Regence websites
Evidence Search Results

- Separate searching and screening was conducted for each of the four cancers
- Number of citations identified by searches

<table>
<thead>
<tr>
<th>Cancer</th>
<th>Number of Studies</th>
</tr>
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<tbody>
<tr>
<td>Breast Cancer</td>
<td>2,005</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>266</td>
</tr>
<tr>
<td>Colon Cancer</td>
<td>431</td>
</tr>
<tr>
<td>Multiple Myeloma</td>
<td>247</td>
</tr>
<tr>
<td>TOTAL</td>
<td>2,949</td>
</tr>
</tbody>
</table>

Risk of Bias for Studies

- Two independent Center researchers evaluated studies for methodological risk of bias, and disagreement among these assessments was settled by a third researcher
- Each study was assessed using Center instruments adapted from international standards and assessments for methodological quality
- A rating of high, moderate, or low risk of bias was assigned to each study or review based on adherence to recommended methods and potential for bias affecting validity
- Risk-of-bias criteria for all study types are in Appendix B of the report
Overall Quality of Evidence

- Center researchers assigned a summary judgment for the overall quality of evidence for each outcome
- Based on GRADE: Grading of Recommendations, Assessment, Development, and Evaluation
- The GRADE system defines the confidence that the estimate of the effect of the intervention on the outcome lies close to the true effect (listed on next slide)

GRADE Definitions of Quality of Evidence

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
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<tbody>
<tr>
<td>High</td>
<td>Very confident that the estimate of the effect of the intervention on the outcome lies close to the true effect</td>
</tr>
<tr>
<td>Moderate</td>
<td>True effect is likely to be close to the estimate of the effect, but there is a possibility that it is different</td>
</tr>
<tr>
<td>Low</td>
<td>Little confidence in the estimate of the effect of the intervention on the outcome and the true effect may be substantially different from the estimate of the effect</td>
</tr>
<tr>
<td>Very Low</td>
<td>No confidence in the estimate of the effect of the intervention on the outcome and the true effect is likely to be substantially different from the estimate of effect</td>
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Clinical Utility of Breast Cancer GEP Tests

Number of Breast Cancer GEP Studies by Test

<table>
<thead>
<tr>
<th>Test</th>
<th>Number of Studies</th>
</tr>
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<tbody>
<tr>
<td>Oncotype DX</td>
<td>38 primary studies from 3 systematic reviews plus 10 additional studies</td>
</tr>
<tr>
<td>MammaPrint</td>
<td>7 primary studies from 2 systematic reviews and 4 additional studies</td>
</tr>
<tr>
<td>Prosigna</td>
<td>1 primary study from a systematic review</td>
</tr>
<tr>
<td>EndoPredict</td>
<td>1 primary study</td>
</tr>
<tr>
<td>BCI</td>
<td>1 primary study</td>
</tr>
<tr>
<td>Mammastrat</td>
<td>1 primary study</td>
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</table>
Oncotype DX: Blok et al. Systematic Review

- Systematic review assessed as having a moderate risk of bias
- Most studies were of patients with LN-negative tumors, although some included patients with LN-negative and LN-positive tumors
- 22 before-after studies (n = 3,743) examined Oncotype DX
- Authors did not provide risk-of-bias assessments for the included studies
- Change, after testing, in proportion of patients with a recommendation for a more invasive treatment: -14.6%
- Change, after testing, in proportion of patients with a recommendation for a less invasive treatment: +51.1%
Oncotype DX: Augustovski et al. Systematic Review

- Assessed systematic review as having a low risk of bias
- Included 15 before-after studies of women with LN-negative, early-stage invasive breast cancer
- Analysis of the 7 studies at lower risk of bias because they used universal subject enrollment vs. selective enrollment
  - Proportion of patients whose treatment decision was altered with use of the Oncotype DX test: 28.97% (95% CI, 26.65% to 31.34%); $I^2 = 0.00$
  - Patients assigned to receive chemotherapy after the test decreased 9.00% (95% CI, 4.00% to 14.00%); $I^2 = 89.00$

Oncotype DX: Scope et al. Systematic Review

- Assessed systematic review as having a high risk of bias
- 28 before-after studies reported outcomes on changes in recommended treatment after Oncotype DX testing
- Authors did not present pooled estimates because of concern about heterogeneity among studies
- Use of Oncotype DX led to changes in treatment recommendations for 21% to 74% of patients
- Change from a recommendation of chemotherapy to no chemotherapy ranged from 6% to 51% of patients after Oncotype DX use
Oncotype DX: Bear et al. RCT

- Assessed as having high risk of bias
- 33 women with Oncotype DX scores of 11 to 25 were randomized to neoadjuvant hormone therapy (NHT) or neoadjuvant chemotherapy (NCT)
- Women who received NHT had lower clinical response rate than women who received NCT 22.2% vs. 36.4%; \( p = .034 \)
  - Clinical response rate is a poor surrogate for survival, and this study provides very little evidence about clinical utility for important patient outcomes

Oncotype DX: Retrospective Cohort Studies

- 6 retrospective cohort studies using databases (Friese et al., Jasem et al. (2016), Jasem et al. (2017), Parsons et al., O’Neill et al., Ray et al.)
  - Studies assessed as having either a moderate or high risk of bias
  - Overall, patients who had Oncotype DX ordered received chemotherapy less often than patients who did not have test
  - Patients with intermediate- and high-risk Oncotype DX scores were more likely to receive chemotherapy than those with low-risk scores
MammaPrint: Blok et al. Systematic Review

- Studies included patients with LN-negative and LN-positive tumors, although most studies were of patients with LN-negative tumors
- Four included studies of 790 patients used the MammaPrint test
- Change, after testing, in proportion of patients with a recommendation for a more invasive treatment: -17%
- Change, after testing, in proportion of patients with a recommendation for a less invasive treatment: +32.2%
MammaPrint: Scope et al. Systematic Review

- Use of MammaPrint led to changes in treatment recommendations for 18% to 40% of patients
- Change from a recommendation of chemotherapy to no chemotherapy ranged from 2% to 32% of patients after MammaPrint use

MammaPrint: Cardosa et al. (MINDACT) RCT

- Cardoso et al. RCT, Microarray in Node-Negative and 1 to 3 Positive Lymph Node Disease May Avoid Chemotherapy (MINDACT)
  - Center researchers assessed this RCT as having a moderate risk of bias
  - 6,693 women with early-stage invasive breast cancer
  - Most women were postmenopausal with ER-positive, HER2-negative, and LN-negative tumors
  - Women underwent clinical risk assessment using a modified version of the Adjuvant! Online tool and genomic risk assessment using MammaPrint
MammaPrint: Cardosa et al. (MINDACT) RCT

- 2,187 women with discordant clinical and genomic risks were randomized to receive or not receive chemotherapy.
- Among women with high clinical risk and low genomic risk, rates of five-year survival without distant metastasis were similar for those treated with chemotherapy and those given no adjuvant chemotherapy: 95.9% vs. 94.4%; aHR, 0.78; 95% CI, 0.50 to 1.21.
- Among women who had low clinical risk and high genomic risk, risks of death and distant metastases were similar in the chemotherapy vs. no chemotherapy groups: 95.8% vs. 95.0%; aHR, 1.17; 95% CI, 0.59 to 2.28.

MammaPrint: Kuijer et al. (2016) Retrospective Cohort

- Center researchers assessed this study as having high risk of bias.
- 2,043 women with breast cancer, surgically treated in the Netherlands.
- Compared women who received MammaPrint test to inform treatment decisions to women whose treatment was determined by standard clinicopathological factors.
- Use of MammaPrint was associated with 9.5% absolute reduction (95% CI, -15.7% to -3.3%) in use of chemotherapy.
MammaPrint: Kuijer et al. (2017) Before-After Study

- Center researchers assessed this study as having a high risk of bias
- 660 women in the Netherlands who had surgically treated early-stage invasive breast cancer and were eligible for adjuvant chemotherapy treatment
- After MammaPrint test, treatment recommendations changed for 51% (95% CI, 46% to 56%)
- Chemotherapy actually administered comported with what was recommended based on the test 90% to 91% of the time

MammaPrint: Tsai et al. Before-After Study

- Center researchers assessed as having a high risk of bias
- Study examined whether MammaPrint test affected treatment decisions among women (n = 840) with an intermediate Oncotype DX score (score of 18 to 30)
- Overall, 33.6% of treatment recommendations changed after the MammaPrint test was administered
- Among all patients, the odds of chemotherapy treatment withdrawal were 0.64 (95% CI, 0.50 to 0.82)
- Physicians were surveyed about how MammaPrint influenced their decision and reported it increased their confidence in the final treatment plan in 78.6%, reduced it in 5.8%, and had no influence in 15.6% of cases
Prosigna Studies

- Blok et al. systematic review included 1 before-after study on a single group of patients (n = 200)
  - Change, after testing, in proportion of patients with a recommendation for a more invasive treatment: -12.9%
  - Change, after testing, in proportion of patients with a recommendation for a less invasive treatment: +37.3%

Two additional studies:

- Hequet et al. before-after study on a single group of patients (n = 210) assessed as having a high risk of bias
  - Treatment recommendation changed for 18% of women
    - Recommendation of no adjuvant chemotherapy to adjuvant chemotherapy for 13% of women
    - Recommendation of adjuvant chemotherapy to no chemotherapy for 5% of women
Prosigna: Wuerstlein et al. Before-After Study

- West German Study Group (WSG) Breast Cancer Intrinsic Subtype before-after study on a single group of patients (n = 198)
- Center researchers assessed as having a high risk of bias
- Treatment recommendation changed for 18%
  - No adjuvant chemotherapy recommendation changed to adjuvant chemotherapy recommendation for 11% of cases
  - Adjuvant chemotherapy recommendation changed to against adjuvant chemotherapy for 2%
  - For 5% of women, there was a change in the particular type of chemotherapy regimen

EndoPredict
EndoPredict: Blok et al. Systematic Review

- Blok et al. systematic review included 1 before-after study on a single group of patients (n = 167)
  - Change, after testing, in proportion of patients with a recommendation for a more invasive treatment: -34%
  - Change, after testing, in proportion of patients with a recommendation for a less invasive treatment: +53.2%
- No additional individual clinical utility studies

Breast Cancer Index
BCI: Sanft et al. Before-After Study

- Center researchers assessed as having a high risk of bias
- Women (n = 96) from a single U.S. institution who had completed at least 3.5 years of adjuvant endocrine therapy and were eligible for extended endocrine treatment
- 26% of women had a change of treatment recommendation after use of the test
- Decline in recommendations for extended adjuvant chemotherapy (74% before the test vs. 54% after the test; OR, 0.14; 95% CI, 0.04 to 0.46)
Mammostrat: Scope et al. Systematic Review

- 1 study of Mammostrat included in the Scope et al. systematic review: Ross et al. (2008)
  - Prospective-retrospective study of 711 women
  - Change in distant recurrence-free interval when treated with tamoxifen:
    - Low risk: improved by 5% from 86% to 91% (HR, 0.4; 95% CI, 0.2 to 0.8)
    - High risk: improved by 21% from 64% to 85% (HR, 0.4; 95% CI, 0.2 to 0.9)
    - Low- and high-risk groups benefited from chemotherapy, whereas patients in the intermediate-risk group did not

Breast Cancer Evidence Summary

- Majority of studies on gene tests to inform treatment of breast cancer have a high risk of bias
- Findings are consistent regarding an association between test use and changes in recommended or actual treatment based on the test result
  - Largest body of evidence for Oncotype DX test
  - Moderate amount of evidence for MammaPrint and Prosigna
  - Very little for BCI, EndoPredict, and Mammostrat
  - Evidence is limited because of lack of information on important patient outcomes such as survival, with the exception of the MINDACT study of MammaPrint
Breast Cancer Key Question 2: Harms

- No studies reported outcomes related to false reassurance or false alarm from these tests
- In general, studies that reported on decisional conflict, anxiety, function, or patient-perceived usefulness of testing found small differences in favor of testing
- Similarly, studies reporting the outcome found physicians perceived testing to be useful and that it increased their confidence in treatment recommendations

Breast Cancer Key Question 3: Subpopulations

- Few studies reported results stratified by subpopulations of interest such as by age, race, or disease characteristics
- Jasem et al. (2017) reported that older patients were more likely to receive testing than younger patients, and that African American women and patients without insurance were less likely to be tested
- Studies reporting differences in subpopulation test receipt or treatment recommendations are difficult to interpret because of small effect sizes, high risk of bias, and residual confounding
Breast Cancer Key Question 4
Economic Outcomes

- Blok et al. systematic review included studies with economic outcomes
- Economic studies published after the Blok et al. systematic review: Hall et al. considered Oncotype DX, MammaPrint, and Prosigna
  - Loncaster et al. reported cost outcomes related to the use of Oncotype DX
- Decision analysis on BCI test by Gustavsen et al.

Breast Cancer: Blok et al. Systematic Review

- 2 studies comparing testing to not testing using patient groups found increased costs per patient ($400 to $1,367) with the use of Oncotype DX
- 26 cost-utility models reported results in costs per QALY:
  - 14 studies on Oncotype DX for women with LN-negative tumors reported cost/QALY ranges of $3,843 to $43,044, CAD$3,206 to CAD$63,064, or £29,502
  - 5 studies evaluated Oncotype DX for women with LN-positive tumors (or studies with mixed LN-negative and LN-positive populations) reported costs/QALY of $1,914 to $49,059, CAD$464 to CAD$14,844, and £5,529
  - 5 studies on MammaPrint reported cost/QALY ranging from $10,000 to $43,044, and €4,614 to €134,000
Breast Cancer: Additional Economic Studies

- Hall et al. assessed as having moderate risk of bias
  - Modeling study to accompany UK NHS feasibility study for Oncotype DX testing (using cutoff score of 25) vs. standard risk assessment or alternative tests (MammaPrint and Prosigna)
  - Mean incremental per-person cost and QALY changes:

<table>
<thead>
<tr>
<th></th>
<th>Cost (£) (95% CI)</th>
<th>QALY (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncotype DX</td>
<td>-108 (-4610 to +4292)</td>
<td>0.20 (-1.07 to 1.40)</td>
</tr>
<tr>
<td>MammaPrint</td>
<td>+195 (-3206 to +3430)</td>
<td>0.18 (-0.87 to 1.10)</td>
</tr>
<tr>
<td>Prosigna</td>
<td>-474 (-4078 to +2955)</td>
<td>0.18 (-0.91 to 1.15)</td>
</tr>
</tbody>
</table>

- Loncaster et al. assessed as having high risk of bias
  - Modeling study showing that use of Oncotype DX test would result in budget savings of £1,325 per patient

- Gustavsen et al. assessed as having high risk of bias
  - Using BCI test for newly diagnosed women with ER-positive, LN-negative breast cancer would result in mean cost savings per patient of $3,803
Breast Cancer Economic Evidence Summary

- Estimates of costs and QALY varied widely among the studies.
- Quality of economic evidence for Oncotype DX and MammaPrint is low when the Blok et al. systematic review and additional economic analysis by Hall et al. are considered together.
- Overall quality of economic evidence about Prosigna, EndoPredict, and Mammostrat is very low.

Breast Cancer GRADE Summary

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Utility—mortality or morbidity</strong></td>
<td>Oncotype DX</td>
</tr>
<tr>
<td></td>
<td>★★★★ Very low</td>
</tr>
<tr>
<td></td>
<td>MammaPrint</td>
</tr>
<tr>
<td></td>
<td>★★★ Moderate</td>
</tr>
<tr>
<td><strong>Clinical Utility—patient management decisions</strong></td>
<td>Oncotype DX Breast</td>
</tr>
<tr>
<td></td>
<td>★★★★ Moderate</td>
</tr>
<tr>
<td></td>
<td>MammaPrint</td>
</tr>
<tr>
<td></td>
<td>★★★ Low</td>
</tr>
<tr>
<td></td>
<td>Prosigna, EndoPredict, BCI, and Mammostrat</td>
</tr>
<tr>
<td></td>
<td>★★★★ Very low</td>
</tr>
</tbody>
</table>
## Breast Cancer GRADE Summary

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical Utility—quality of life</strong></td>
<td>Oncotype DX, Prosigna, and BCI</td>
</tr>
<tr>
<td></td>
<td>●◌◌◌ Very low</td>
</tr>
<tr>
<td></td>
<td>Other tests</td>
</tr>
<tr>
<td></td>
<td>Not applicable (no eligible studies)</td>
</tr>
<tr>
<td><strong>Harms</strong></td>
<td>Oncotype DX</td>
</tr>
<tr>
<td></td>
<td>●◌◌◌ Very low</td>
</tr>
<tr>
<td></td>
<td>Other tests</td>
</tr>
<tr>
<td></td>
<td>Not applicable (no eligible studies)</td>
</tr>
<tr>
<td><strong>Cost-effectiveness and other economic outcomes</strong></td>
<td>Oncotype DX and MammaPrint:</td>
</tr>
<tr>
<td></td>
<td>●●◌◌ Low</td>
</tr>
<tr>
<td></td>
<td>EndoPredict, Mammostrat, Prosigna, BCI:</td>
</tr>
<tr>
<td></td>
<td>●◌◌◌ Very low</td>
</tr>
</tbody>
</table>

## Breast Cancer Guidelines

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Methodological quality assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Society of Clinical Oncology (ASCO, 2016)</td>
<td>Good</td>
</tr>
<tr>
<td>European Group on Tumor Markers (EGTM) 2017</td>
<td>Poor</td>
</tr>
<tr>
<td>European Society for Medical Oncology (ESMO) 2015</td>
<td>Poor</td>
</tr>
<tr>
<td>National Institute for Health and Care Excellence (NICE) 2013</td>
<td>Good</td>
</tr>
<tr>
<td>National Comprehensive Cancer Network (NCCN) 2017</td>
<td>Fair</td>
</tr>
</tbody>
</table>
Breast Cancer Guidelines

- When these guidelines recommend a GEP test, the recommendations generally include these restrictions:
  - Early-stage breast cancer (usually stage 1 and stage 2)
  - ER-positive (sometimes also includes PR-positive)
  - HER2-negative
  - Test results will affect treatment decisions
  - LN-negative patients (sometimes also includes 1-3 positive lymph nodes) – see next slide

<table>
<thead>
<tr>
<th>Test</th>
<th>ASCO</th>
<th>NCCN</th>
<th>NICE</th>
<th>ESMO**</th>
<th>EGTM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncotype DX</td>
<td>LN-negative</td>
<td>LN-negative</td>
<td>LN-negative</td>
<td>LN-negative</td>
<td>LN-negative</td>
</tr>
<tr>
<td>MammaPrint</td>
<td>LN-negative</td>
<td>Not recommended*</td>
<td>Not recommended</td>
<td>LN-negative</td>
<td>LN-negative</td>
</tr>
<tr>
<td>EndoPredict</td>
<td>LN-negative</td>
<td>Not recommended*</td>
<td>No guideline recommended</td>
<td>LN-negative</td>
<td>LN-negative</td>
</tr>
<tr>
<td>Prosigna</td>
<td>LN-negative</td>
<td>Not recommended*</td>
<td>No guideline recommended</td>
<td>LN-negative</td>
<td>LN-negative</td>
</tr>
<tr>
<td>Breast Cancer Index</td>
<td>LN-negative</td>
<td>Not recommended*</td>
<td>No guideline recommended</td>
<td>No guideline recommended</td>
<td>LN-negative</td>
</tr>
<tr>
<td>Mammostrat</td>
<td>Not recommended</td>
<td>Not recommended*</td>
<td>Not recommended</td>
<td>No guideline recommended</td>
<td>No guideline recommended</td>
</tr>
</tbody>
</table>

*NCCN guidelines stated that prognostic multigene assays other than Oncotype DX may be considered to help assess risk of recurrence but have not been validated to predict response to chemotherapy.

**ESMO guidelines did not distinguish between LN-negative and LN-positive cancers.
Breast Cancer Payer Policies

- No Medicare National Coverage Determinations (NCDs) were found for any of the GEP tests for breast cancer.
- Local Coverage Determinations (LCDs) applying to Washington provide coverage for EndoPredict, Prosigna, and BCI.
- No LCDs applying to Washington provide coverage for Oncotype DX, MammaPrint, or Mammostrat.

Breast Cancer Private Payer Policies

<table>
<thead>
<tr>
<th></th>
<th>Aetna</th>
<th>Cigna</th>
<th>Regence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncotype DX</td>
<td>LN-negative</td>
<td>LN-negative</td>
<td>LN-negative</td>
</tr>
<tr>
<td></td>
<td>LN-positive</td>
<td>LN-positive</td>
<td></td>
</tr>
<tr>
<td>MammaPrint</td>
<td>LN-negative</td>
<td>LN-negative</td>
<td>No coverage</td>
</tr>
<tr>
<td></td>
<td>LN-positive</td>
<td>LN-positive</td>
<td></td>
</tr>
<tr>
<td>EndoPredict</td>
<td>LN-negative</td>
<td>No coverage</td>
<td>LN-negative</td>
</tr>
<tr>
<td>Prosigna</td>
<td>LN-negative</td>
<td>LN-negative</td>
<td>No coverage</td>
</tr>
<tr>
<td>BCI</td>
<td>LN-negative</td>
<td>No coverage</td>
<td>LN-negative</td>
</tr>
<tr>
<td>Mammostrat</td>
<td>No coverage</td>
<td>No coverage</td>
<td>No coverage</td>
</tr>
</tbody>
</table>
Clinical Utility of Prostate Cancer GEP Tests

Prostate Cancer Evidence

- Total of 8 individual studies identified for prostate cancer
- All studies were assessed as having a high risk of bias
- All studies used before-after designs that reported treatment recommendations before and after the test result was available
  - Four of these studies used a single group of patients and tracked decision outcomes before and after the test results were provided
  - Four studies employed a historical group from a time period when treatment decisions were made without the assistance of genomic testing
Prostate Cancer Evidence

- Test used after an initial diagnosis of prostate cancer to predict the cancer’s aggressiveness and thus inform treatment decisions
  - Oncotype DX: 4 before-after studies
  - Prolaris: 2 before-after studies
- Test used after radical prostatectomy to predict the probability of metastasis and inform clinical decisions on the use of adjuvant prostate cancer treatments
  - Decipher: 2 before-after studies

Oncotype DX Prostate Studies

- 3 studies used historical comparison groups
  - Albala et al. reported that more men received recommendations for active surveillance after testing (59% vs. 38%)
  - Dall-Era et al. reported that use of active surveillance increased after testing (67% vs. 43%)
  - Eure et al. reported 51% of patients switched from interventional treatment to active surveillance after testing
- Badani et al. before-after study on a single group of patients
  - After testing, recommended treatment intensity decreased for 15.8% of men and increased for 8.9%
Prolaris Studies

- Crawford et al. before-after study using a historical comparison
  - For 37% of subjects, recommendation for interventional treatment changed to active surveillance or watchful waiting after testing
- Shore et al. before-after study on a single group of patients
  - After testing, treatment recommendations changed for 47.8% of subjects
    - Nearly 75% of treatment modifications were changing to decreased treatment intensity

Decipher Studies

- Decipher: 2 before-after studies (each using a single group of patients) of men who have had a radical prostatectomy
- Gore et al.: Decipher test use is associated with changes in treatment recommendations
  - Men considering adjuvant radiotherapy: OR, 1.48; 95% CI, 1.19 to 1.85
  - Men considering salvage radiotherapy: OR, 1.30; 95% CI, 1.03 to 1.65
- Michalopoulos et al.: Changes in treatment recommendations before-after Decipher test
  - 42% of patients who had a recommendation of any active treatment experienced a change to observation only
  - 18% with an initial recommendation of observation had a posttest recommendation of an active treatment strategy
Prostate Cancer

- Key Question 2: Harms
  - No studies met inclusion criteria for this key question

- Key Question 3: Subpopulations
  - No studies met inclusion criteria for this key question, except that Oncotype DX and Prolaris are used in different clinical situations than the Decipher test

Prostate Cancer Key Question 4
Economic Outcomes

- Ontario Health Technology Advisory Committee study of Prolaris, assessed as having a moderate risk of bias
  - Budget impact analysis showed that use of test increased costs for province of Ontario

- Lobo et al. cost-effectiveness study of Decipher, assessed as having a high risk of bias
  - Test-based care increased per-person cost of care by $5,453; increased the mean QALY per individual by 0.066; with an incremental cost-effectiveness ratio of $90,883

- Albala et al. study of Oncotype DX, assessed as having a high risk of bias
  - Total cost of care was $2,286 less for men who had received the test compared to historical costs
Prostate Cancer GRADE Summary

- Study findings are consistent regarding an association between use of Oncotype DX, Prolaris, or Decipher and recommendations for decreased treatment intensity and increased decision confidence for patients and physicians.
- Quality of evidence very low for these findings because of high risk of bias and other limitations, including:
  - Use of before-after designs
  - Reporting of recommended rather than actual treatments
  - Lack of important patient outcomes such as survival or treatment-related morbidity
- Quality of evidence very low for economic outcomes

Prostate Cancer Guidelines

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Methodological Quality</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Urological Association, American Society for Radiation Oncology, and Society of Urologic Oncology (2017)</td>
<td>Good</td>
<td>Tissue-based genomic biomarkers have not shown a clear role in active surveillance for localized prostate cancer</td>
</tr>
<tr>
<td>National Comprehensive Cancer Network (NCCN, 2017)</td>
<td>Fair</td>
<td>May consider the use of tumor-based molecular assays; specific recommendations on when to use Decipher, Prolaris, and Oncotype DX</td>
</tr>
</tbody>
</table>
## Prostate Cancer Payer Policies

<table>
<thead>
<tr>
<th>Payer</th>
<th>Coverage policies for Decipher, Prolaris, and Oncotype DX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare National Coverage Determination</td>
<td>Not found</td>
</tr>
<tr>
<td>Medicare Local Coverage Determination applying to WA</td>
<td>Coverage for Decipher, Prolaris, and Oncotype DX under certain conditions</td>
</tr>
<tr>
<td><strong>Private Payers</strong></td>
<td></td>
</tr>
<tr>
<td>Aetna</td>
<td>No coverage</td>
</tr>
<tr>
<td>Cigna</td>
<td>Not included on the list of medically necessary prostate cancer prognostic tests</td>
</tr>
<tr>
<td>Regence</td>
<td>No coverage</td>
</tr>
</tbody>
</table>

## Clinical Utility of Colon Cancer GEP Tests
Colon Cancer Evidence

- ColoPrint: no systematic reviews or individual studies
- Oncotype DX: no systematic reviews; 2 individual studies
- Both individual studies for Oncotype DX were assessed as having a high risk of bias
  - Srivastava et al.: use of the test resulted in changes in treatment recommendations
    - Increased intensity of recommended therapy for 11.4%
    - Decreased intensity recommendations for 32.9%
  - Brenner et al.: actual treatment received compared to treatment recommended before the test results were known
    - Increased intensity of treatment for 9.7%
    - Decreased intensity for 28.3%

Colon Cancer

- Key Question 2: Harms
  - No studies met inclusion criteria for this key question
- Key Question 3: Subpopulations
  - No studies met inclusion criteria for this key question

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Colon Cancer Key Question 4
Economic Outcomes

- Alberts et al. study of Oncotype DX colon cancer test
  - Assessed as having a moderate risk of bias
  - Cost-effectiveness of using Oncotype DX to guide therapy for patients with resected stage 2 MMR-P colon cancer
  - Slightly lower total lifetime costs ($991 less) with the test ($103,775) than without it ($104,767)

Colon Cancer GRADE Summary

- Quality of evidence very low for Oncotype DX clinical and economic outcomes
- No evidence found for ColoPrint
Colon Cancer Guidelines

- No clinical practice guidelines were found that included recommendations for the use of ColoPrint or Oncotype DX for colon cancer
- NCCN guideline on colon cancer, assessed as having fair methodological quality
  - “There is no evidence of predictive value in terms of the potential benefit of chemotherapy to any of the multigene assays”

Colon Cancer Payer Policies

<table>
<thead>
<tr>
<th>Payer</th>
<th>Coverage policies for ColoPrint and Oncotype DX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare National Coverage Determination</td>
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</tr>
<tr>
<td>Medicare Local Coverage Determination applying to WA</td>
<td>Not found</td>
</tr>
<tr>
<td>Private Payers</td>
<td></td>
</tr>
<tr>
<td>Aetna</td>
<td>No coverage</td>
</tr>
<tr>
<td>Cigna</td>
<td>No coverage</td>
</tr>
<tr>
<td>Regence</td>
<td>No coverage</td>
</tr>
</tbody>
</table>
Multiple Myeloma

GEP tests

- No multiple myeloma studies found for clinical utility or economic outcomes
Multiple Myeloma Guidelines

- NCCN (2017) guidelines on multiple myeloma, assessed as having fair methodological quality
  - No recommendation provided
  - Stated that although GEP tests are not routinely used, they could be helpful in selected patients to estimate the aggressiveness of disease and/or individualize treatment
- European Society for Medical Oncology (ESMO, 2017), assessed as having fair methodological quality
  - Gene-expression profiling is not currently used routinely, and more research is needed to identify molecular markers, which could lead to advances in this area

Multiple Myeloma Payer Policies

<table>
<thead>
<tr>
<th>Payer</th>
<th>Coverage policies for MyPRS and SKY92</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicare National Coverage Determination</td>
<td>Not found</td>
</tr>
<tr>
<td>Medicare Local Coverage Determination applying to WA</td>
<td>Not found</td>
</tr>
<tr>
<td><strong>Private Payers</strong></td>
<td></td>
</tr>
<tr>
<td>Aetna</td>
<td>No coverage for MyPRS</td>
</tr>
<tr>
<td></td>
<td>Does not mention SKY92</td>
</tr>
<tr>
<td>Cigna</td>
<td>Does not mention MyPRS or SKY92</td>
</tr>
<tr>
<td>Regence</td>
<td>Does not cover MyPRS or SKY92</td>
</tr>
</tbody>
</table>
Overall Summary

Limitations

- Risk of bias of included studies varied, but was often high
- Evidence base limited for assessing the clinical utility, harms, and cost-effectiveness of most of the tests
- Clinical utility limited to influence on clinical decision making for nearly all tests
- Without evidence of clinical endpoint data, cannot be certain that effects on decision making are actually improving care
- Populations included were generally not diverse in terms of race, ethnicity, or socioeconomic factors
- Many studies were conducted in Europe, which could limit generalizability to the U.S. context
- Given limited evidence on effectiveness, economic modeling studies were not able to use solid estimates of effectiveness
Overall Summary

- There was no high-quality evidence of clinical utility to guide decisions about any GEP tests
- Only condition with quality of evidence ratings above very low was breast cancer and only for the MammaPrint and Oncotype DX
- Based on 1 RCT, there is moderate-quality evidence that women with early-stage invasive breast cancer who are at high clinical risk by the Adjuvant! Online risk assessment tool may safely forego adjuvant systemic chemotherapy if their MammaPrint genomic risk score is low

Overall Summary

- Moderate-quality evidence supports the use of Oncotype DX because of its impact on clinical treatment recommendations
- Based primarily on modeling studies, there is low-quality evidence that both Oncotype DX and MammaPrint are cost-effective at conventional thresholds of cost/QALY
- For prostate cancer, colon cancer, and multiple myeloma, there is very low-quality evidence or a complete absence of evidence to support use of these tests to improve clinical decision making and important patient outcomes
FINAL key questions and background

Gene expression profile testing of cancer tissue

Background

The lifetime risk of developing cancer is about 40%, and one in every five Americans will die from cancer. Strategies for reducing the burden of cancer include preventing the disease, early diagnosis of cancer, and appropriate treatments of diagnosed cancers. Common treatments for cancer include surgery, chemotherapy, radiation therapy, hormone therapy, and immunotherapy. The most appropriate treatments for a particular cancer depend on the cancer’s severity (e.g., cancer stage and grade), the patient’s age and health status, response to previous treatments, and other factors.

In recent years, gene expression profile testing of cancer tissue has been used to help inform decisions on the most appropriate treatments. Gene expression profile testing identifies the genes in a cancer cell or tissue that are making messenger RNA, which carry the genetic information that cancer cells need to make proteins. Some gene expression profile tests are designed to increase the accuracy of the prognosis for a patient with cancer. If a test predicts that a cancer is slow growing or is unlikely to metastasize, then active surveillance of the cancer could be the most appropriate course. If a test predicts that a cancer is at high risk for progression and metastasis, then more aggressive treatments could be warranted.

Policy context

There are a growing number of gene expression profile tests for cancer tissue designed to inform treatment decisions after diagnosis. Potential benefits of these tests are more appropriate treatment decisions and better patient outcomes, including avoiding treatment-related side effects and the potential cost savings from forgoing unnecessary treatments. This topic was selected for a health technology assessment because of medium concerns for the safety of these tests, medium/high concerns for efficacy, and high concerns for cost.

This evidence review will help to inform Washington’s independent Health Technology Clinical Committee as the committee determines coverage regarding selected gene expression profile tests for patients with eligible breast, prostate, or colon cancers or multiple myeloma.

Proposed Scope

Population: Adults with breast, prostate, or colon cancers or multiple myeloma

Interventions: Gene expression profile testing of cancer tissue to inform treatment decisions, including the following tests by cancer type:
- Breast Cancer—Oncotype DX Breast Cancer Assay, EndoPredict, MammaPrint, Prosigna Breast Cancer Prognostic Gene Signature Assay (PAM50), Mammostrat, Breast Cancer Index (BCI)
- Prostate Cancer—Prolaris, Decipher, Oncotype DX Prostate Cancer Assay
- Colon Cancer—Oncotype DX Colon Cancer Assay, ColoPrint
- Multiple Myeloma—Myeloma Prognostic Risk Signature (MyPRS), SKY92-signal (formerly EMC92)

**Comparators:** Usual care without gene expression profile testing of cancer tissue, alternate gene expression profile tests (i.e., one test intervention listed above versus another)

**Outcomes:**
- Patient management decisions (including selection of active surveillance rather than active treatment)
- Clinical outcomes (e.g., morbidity, mortality, quality of life)
- Harms, such as consequences of false-positive or false-negative test results
- Cost-effectiveness and other economic outcomes

**Time period for literature search:** 2007 to 2017

**Key Questions**

1. Effectiveness: What is the clinical utility of gene expression profile testing of cancer tissue to inform treatment decisions for patients with breast, prostate, and colon cancers and multiple myeloma?
   a. Is there evidence that test results affect treatment decisions?
   b. Do treatment decisions guided by gene expression profile testing of cancer tissue result in clinically meaningful improvements in patient outcomes?

2. Harms: What harms are associated with conducting gene expression profile testing of cancer tissue?

3. Special populations: Compared with usual care, do treatment decisions, patient outcomes, or harms after gene expression profile testing of cancer tissue vary by:
   a. Patient demographics (e.g., age, sex, race/ethnicity)?
   b. Clinical history (e.g., means of diagnosis, stage or grade of cancer, results of other testing, previous treatments, chronicity)?
   c. Medical comorbidities?
   d. Provider type or care setting?

4. What are the cost-effectiveness and other economic outcomes of gene expression profile testing used to inform treatment management decisions?
Eligible Studies

Randomized controlled trials, nonrandomized comparative studies, and systematic reviews of these two types of studies that assess clinical utility will be considered for Key Questions 1, 2, and 3. Cost-effectiveness studies and other comparative economic evaluations, along with systematic reviews of these types of studies, will be considered for Key Question 4.

Analytic framework

The analytic framework below will guide the selection, synthesis, and interpretation of available evidence.

![Diagram showing the analytic framework for gene expression profile testing of cancer tissue to inform treatment decisions, with patients, intervention, outcomes, and harms as key components.]

References


Public comment and response

See Draft key questions: Comment and response document published separately.
HTCC Coverage and Reimbursement Determination

Analytic Tool

HTA’s goal is to achieve better health care outcomes for enrollees and beneficiaries of state programs by paying for proven health technologies that work.

To find best outcomes and value for the state and the patient, the HTA program focuses on three questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are evidence-based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective\(^1\) as expressed by the following standards\(^2\):

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms\(^3\):

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially

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\(^1\) Based on Legislative mandate: See RCW 70.14.100(2).

\(^2\) The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

\(^3\) The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm
within the population, coverage or reimbursement determinations may be more selective based on the variation.

- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

Using evidence as the basis for a coverage decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. **Availability of Evidence:**

   Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

2. **Sufficiency of the Evidence:**

   Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence using characteristics such as:

   - Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
   - The amount of evidence (sparse to many number of evidence or events or individuals studied);
   - Consistency of evidence (results vary or largely similar);
   - Recency (timeliness of information);
   - Directness of evidence (link between technology and outcome);
   - Relevance of evidence (applicability to agency program and clients);
   - Bias (likelihood of conflict of interest or lack of safeguards).

   Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

<table>
<thead>
<tr>
<th>Not Confident</th>
<th>Confident</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.</td>
<td>Very certain of evidentiary support. Further information is unlikely to change confidence</td>
</tr>
</tbody>
</table>

3. **Factors for Consideration - Importance**

   At the end of discussion a vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage

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4 Based on GRADE recommendation.
decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- Risk of event occurring;
- The degree of harm associated with risk;
- The number of risks; the burden of the condition;
- Burden untreated or treated with alternatives;
- The importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- The degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- Value variation based on patient preference.

Clinical Committee Findings and Decisions

Efficacy Considerations

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
  - Direct outcome or surrogate measure
  - Short term or long term effect
  - Magnitude of effect
  - Impact on pain, functional restoration, quality of life
  - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value?
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests’ accuracy?
  - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices?

Safety

- What is the evidence of the effect of using the technology on significant morbidity?
  - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
  - Adverse effect on health that can result in lasting harm or can be life-threatening?
- Other morbidity concerns?
- Short term or direct complication versus long term complications?
• What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

**Cost Impact**

• Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

**Overall**

• What is the evidence about alternatives and comparisons to the alternatives?
• Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?

**Next Step: Cover or No Cover**

If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

**Next Step: Cover with Conditions**

If covered with conditions, the Committee will continue discussion.

1) Does the committee have enough information to identify conditions or criteria?
   • Refer to evidence identification document and discussion.
   • Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
   • Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.

2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
   • What are the known conditions/criteria and evidence state
   • What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

**Clinical Committee Evidence Votes**

**First Voting Question**

The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.
**Discussion Document:** What are the key factors and health outcomes and what evidence is there? ( Applies to the population in the PICO for this review)

<table>
<thead>
<tr>
<th>Safety Outcomes</th>
<th>Importance of Outcome</th>
<th>Safety Evidence / Confidence in Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse effects</td>
<td></td>
<td></td>
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<tr>
<td>False positive or negative</td>
<td></td>
<td></td>
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<tr>
<td>Harms associated with testing</td>
<td></td>
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<td>Anxiety</td>
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<thead>
<tr>
<th>Efficacy – Effectiveness Outcomes</th>
<th>Importance of Outcome</th>
<th>Efficacy / Effectiveness Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Utility –Morbidity/Mortality</td>
<td></td>
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<tr>
<td>Clinical Utility- Patient management decisions</td>
<td></td>
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<tr>
<td>Quality of life</td>
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<table>
<thead>
<tr>
<th>Cost Outcomes</th>
<th>Importance of Outcome</th>
<th>Cost Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs of testing</td>
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<tr>
<td>Cost effectiveness</td>
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<thead>
<tr>
<th>Special Population / Considerations Outcomes</th>
<th>Importance of Outcome</th>
<th>Special Populations/ Considerations Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
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<td>Gender</td>
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<td>Race/ethnicity</td>
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<td>Clinical history</td>
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<td>Comorbidities</td>
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<tr>
<td>Care setting</td>
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</tbody>
</table>
For Safety: Is there sufficient evidence that the technology is safe for the indications considered?

<table>
<thead>
<tr>
<th>Unproven (no)</th>
<th>Less (yes)</th>
<th>Equivalent (yes)</th>
<th>More in some (yes)</th>
<th>More in all</th>
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For Efficacy/Effectiveness: Is there sufficient evidence that the technology has a meaningful impact on patients and patient care?

<table>
<thead>
<tr>
<th>Unproven (no)</th>
<th>Less (yes)</th>
<th>Equivalent (yes)</th>
<th>More in some (yes)</th>
<th>More in all</th>
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</table>

For Cost Outcomes/Cost-Effectiveness: Is there sufficient evidence that the technology is cost-effective for the indications considered?

<table>
<thead>
<tr>
<th>Unproven (no)</th>
<th>Less (yes)</th>
<th>Equivalent (yes)</th>
<th>More in some (yes)</th>
<th>More in all</th>
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</table>

Discussion

Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

Second Vote

Based on the evidence about the technologies’ safety, efficacy, and cost-effectiveness, it is

_____ Not Covered  _____ Covered Unconditionally  _____ Covered Under Certain Conditions
Discussion Item
Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

Next Step: Proposed Findings and Decision and Public Comment
At the next public meeting the committee will review the proposed findings and decision and consider any public comments as appropriate prior to a vote for final adoption of the determination.

1) Based on public comment was evidence overlooked in the process that should be considered?
2) Does the proposed findings and decision document clearly convey the intended coverage determination based on review and consideration of the evidence?

Next Step: Final Determination
Following review of the proposed findings and decision document and public comments:

Final Vote
Does the committee approve the Findings and Decisions document with any changes noted in discussion?

If yes, the process is concluded.
If no, or an unclear (i.e., tie) outcome Chair will lead discussion to determine next steps.

Medicare and Coverage Guidelines
[From page 25 of the Final Evidence Report]

No Medicare National Coverage Determinations (NCDs) were found for any of the gene expression profile tests for breast cancer. Center researchers identified Local Coverage Determinations (LCDs) by Noridian Healthcare Solutions, which apply to Washington, that provide coverage for EndoPredict, Prosigna, and BCI.

The EndoPredict LCD provides coverage for women with T1-3, N0-1 breast cancer when the following criteria are met:

- Patient is postmenopausal
- Pathology reveals invasive carcinoma of the breast that is ER-positive, HER2-negative
- Patient is either LN-negative or has 1 to 3 positive lymph nodes
- Patient has no evidence of distant metastasis
- Test result will be used to determine treatment choice between endocrine therapy alone vs. endocrine therapy plus chemotherapy\textsuperscript{72}

The Prosigna LCD provides coverage for postmenopausal women with either of the following:

- ER-positive, LN-negative, stage 1 or 2 breast cancer or
- ER-positive, LN-positive (one to three positive nodes), stage 2 breast cancer\textsuperscript{73}
The BCI LCD provides coverage for patients who have non-relapsed, ER-positive, LN-negative breast cancer, among other criteria. No Medicare LCDs covering Washington were found for the Oncotype DX breast cancer assay, MammaPrint, or Mammostrat.

Center researchers assessed private payer policies for Aetna, Cigna, and Regence. The Aetna policy on tumor markers provides coverage for the Oncotype DX breast cancer assay, MammaPrint, EndoPredict, Prosigna, and BCI to assess the necessity of adjuvant chemotherapy in females or males with recently diagnosed breast tumors. Oncotype DX and MammaPrint are covered for breast cancers that are LN-negative or with one to three involved ipsilateral axillary lymph nodes. EndoPredict, Prosigna, and BCI are covered for only LN-negative cancers. Coverage for all of these tests requires that adjuvant chemotherapy is not precluded by any other factor (e.g., advanced age or significant comorbidities) and that the patient and physician have discussed the potential results of the test and agree to use the results to guide therapy, among other criteria. Aetna does not cover Mammostrat.

The Cigna policy on gene expression assays covers the Oncotype DX breast cancer assay, MammaPrint, and Prosigna under certain conditions, and does not provide coverage for EndoPredict, BCI, or Mammostrat. Oncotype DX and MammaPrint are covered for LN-negative cancers and for cancers with up to three positive nodes, and Prosigna is covered for only LN-negative cancers. The Regence policy on gene expression testing for breast cancer provides coverage for the Oncotype DX breast cancer assay, EndoPredict, and BCI under certain conditions, and does not cover MammaPrint, Prosigna, or Mammostrat. Regence covers the Oncotype DX breast cancer assay, EndoPredict, and BCI for women with primary breast cancer, stages 1, 2, or 3, that are LN-negative, among other criteria.

**Prostate Cancer**

No Medicare NCDs were found for Decipher, Prolaris, or Oncotype DX for prostate cancer. There are LCDs for Noridian Healthcare Solutions, applying to the state of Washington, that provide coverage for Decipher, Prolaris, and Oncotype DX for prostate cancer under certain conditions. The LCD for Decipher provides coverage after radical prostatectomy when certain conditions are met. There are two LCDs providing coverage for Prolaris, under certain conditions, one for patients with early stage, needle-biopsy-proven prostate cancer and the other for patients with favorable intermediate-risk, needle-biopsy-proven prostate cancer. The LCD for Oncotype DX for early-stage, needle-biopsy-proven prostate cancer provides coverage with specified conditions.

The coverage policies for Aetna and Regence consider Decipher, Prolaris, and Oncotype DX prostate cancer assay to be experimental or investigational. Cigna does not include Decipher, Prolaris, or Oncotype DX prostate cancer assay in the list of medically necessary prostate cancer prognostic tests.

**Colon Cancer**

No Medicare National or Local Coverage Determinations were found for ColoPrint or the Oncotype DX colon cancer assay. The policies for Aetna, Cigna, and Regence do not cover ColoPrint or Oncotype DX colon cancer assay.

**Multiple Myeloma**

No Medicare National or Local Coverage Determinations were found for MyPRS or SKY92. The policy for Aetna does not cover MyPRS and does not mention SKY92. Cigna’s coverage policy on tumor markers does not mention MyPRS or SKY92. The Regence coverage policy states that all microarray-based gene expression profile testing for multiple myeloma is considered investigational.
Guidelines

[From page 73 of Final Evidence Report]

Clinical Practice Guidelines

Breast Cancer

The most detailed clinical practice guideline, *Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women with Early-Stage Invasive Breast Cancer*, was published by the American Society of Clinical Oncology (ASCO) in 2016. ASCO published a guideline update in 2017 modifying the recommendations regarding MammaPrint, which draws upon recently published studies. Both of these guidelines were rated as having good methodological quality. The detailed ASCO recommendations for the use of biomarkers in early-stage breast cancer are in Appendix G.

The ASCO guidelines outlined recommendations for when Oncotype DX breast cancer assay, MammaPrint, EndoPredict, Prosigna, BCI, and Mammostrat should or should not be used in patients with early-stage breast cancer. All of these tests, except for Mammostrat, are recommended for use in patients who have ER-positive/PR-positive, HER2-negative, LN-negative breast cancer. The guidelines recommend against the use of MammaPrint for the following categories of breast cancers: ER-positive/PR-positive, HER2-negative (LN-positive or negative); HER2-positive; or ER-negative/PR-negative, HER2-negative, LN-negative.

According to the ASCO guidelines, MammaPrint should not be used in patients with low clinical risk (as defined by the Adjuvant! Online tool as used in the MINDACT study), because women in the low clinical risk category had very good outcomes and did not appear to benefit from chemotherapy even with a genomic high-risk cancer. MammaPrint can be used in patients with ER-positive/PR-positive, HER2-negative, LN-negative breast cancer who have one to three positive nodes and are at high clinical risk per MINDACT categorization. Still, these patients should be informed that a benefit of chemotherapy cannot be excluded, particularly among patients with more than one involved lymph node. The ASCO guidelines recommended against using the other tests in patients with ER-positive/PR-positive, HER2-negative, LN-positive breast cancer; HER2-positive breast cancer; or ER-negative/PR-negative, HER2-negative, LN-negative breast cancer. The authors of the 2017 NCCN clinical practice guidelines on breast cancer discussed the evidence for Oncotype DX (21-gene breast cancer assay), MammaPrint (70-gene assay), and Prosigna (50-gene assay). According to the guidelines, Oncotype DX can be considered for ER-positive/PR-positive, HER2-negative cancers with pT1, pT2, or pT3, and pN0 or pN1mi ≤ 2 mm axillary node metastasis and a tumor greater than 0.5 cm. Oncotype DX can also be considered in certain patients with one to three involved ipsilateral axillary lymph nodes to guide the addition of combination chemotherapy to standard hormone therapy. The NCCN guideline authors stated that the other gene expression profile tests can be considered to assess risk of cancer recurrence, but that they have not been validated to predict response to chemotherapy. Center researchers rated the NCCN guidelines as having fair methodological quality.

NICE published guidelines in 2013 that assessed the use of Oncotype DX breast cancer assay, MammaPrint, Mammostrat, and immunohistochemical 4 (IHC4) score in early-stage breast cancer. The guidelines recommend Oncotype DX as an option for guiding adjuvant chemotherapy decisions for people with ER-positive, HER2-negative, LN-negative early-stage breast cancer when the patient is assessed as being at intermediate risk. According to the guidelines, Oncotype DX should only be used when the test results are likely to help in predicting the course of the disease, and therefore in the decision of whether to prescribe chemotherapy. MammaPrint and Mammostrat are only recommended for use in research in patients with ER-positive, HER2-negative, LN-negative early-stage breast cancer. Center researchers rated the NICE guidelines as having good methodological quality.
The European Society for Medical Oncology (ESMO) published breast cancer clinical practice guidelines in 2015. The ESMO guidelines recommend that gene expression profile tests, such as Oncotype DX breast cancer assay, MammaPrint, EndoPredict, and Prosigna, can be used to complement pathology assessments to predict the benefit of adjuvant chemotherapy. In cases when decisions might be challenging, such as in luminal B HER2-negative and LN-negative breast cancer, Oncotype DX, EndoPredict, and Prosigna can be used. For all types of breast cancer (pN0–1), MammaPrint can be used in conjunction with clinicopathological factors to help in decision making about treatment. Center researchers rated the ESMO guidelines as having poor methodological quality.

The European Group on Tumor Markers (EGTM) published a guideline in 2017 on the use of biomarkers in breast cancer. These guidelines recommend that the Oncotype DX breast cancer assay, MammaPrint, EndoPredict, Prosigna, and BCI can be used to aid in adjuvant therapy decision making in ER-positive, HER2-negative, LN-negative patients. In addition, Oncotype DX, MammaPrint, EndoPredict, and Prosigna can be used in patients with one to three metastatic lymph nodes. Center researchers rated the EGTM guidelines as having poor methodological quality. The detailed recommendations from the EGTM are in Appendix G. Table 1 summarizes these five guidelines on breast cancer, indicating whether the gene expression profile tests are recommended for LN-negative and/or LN-positive cancers.

### Table 1. Recommendations for Lymph Node Status in Guidelines on the Use of Gene Expression Tests in Early-Stage Breast Cancer

<table>
<thead>
<tr>
<th>Test</th>
<th>ASCO</th>
<th>NCCN</th>
<th>NICE</th>
<th>ESMO**</th>
<th>EGTM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oncotype DX</td>
<td>LN-negative</td>
<td>LN-negative</td>
<td>LN-negative</td>
<td>LN-negative</td>
<td>LN-negative</td>
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<tr>
<td></td>
<td></td>
<td>LN-positive</td>
<td></td>
<td>LN-negative</td>
<td>LN-positive</td>
</tr>
<tr>
<td>MammaPrint</td>
<td>LN-negative</td>
<td>Not recommended*</td>
<td>Not recommended</td>
<td>LN-negative</td>
<td>LN-negative</td>
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<tr>
<td></td>
<td>LN-positive</td>
<td></td>
<td></td>
<td>LN-negative</td>
<td>LN-positive</td>
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<tr>
<td>EndoPredict</td>
<td>LN-negative</td>
<td>Not recommended*</td>
<td>No guideline recommendation</td>
<td>LN-negative</td>
<td>LN-negative</td>
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<td>LN-positive</td>
<td>LN-positive</td>
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<tr>
<td>Prosigna</td>
<td>LN-negative</td>
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<td>No guideline recommendation</td>
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<td></td>
<td>LN-positive</td>
<td>LN-positive</td>
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<tr>
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<td>LN-negative</td>
<td>Not recommended*</td>
<td>No guideline recommendation</td>
<td>No guideline recommendation</td>
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<tr>
<td>Mammastrat</td>
<td>Not recommended*</td>
<td>Not recommended*</td>
<td>Not recommended</td>
<td>No guideline recommendation</td>
<td>No guideline recommendation</td>
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</table>

*NCCN guidelines state that prognostic multigene assays other than Oncotype DX may be considered to help assess risk of recurrence but have not been validated to predict response to chemotherapy. **The ESMO guideline authors did not distinguish between LN-negative and LN-positive cancers in their recommendations.

### Prostate Cancer

Two clinical practice guidelines were identified that included recommendations on the use of Decipher, Prolaris, and Oncotype DX prostate cancer assay. The 2017 NCCN guidelines on prostate cancer stated that men with clinically localized prostate cancer may consider the use of tumor-based molecular assays, and the authors made specific recommendations on the use of Decipher, Prolaris, and Oncotype DX for prostate cancer. The guidelines recommend Decipher after a radical prostatectomy for patients with pT2 (confined to prostate) with positive margins, any pT3 (extraprostatic extension) disease, and a rising PSA level. Prolaris and Oncotype DX are recommended post-biopsy for low- and very low-risk prostate cancer in patients with at least 10 years of life expectancy who have not received other active treatment for prostate cancer and who are candidates for active surveillance or definitive therapy. Center researchers rated the NCCN guidelines as having fair methodological quality.
A guideline on clinically localized prostate cancer has been jointly published by the American Urological Association, American Society for Radiation Oncology, and Society of Urologic Oncology in 2017. These guidelines include the following recommendation based on expert opinion: “Tissue-based genomic biomarkers have not shown a clear role in active surveillance for localized prostate cancer and are not necessary for follow up.” Center researchers rated these guidelines as having good methodological quality.

**Colon Cancer**

No clinical practice guidelines were found that included recommendations for the use of ColoPrint or Oncotype DX for colon cancer. The American Society for Clinical Pathology, College of American Pathologists, Association for Molecular Pathology, and ASCO published a guideline on molecular biomarkers for colorectal cancer in 2017. This guideline stated, “A problem of quantitative assays, such as gene expression, microRNA expression, and methylation levels, tested in solid tumors, results from the intrinsic mixed nature of the tissue with significant variability of tumor and non-tumor tissue content. Another limitation of molecular biomarker discovery approaches that rely on expression levels is that these biomarkers have not been evaluated in the context of complex molecular regulation of individual cancer subtypes.” Center researchers rated these guidelines as having good methodological quality.

The fair-methodological-quality 2017 NCCN guidelines on colon cancer discussed multigene assays, including ColoPrint and Oncotype DX colon cancer assay, and concluded that there is no evidence of predictive value in terms of the potential benefit of chemotherapy for any of the multigene assays. Similarly, the 2016 guidelines on metastatic colon cancer from ESMO concluded that gene expression signatures have failed to accurately predict disease recurrence and prognosis. Center researchers rated the ESMO guidelines as having poor methodological quality.

**Multiple Myeloma**

The authors of the 2017 NCCN guidelines on multiple myeloma discussed gene expression profiling tests, including MyPRS and SKY92, but did not make any recommendations about the use of these tests. The NCCN panel unanimously agreed that although gene expression profile tests are not routinely used, they could be helpful in selected patients to estimate the aggressiveness of the disease and to individualize treatment. Center researchers rated the NCCN guidelines as having fair methodological quality. The authors of the 2017 guidelines on multiple myeloma from ESMO stated that gene-expression profiling is not currently used routinely, and more research is needed to identify molecular markers, which could lead to advances in this area. Center researchers rated the ESMO guidelines as having fair methodological quality. No other clinical practice guidelines were found that included recommendations for the use of My Prognostic Risk Signature (MyPRS) or SKY92 tests.