

The Medical Letter®

On Drugs and Therapeutics

Published by The Medical Letter, Inc. • 1000 Main Street, New Rochelle, NY 10801 • A Nonprofit Publication

www.medicalletter.org

BRCA Screening

Direct-to-consumer advertisements are urging women to be tested for mutations in *BRCA1* and *BRCA2* genes, which are the most common known causes of an inherited predisposition to breast and ovarian cancer. Clinically important *BRCA* mutations have been found in about 2% of Ashkenazi Jewish women, and are estimated to occur in about 1 in 300 to 500 women in the general non-Jewish US population.¹ The prevalence appears to be lower in non-whites.

WHO SHOULD BE SCREENED? — If the youngest woman in the family who has breast or ovarian cancer tests negative for *BRCA* mutations, further testing of the family may not be indicated.

BRCA genes can be inherited from either parent. The family histories that warrant consideration of testing, according to the US Preventive Services Task Force, are listed in the table below.

When a woman tests positive, her first- and second-degree female relatives, and possibly her female cousins, should also be tested.

MANAGEMENT OF A POSITIVE TEST — A recent meta-analysis calculated that women who test positive for the *BRCA1* mutation have a 57% risk of developing breast cancer and a 40% risk of developing ovarian cancer before age 70, and those who test positive for the *BRCA2* mutation have a 49% risk of developing breast cancer and an 18% risk of developing ovarian cancer.²

Since the onset of cancer occurs at an earlier age in *BRCA* mutation carriers than in the general population, *BRCA*-positive women might consider having breast and gynecological exams every 6 months beginning at age 25 and an annual breast MRI, with or without mammography, at age 30. MRIs detect twice as many cancers as either mammography or ultrasound.³⁻⁵ A mammogram in addition to an MRI would further increase the sensitivity of breast cancer detection, but ionizing radiation may itself induce cancer in *BRCA*-mutation carriers, and the benefit may not justify the radiation exposure before age 35.⁶ Use of a mammogram, MRI and ultrasound all together increases the sensitivity of breast cancer detection from about 75% with an MRI alone to about 95%.

At some point, *BRCA*-positive women should consider a bilateral salpingo-oophorectomy, which reduces the risk of ovarian cancer by at least 80% and also reduced the risk of breast cancer by 50% in some reports.^{7,8} Preventive bilateral mastectomy can reduce the risk of breast cancer by 90% or more.

CONCLUSION — Women with no family history of breast or ovarian cancer on either side of the family generally should not be tested for *BRCA* mutations. Women with a strong family history of breast or ovarian cancer and female relatives of women who test positive for *BRCA* mutations probably should be tested because effective surveillance and preventive measures are available. □

1. US Preventive Services Task Force. Genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility: recommendation statement. *Ann Intern Med* 2005; 143:355.

2. S Chen and G Parmigiani. Meta-analysis of *BRCA1* and *BRCA2* penetrance. *J Clin Oncol* 2007; 25:1329.

3. M Robson and K Offit. Clinical practice. Management of an inherited predisposition to breast cancer. *N Engl J Med* 2007; 357:154.

4. D Saslow et al. American Cancer Society guidelines for breast screening with MRI as an adjunct to mammography. *CA Cancer J Clin* 2007; 57:75.

Table 1. USPSTF Recommendations*

Ashkenazi Jewish Women: <ul style="list-style-type: none">• Any first-degree relative with breast or ovarian cancer• Two second-degree relatives on the same side of the family with breast or ovarian cancer
Non-Ashkenazi Women: <ul style="list-style-type: none">• Two first-degree relatives with breast cancer (including one diagnosed ≤ age 50)• Three or more first- or second-degree relatives with breast cancer• Both breast cancer and ovarian cancer among first- and second-degree relatives• A first-degree relative with bilateral breast cancer• Two or more first- or second-degree relatives with ovarian cancer• A first- or second-degree relative with both breast and ovarian cancer• A male relative with breast cancer

* US Preventive Services Task Force. *Ann Intern Med* 2005; 143:355.

5. E Warner et al. Surveillance of BRCA1 and BRCA2 mutation carriers with magnetic resonance imaging, ultrasound, mammography, and clinical breast examination. JAMA 2004; 292:1317.
6. F Sardanelli and F Podo. Management of an inherited predisposition to breast cancer. N Engl J Med 2007; 357:1663.
7. A Finch et al. Salpingo-oophorectomy and the risk of ovarian, fallopian tube, and peritoneal cancers in women with a BRCA1 or BRCA2 mutation. JAMA 2006; 296:185.
8. A Eisen et al. Breast cancer risk following bilateral oophorectomy in BRCA1 and BRCA2 mutation carriers: an international case-control study. J Clin Oncol 2005; 23:7491.

The Medical Letter®
On Drugs and Therapeutics

EDITOR: Mark Abramowicz, M.D.
DEPUTY EDITOR: Gianna Zuccotti, M.D., M.P.H., Weill Medical College of Cornell University
EDITOR, DRUG INFORMATION: Jean-Marie Pflomm, Pharm.D.
CONTRIBUTING EDITOR, DRUG INTERACTIONS: Philip D. Hansten, Pharm.D., University of Washington
ADVISORY BOARD:
Jules Hirsch, M.D., Rockefeller University
David N. Juurlink, BPhM, M.D., PhD, Sunnybrook Health Sciences Centre
James D. Kenney, M.D., Yale University School of Medicine
Richard B. Kim, M.D., University of Western Ontario
Gerald L. Mandell, M.D., University of Virginia School of Medicine
Hans Meinertz, M.D., University Hospital, Copenhagen
Dan M. Roden, M.D., Vanderbilt University School of Medicine
F. Estelle R. Simons, M.D., University of Manitoba
Neal H. Steigbigel, M.D., New York University School of Medicine
EDITORIAL FELLOWS:
Vanessa K. Dalton, M.D., M.P.H., University of Michigan Medical School
Eric J. Epstein, M.D., Albert Einstein College of Medicine
DRUG INTERACTIONS FELLOW: Emily Ung, BScPhM, Children's Hospital of Western Ontario
SENIOR ASSOCIATE EDITORS: Donna Goodstein, Amy Faucard
ASSISTANT EDITOR: Cynthia Macapagal Covey
MANAGING EDITOR: Susie Wong
PRODUCTION COORDINATOR: Cheryl Brown
VP FINANCE & OPERATIONS: Yosef Wissner-Levy
 Founded in 1959 by
 Arthur Kallet and Harold Aaron, M.D.

Copyright and Disclaimer: The Medical Letter is an independent nonprofit organization that provides healthcare professionals with unbiased drug prescribing recommendations. The editorial process used for its publications relies on a review of published and unpublished literature, with an emphasis on controlled clinical trials, and on the opinions of its consultants. The Medical Letter is supported solely by subscription fees and accepts no advertising, grants or donations. The content of The Medical Letter is controlled by the Editor, who declares no conflict. The members of the Advisory Board are required to disclose any potential conflict of interest.

No part of the material may be reproduced or transmitted by any process in whole or in part without prior permission in writing. The editors do not warrant that all the material in this publication is accurate and complete in every respect. The editors shall not be held responsible for any damage resulting from any error, inaccuracy or omission.

Subscription Services

<p>Mailing Address: The Medical Letter, Inc. 1000 Main Street New Rochelle, NY 10801-7537</p> <p>Customer Service: Call: 800-211-2769 or 914-235-0500 Fax: 914-632-1733 Web Site: www.medicalletter.org E-mail: custserv@medicalletter.org</p> <p>Permissions: To reproduce any portion of this issue, please e-mail your request to: permissions@medicalletter.org</p>	<p>Subscriptions (US): 1 year - \$89; 2 years - \$151; 3 years - \$214. \$44.50 per year for students, interns, residents and fellows in the US and Canada. CME: \$44 for 26 credits.</p> <p>E-mail site license inquiries to: info@medicalletter.org or call 800-211-2769 x315. Special fees for bulk subscriptions. Special classroom rates are available. Back issues are \$12 each. Major credit cards accepted.</p>
--	---

Copyright 2007. ISSN 1523-2859