

A REVIEW OF QUALITATIVE INDICATORS IN BREAST CANCER DIAGNOSIS

Hadeel Naji Al-Tamimi

Department of Pathology, College of Medicine, Al-Muthanna University, Samawah, Iraq.

DOI:<https://doi.org/10.5281/zenodo.15480973>

Abstract: Though breast cancer that has not spread is curable in 70 to 80 percent of cases diagnosed in earlier stages of the disease. [1] Breast cancer is the most prevalent cancer diagnosed in women globally. Currently, metastatic breast cancer, indicated by distant organ metastasis, is an incurable disease. These include genetic characteristics such as sensitivities promoted by BRCA mutations, hormone receptors (oestrogen and progesterone receptors) and human epidermal growth factor receptor 2 (HER2, encoded by ERBB2) reported to be associated with breast cancer. Note: Treatment depends on molecular subtype. Breast cancer is treated in a multidisciplinary setting with systemic therapy (including chemotherapy and endocrine therapy) and locoregional (surgical and radiation therapy) procedures. These include endocrine therapy for estrogen receptor-positive tumors, anti-HER2 therapy, bone-stabilizing agents, and for BRCA mutation carriers, poly(ADP-ribose) polymerase inhibitors, chemotherapy, and, most recently, immunotherapy. Such future therapeutic concepts in breast cancer where there is the aim to escalate or de-escalate a treatment based on tumor biology, early therapy response and even treating patients according to their genomic profile. New therapeutic development is surpassed only by equitable access to the latest therapeutics regardless of socioeconomic status as the greatest challenge in breast cancer treatment of the future

Keywords: Breast cancer, causes, risk

Introduction:

One tumor that grows to beçky is Breast flesh. [1] A ache on a a breast knob, a change in breast shape, a dimpled peel, a move conflicting to milk, nip fluid, a new-inverted nip, or even a sore or scaly square of peel are all examples of breast tumor. [1] People of the disease actually gone could suffer as bone pain, a bloated lymph mass, a yellow skin & a shortness of breath. [2]

Obesity, physical inactivity, alcohol use, premenopausal hormone replacement therapy, previous ionizing radiation exposure, early age at menarche, later age at first childbirth (and nulligravidity), older age, breast cancer in family history of , and breast cancer personal history. However, only 5–10% of cases are linked to inherited genetic predisposition (e.g. BRCA mutations) 1[3]. [4] Breast cancer typically starts in the cells that make up the lining of milk ducts or in the lobules that give milk to these ducts. [1] Lobular carcinomas originate in the lobules and ductal carcinomas originate in the ducts. [1] There are over eighteen subtypes of breast cancer. Some begin as pre-invasive lesions such as ductal carcinoma in situ. [2] A biopsy of the affected tissue confirms breast cancer. [1] Following diagnosis, more screening tests are conducted to figure out the most effective therapy and if the cancer has spread outside the breast. [5]

Because the size and spread of breast cancer are among the most important criteria in judging the disease's prognosis, screening for the disease can be extremely useful. Breast cancers that are found through screening are smaller and less likely to have spread beyond the breast. Mammography is under a 2013 Cochrane research instead many women who have positive mammography test results ultimately have no cancer and the procedure may even do more bad than good to the people. [6] A 2009 study from the US Preventive Services Task Force found screening was beneficial between the ages of 40 and 70 [8], and the group recommends biennial screening between ages 50 and 74. [7] In women at increased risk for having breast cancer, the drugs raloxifene or tamoxifen are used to attempt to prevent the condition. Having both breasts surgically removed is another option that some high-risk women choose as a prophylactic one. Cancer treatment spans a wide variety of approaches like hormone therapy, targeted therapy, chemotherapy, radiation therapy, surgery, etc.[2] [9] Surgical options can include mastectomy or breast-conserving techniques. [10] Breast reconstruction can occur at the time of surgery or afterwards. [11] The focus of treatment is on improving the comfort and quality of life in these patients whose cancer has metastasized to the other body parts. [12]

Epidemiology

Breast cancer is the most prevalent malignant tumor in females worldwide. 36% Breast: No Patients with Cancer. Approximately 2.089 million new breast cancer diagnoses in women occurred in 2018 [13]. Although this tumor is increasingly frequent worldwide, developed countries are reporting the highest incidence. Developed countries make up over half of all-of-cases globally. [14]. Therefore, this trend predominantly follows the so-called Western lifestyle and is linked to poor diet, nicotine, high levels of stress and exercise. [15] Mammograms are a widely accepted method of screening for breast cancer. Mammography mammography values are the highest in women from 50 to 69 years of age [16]. Mammography classical sensitivity and specificity is found from 75–95% and 80–95%, respectively. [14]. Magnetic Resonance Mammography (MRM) A breast cancer screen for some women who may have inherited breast cancer. If a mammogram demonstrates a concern lesion, the patient undergoes a coarser needle biopsy, an ultrasound and a tumor histological study.

1. Kinds of Breast Growth

Breast cancer is classified by its origin and molecular features:

- DCIS or ductal carcinoma in situ: a non-invasive cancer that affects only the milk duct. The most common type, IDC starts in the milk ducts and spreads to surrounding tissue.
- ILC This cancer starts in the lobules that produce milk and can spread to other types of areas.
- Triple-negative breast cancers (TNBC) are rns negative for HER2, progesterone receptors (PR), and estrogen receptors (ER). It is hateful and aggressive and heartless and ever harder to cure.
- HER2-positive breast cancer: This form of cancer grows rapidly from overexpression of the HER2 protein.
- Hormone Receptor-Positive Breast Cancer: As its name implies, this type of breast cancer is driven by estrogen or progesterone receptors and responds to hormone therapy.

2. Common Characteristics

- Lump or Mass: The most typical symptom is a firm, painless lump in the breast.
- Skin Changes: The skin may become thicker, redder, or dimplified (like an orange peel).
- Changes to the breasts: inversion, scaling, or discharge (particularly bloody).
- Asymmetry or bulge in unique breast are instances of vagaries in breast scope or shape.

- Pain: In severe cases, pain may arise, albeit it is uncommon in the early stages.
- 3. Molecular and Genetic Features
 - Hormone Receptors: Presence or absence of estrogen (ER) and progesterone (PR) receptors.
 - HER2 Position: Overexpression of the HER2 protein.
 - Genetic Mutations: Mutations in genes like BRCA1, BRCA2, TP53, and PTEN increase the danger of breast tumor.
- 4. Staging

Tumor size, involvement of lymph nodes, and metastasis are used to stage breast growth:

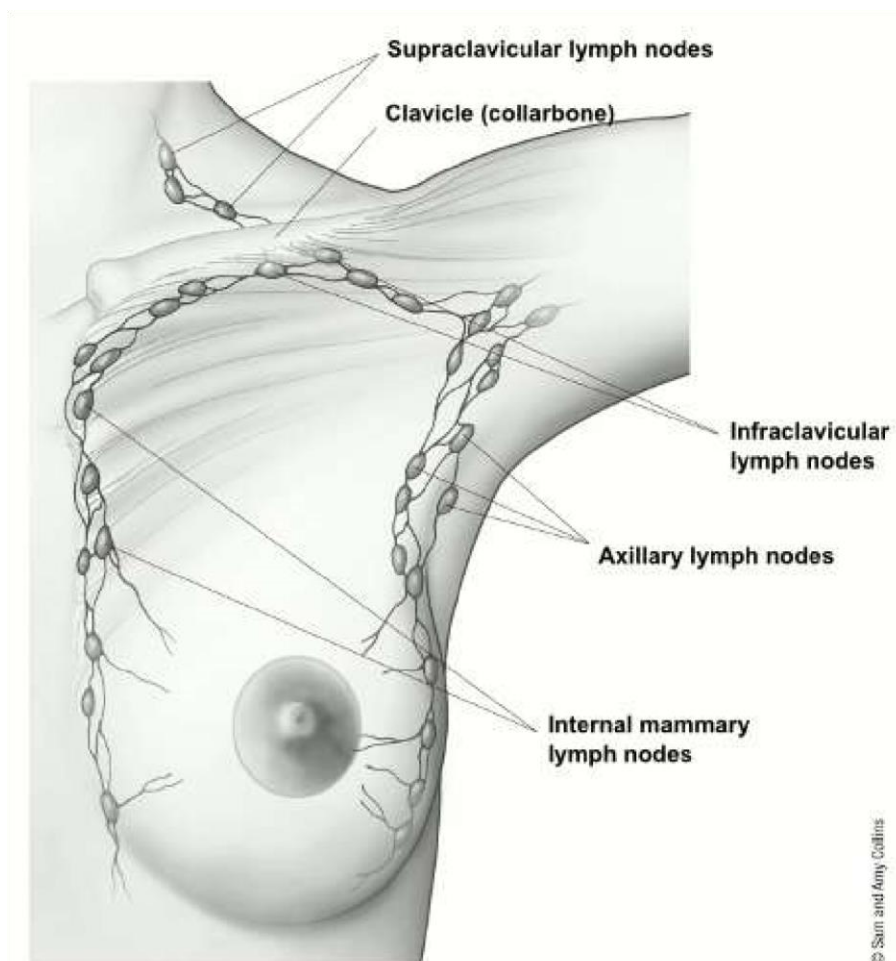
 - Phase 0: DCIS and other non-invasive procedures.
 - Stage I: Breast-specific little tumor.
 - Stage II: A larger tumor or lymph node spread.
 - Stage III: Cancer that has spread locally and affected numerous lymph bulges.
 - Phase IV: Cancer that takes metastasized to extra organs, such equally the liver, lungs, or bones.
- 5. Risk Causes
 - Gender: Women are at higher risk, though men can also grow breast cancer.
 - Period: Risk increases with age, chiefly after the age of fifty.
 - Family Past: Genetic mutations (e.g., BRCA1/2) or a strong family history.
 - Hormonal Factors: hormone replacement treatment, late menopause, or early menstruation.
 - Lifestyle Factors: Lack of physical activity, alcohol use, and obesity.
- 6. Diagnostic Tools
 - Mammography: Primary screening tool for detecting breast abnormalities.
 - Ultrasound: Used to differentiate among solid masses then fluid-filled lumps.
 - MRI: For high-risk individuals or detailed imaging.
 - Biopsy: Definitive diagnosis through flesh sampling.
- 7. Treatment Options
 - Surgery: mastectomy (breast removal) or lumpectomy (tumor removal). After operation, radiation healing is used to destroy any cancer lockups that remain.

Chemotherapy: A systemic approach to cancer cell death.

 - Hormone therapy: For tumors that express hormone receptors (tamoxifen, aromatase inhibitors, etc.).

Targeted therapy, such as trastuzumab, is used for HER2-positive tumors.

 - Immunotherapy: For some triple-negative or advanced breast tumors.



Lymph nodes in relation to the breast

References:

- Henry NL, Shah PD, Haider I, Freer PE, Jagsi R, Sabel MS. Chapter 88: Cancer of the Breast. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology*. 6th ed. Philadelphia, Pa: Elsevier; 2020.
- Jagsi R, King TA, Lehman C, Morrow M, Harris JR, Burstein HJ. Chapter 79: Malignant Tumors of the Breast. In: *DeVita VT, Lawrence TS, Lawrence TS, Rosenberg SA, eds.*
- DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology*. 11th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2019.

National Cancer Institute. Physician Data Query (PDQ). Breast Cancer Treatment – Patient Version. 2021. Accessed at <https://www.cancer.gov/types/breast/patient/breast-treatmentpdq> on June 24, 2021.

Brinton L.A., Schairer C., Hoover R.N., Fraumeni J.F., Jr. Menstrual Factors and Risk of Breast Cancer. *Cancer Invest.* 1988;6:245–254. doi: 10.3109/07357908809080645.

Collaborative Group on Hormonal Factors in Breast Cancer Menarche, menopause, and breast cancer risk: Individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. *Lancet Oncol.* 2012;13:1141–1151. doi:

10.1016/S1470-2045(12)70425-4.

De Blok C.J.M., Wiepjes C.M., Nota N.M., van Engelen K., Adank M.A., Dreijerink K.M.A., Barbé E., Konings I.R.H.M., den Heijer M. Breast cancer risk in transgender people receiving hormone treatment: Nationwide cohort study in the Netherlands. *BMJ.* 2019;365:l1652. doi: 10.1136/bmj.l1652.

Vinogradova Y., Coupland C., Hippisley-Cox J. Use of hormone replacement therapy and risk of breast cancer: Nested case-control studies using the QResearch and CPRD databases. *BMJ.* 2020;371:m3873. doi: 10.1136/bmj.m3873.

Yue W., Wang J.P., Li Y., Fan P., Liu G., Zhang N., Conaway M., Wang H., Korach K.S., Bocchinfuso W., et al. Effects of estrogen on breast cancer development: Role of estrogen receptor independent mechanisms. *Int. J. Cancer.* 2010;127:1748–1757. doi: 10.1002/ijc.25207. [DOI] [PMC free article] [PubMed] [Google Scholar]

Dall G.V., Britt K.L. Estrogen Effects on the Mammary Gland in Early and Late Life and Breast Cancer Risk. *Front. Oncol.* 2017;7:110. doi: 10.3389/fonc.2017.00110. [DOI] [PMC free article] [PubMed] [Google Scholar]

Singletary S.E. Rating the risk factors for breast cancer. *Ann. Surg.* 2003;237:474–482. doi: 10.1097/01.SLA.0000059969.64262.87. [DOI] [PMC free article] [PubMed] [Google Scholar]

Harlow S.D., Paramsothy P. Menstruation and the menopausal transition. *Obstet. Gynecol. Clin. N. Am.* 2011;38:595–607. doi: 10.1016/j.ogc.2011.05.010. [DOI] [PMC free article] [PubMed] [Google Scholar]

Kelsey J.L., Gammon M.D., John E.M. Reproductive factors and breast cancer. *Epidemiol. Rev.* 1993;15:36–47. doi: 10.1093/oxfordjournals.epirev.a036115. [DOI] [PubMed] [Google Scholar]

Hershman, D. L. et al. Prevention and management of chemotherapy-induced peripheral neuropathy in survivors of adult cancers: American Society of Clinical Oncology clinical practice guideline. *J. Clin. Oncol.* 32, 1941–1967 (2014).

- Hanai, A. et al. Effects of cryotherapy on objective and subjective symptoms of paclitaxel-induced neuropathy: prospective self-controlled trial. *J. Natl Cancer Inst.* 110, 141–148 (2018).
- Kadakia, K. C., Rozell, S. A., Butala, A. A. & Loprinzi, C. L. Supportive cryotherapy: a review from head to toe. *J. Pain Symptom Manage.* 47, 1100–1115 (2014).
- Hou, S., Huh, B., Kim, H. K., Kim, K.-H. & Abdi, S. Treatment of chemotherapy-induced peripheral neuropathy: systematic review and recommendations. *Pain Physician* 21, 571–592 (2018).
- Ahmed, R. L., Schmitz, K. H., Prizment, A. E. & Folsom, A. R. Risk factors for lymphedema in breast cancer survivors, the Iowa Women's Health Study. *Breast Cancer Res. Treat.* 130, 981–991 (2011).
- Gillespie, T. C., Sayegh, H. E., Brunelle, C. L., Daniell, K. M. & Taghian, A. G. Breast cancer-related lymphedema: risk factors, precautionary measures, and treatments. *Gland. Surg.* 7, 379–403 (2018).
- Runowicz, C. D. et al. American Cancer Society/ American Society of Clinical Oncology breast cancer survivorship care guideline. *J. Clin. Oncol.* 34, 611–635 (2016).
- Velikova, G. et al. Quality of life after postmastectomy radiotherapy in patients with intermediate-risk breast cancer (SUPREMO): 2-year follow-up results of a randomised controlled trial. *Lancet Oncol.* 19, 1516–1529 (2018).
- Hofmann, D. et al. WSG ADAPT — adjuvant dynamic marker-adjusted personalized therapy trial optimizing risk assessment and therapy response prediction in early breast cancer: study protocol for a prospective, multi-center, controlled, non-blinded, randomized, investigator initiated phase II/III trial. *Trials* 14, 261 (2013).
- Robertson, J. F. R., Dowsett, M. & Bliss, J. M. Peri-operative aromatase inhibitor treatment in determining or predicting long-term outcome in early breast cancer — the POETIC Trial (CRUK/07/015) [abstract]. *SABCS GS1-03* (2017).
- Kim, S.-B. et al. Ipatasertib plus paclitaxel versus placebo plus paclitaxel as first-line therapy for metastatic triple-negative breast cancer (LOTUS): a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet Oncol.* 18, 1360–1372 (2017).
- Schmid, P. et al. AZD5363 plus paclitaxel versus placebo plus paclitaxel as first-line therapy for metastatic triple-negative breast cancer (PAKT): a randomised, double-blind, placebo-controlled, phase II trial. *J. Clin. Oncol.* 36 (15 Suppl.), 1007 (2018).
- Jones, R. H. et al. Capivasertib (AZD5363) plus fulvestrant versus placebo plus fulvestrant after relapse or progression on an aromatase inhibitor in metastatic ER-positive breast cancer (FAKTION): a randomized, double-blind, placebo-controlled, phase II trial [abstract]. *J. Clin. Oncol.* 37 (no. 15_suppl), 1005–1005 (2019).

- Yardley, D. A. et al. Randomized phase II, doubleblind, placebo-controlled study of exemestane with or without entinostat in postmenopausal women with locally recurrent or metastatic estrogen receptorpositive breast cancer progressing on treatment with a nonsteroidal aromatase inhibitor. *J. Clin. Oncol.* 31, 2128–2135 (2013).
- Ogitani, Y. et al. DS-8201a, a novel HER2-targeting ADC with a novel DNA Topoisomerase I inhibitor, demonstrates a promising antitumor efficacy with differentiation from T-DM1. *Clin. Cancer Res.* 22, 5097–5108 (2016).
- Tamura, K. et al. Trastuzumab deruxtecan (DS-8201a) in patients with advanced HER2positive breast cancer previously treated with trastuzumab emtansine: a dose-expansion, phase 1 study. *Lancet Oncol.* 20, 816–826 (2019).
- Burris III, H. A., Giaccone, G. & Im, S. A. Updated findings of a first-in-human phase 1 study of margetuximab, an Fc-optimized chimeric monoclonal antibody, in patients with HER2-positive advanced solid tumors [abstract]. *Am. Soc. Clin. Oncol. Meet.* 33 (no. 15_suppl), A523 (2015).
- Rugo, H. S. et al. SOPHIA primary analysis: a phase 3 (P3) study of margetuximab (M) + chemotherapy (C) versus trastuzumab (T) + C in patients (pts) with HER2+ metastatic (met) breast cancer (MBC) after prior anti-HER2 therapies (Tx) [abstract]. *J. Clin. Oncol.* 37 (Suppl.), Abstr 1000 (2019).
- Hyman, D. M., Piha-Paul, S. & Rodon, J. Neratinib in HER2- or HER3-mutant solid tumors: SUMMIT, a global, multi-histology, open-label, phase 2 ‘basket’ study [abstract]. *Am. Assoc. Cancer Res. Meet.* CTO01 (2017).
- Kanemura, S., I. Tsuji, N. Ohuchi, H. Takei, T. Yokoe, Y. Koibuchi, K. Ohnuki, A. Fukao, S. Satomi, and S. Hisamichi. 1999. "A case control study on the effectiveness of breast cancer screening by clinical breast examination in Japan." *Jpn J Cancer Res* no. 90 (6):60713. doi: S0910505099801240 [pii].
- Kardinah, D., B. O. Anderson, C. Duggan, I. A. Ali, and D. B. Thomas. 2013. "Short report: Limited effectiveness of screening mammography in addition to clinical breast examination by trained nurse midwives in rural Jakarta, Indonesia." *Int J Cancer.* doi: 10.1002/ijc.28442.
- Kuroishi, T., K. Hirose, T. Suzuki, and S. Tominaga. 2000. "Effectiveness of mass screening for breast cancer in Japan." *Breast Cancer* no. 7 (1):1-8. Lauer, J. A., K. Rohrich, H. Wirth, C. Charette, S. Gribble, and C. J. Murray. 2003. "PopMod: a longitudinal population model with two interacting disease states." *Cost Eff Resour Alloc* no. 1 (1):6.
- Lee, S. G., Y. G. Jee, H. C. Chung, S. B. Kim, J. Ro, Y. H. Im, S. A. Im, and J. H. Seo. 2009. "Cost-effectiveness analysis of adjuvant therapy for node positive breast cancer in Korea: docetaxel, doxorubicin and cyclophosphamide (TAC) versus fluorouracil, doxorubicin and cyclophosphamide (FAC)." *Breast Cancer Res Treat* no. 114 (3):589-95.

doi: 10.1007/s10549-008-0035-0.

- Lee, S. Y., S. H. Jeong, Y. N. Kim, J. Kim, D. R. Kang, H. C. Kim, and C. M. Nam. 2009. "Cost-effective mammography screening in Korea: high incidence of breast cancer in young women." *Cancer Sci* no. 100 (6):1105-11. doi: 10.1111/j.1349-7006.2009.01147.x.
- Love, R. R., N. B. Duc, D. C. Allred, N. C. Binh, N. V. Dinh, N. N. Kha, T. V. Thuan, S. K. Mohsin, D. Roanh le, H. X. Khang, T. L. Tran, T. T. Quy, N. V. Thuy, P. N. The, T. T. Cau, N. D. Tung, D. T. Huong, M. Quang le, N. N. Hien, L. Thuong, T. Z. Shen, Y. Xin, Q. Zhang, T. C. Havighurst, Y. F. Yang, B. E. Hillner, and D. L. DeMets. 2002. "Oophorectomy and tamoxifen adjuvant therapy in premenopausal Vietnamese.
- Murray, C.J.L., and A.D. Lopez. 1996. "The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases, Injuries, and Risk Factors in 1990 and Projected to 2020." In *Global Burden of Disease and Injury*. Cambridge, MA: Harvard School of Public Health.
- Nelson, H. D., K. Tyne, A. Naik, C. Bougatsos, B. K. Chan, and L. Humphrey. 2009. "Screening for breast cancer: an update for the U.S. Preventive Services Task Force." *Ann Intern Med* no. 151 (10):727-37, W237-42. doi: 10.7326/0003-4819-151-10-20091117000009.
- Nguyen, L.H., W. Laohasiriwong, J.F. Stewart, and et al. 2013. "Cost-effectiveness analysis of a screening program for breast cancer in Vietnam. ." *Value in Health Regional Issues* no. 2:21-28.
- Okonkwo, Q. L., G. Draisma, A. der Kinderen, M. L. Brown, and H. J. de Koning. 2008. "Breast cancer screening policies in developing countries: a cost-effectiveness analysis for India." *J Natl Cancer Inst* no. 100 (18):1290-300. doi: 10.1093/jnci/djn292.
- Parkin, D. M., and L. M. Fernandez. 2006. "Use of statistics to assess the global burden of breast cancer." *Breast J* no. 12 Suppl 1:S70-80.
- Perloff, M., G. J. Lesnick, A. Korzun, F. Chu, J. F. Holland, M. P. Thirlwell, R. R. Ellison, R. W. Carey, L. Leone, V. Weinberg, and et al. 1988. "Combination chemotherapy with mastectomy or radiotherapy for stage III breast carcinoma: a Cancer and Leukemia Group B study." *J Clin Oncol* no. 6 (2):261-9.
- Pisani, P., D. M. Parkin, C. Ngelangel, D. Esteban, L. Gibson, M. Munson, M. G. Reyes, and A. Laudico. 2006. "Outcome of screening by clinical examination of the breast in a trial in the Philippines." *Int J Cancer* no. 118 (1):149-54.
- Poon, D., B. O. Anderson, L. T. Chen, K. Tanaka, W. Y. Lau, E. Van Cutsem, H. Singh, W. C. Chow, L. L. Ooi, P. Chow, M. W. Khin, and W. H. Koo. 2009. "Management of hepatocellular carcinoma in Asia: consensus statement from the Asian Oncology Summit 2009." *Lancet Oncol* no. 10 (11):1111-8.
- Salomon, J. A., N. Carvalho, C. Gutierrez-Delgado, R. Orozco, A. Mancuso, D. R. Hogan, D. Lee, Y. Murakami, L. Sridharan, M. E. Medina-Mora, and E. Gonzalez-Pier. 2012. "Intervention strategies to reduce the burden of non-communicable diseases in Mexico: cost effectiveness analysis." *Bmj* no. 344:e355. doi: 10.1136/bmj.e355.