

Prognosis of Breast Cancer in Relation with Estrogen-Progesterone and HER-2 Receptor Status

Shamsun Nahar¹, Nazir Uddin Mollah¹, Md Saidul Haque¹, Md Jamal Uddin¹, Sarwar Alam¹, Faruk Ahammad², Khursheda Akhter³, Shejuti Sharmin⁴, Afsana Sharmin Anika⁴, Nasrin Akhter⁵

¹Department of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

²Department of Medicine, Bangabandhu Sheikh Mujib Medical College, Faridpur, Bangladesh

³Department of Community Medicine, National Institute of Preventive and Social Medicine, Dhaka, Bangladesh

⁴Radiation Oncology, Lab Aid Cancer Hospital and Super Speciality Center, Dhaka, Bangladesh

⁵Department of Haematology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

Email address:

shamsunnahar75@yahoo.com (Shamsun Nahar)

To cite this article:

Shamsun Nahar, Nazir Uddin Mollah, Md Saidul Haque, Md Jamal Uddin, Sarwar Alam et al. (2023). Prognosis of Breast Cancer in Relation with Estrogen-Progesterone and HER-2 Receptor Status. *Cancer Research Journal*, 11(4), 156-160.

<https://doi.org/10.11648/j.crj.20231104.15>

Received: May 16, 2023; **Accepted:** June 10, 2023; **Published:** December 14, 2023

Abstract: *Introduction:* Worldwide, breast cancer is the second most common cause of death. The occurrence of breast cancer is roughly 2.3 million women of all ages worldwide. Both the normal breast cells and some breast cancer cells have the receptors that attach to the estrogen and progesterone hormone and play vital roles for normal and even abnormal growth of breast cells. The aim of this study was to evaluate the prognosis of breast cancer in relation with receptor status. *Methods:* This prospective observational study was carried out in the Department of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh during the period from December 2011 to December 2021. In total 100 breast cancer patients of several stages and grades were enrolled in this study as study subjects. Proper written consents were taken from all the participants before data collection. All data were processed, analyzed and disseminated by using MS Excel and SPSS version 25.0 as per need. *Result:* In this study, among total 100 cases, estrogen receptors were analyzed in 88 cases; among them in majority (86%), positive estrogen receptors were found whereas negative receptors were found in 14% cases. Progesterone receptors were analyzed in 85 cases; among them in majority (69%), positive progesterone receptors were found whereas negative receptors were found in 31% cases. HER 2 receptors were analyzed in 52 cases; among them in majority (67%), negative HER 2 receptors were found whereas positive receptors were found in 33% cases. highest death (12%) occurred in patients with ER-/PR-. In contrast, no death was seen in ER+/PR+ patients. In comparing the estrogen receptor status among participants, we did not find any significant correlation considering the stages or grades of carcinoma; the P values were >0.05. *Conclusion:* This study concluded that, compared to women of breast cancer with ER+/PR+ tumors, women with ER+/PR-, ER-/PR+, or ER-/PR- tumors experienced higher risks of mortality and distant metastasis. Receptor status of breast cancer may be considered as potential indicator for proper management of patients with breast cancer. Preliminary diagnosis and treatment of breast cancers have a certain survival advantage. Thus, we should need to assess the hormone receptor status for every patient before commencing treatment. To get robust data, multicenter studies are in great need of policymakers to interpret the demonstrable scenario and to take necessary steps towards mitigating this problem.

Keywords: Receptors, Diagnosis, Breast Carcinoma, Tumors, Oncology

1. Introduction

Worldwide breast cancer is ranked as the 5th cause of death among all forms of cancers in both sex and it is the 2nd most

common cancer next to lung cancer. [1] Cancer has become the leading reason of morbidity and mortality on a global scale in recent decades. The female population with first-degree relation carcinoma are at increased threat of death over the

century [2]. Despite the enormous reports on the incidence and survival rates of breast cancer in the developed nation, data are not so available from countries in Asia, Africa and Central America [3]. Around 2.3 million women have been diagnosed with breast cancer and 685,000 deaths occurred worldwide in the year of 2020. [4] The prevalence of breast cancer is approximately 22.5 per 1 lakhs females of all ages in 2020. For women of aged between 15-44 years, breast cancer has the maximum prevalence rate of 19.3 per 1 lakh in contrast with any other section of carcinoma [5]. There are many distinct types of breast cancer defined by where the breast cancer starts to develop, how much it has developed or spread, and certain features that influence how cancer behaves. The three types of breast cancers mostly found in women are invasive breast carcinoma, lobular breast carcinoma and medullary carcinoma [6]. Receptors are basically proteins in cells which can confer to definite elements in blood and normal breast cells along with some breast cancer cells have receptors that attach to estrogen and progesterone and these hormones for the cells to develop [7]. Women's threat of breast cancer is directly related to estrogen as well as progesterone and the cancer cells have the receptors which attach to these hormones which help the cell to increase. Breast cancer patients with tumours that are estrogen receptor (ER)-positive and/or progesterone (ER)-positive have the minimum threat of mortality after their diagnosis in contrast with women with ER- and/or PR-negative disease [8]. Estrogen causes an increased reason for breast carcinoma. On the other hand, progesterone prevents breast cancer [9, 10]. Estrogen may aid normal healthy cells to grow and function. Experts' opinion related to estrogen is that, several facts may act as a spark which turns normal cells into cancerous ones [11]. Progesterone acts in recital with estrogen to endorse proliferative and pro-survival gene programs in breasts and it constrains estrogen-driven growth in the uterus and keeps the ovary from neoplastic transformation [12]. Grade 1 is usually less likely to spread whereas grade 3 is usually faster-growing cancer that's more likely to spread. Grade 2 is developing more rapidly than grade 1, however slower compared to grade 3 cancers [13]. People with early breast cancer have a great chance of surviving. In a study, it was reported that, for an instance, diagnosed women with early breast cancer had not spread beyond the breast was 99% [14]. Keeping a healthy weight, avoiding OCP and tobacco, and lessening the percentage of alcohol are considered as the basic measures to prevent carcinoma to large extent [15]. On the other hand, hormone therapy can slow or stop cancer's growth and lessen the possibility of return and it may be used to reduce symptoms [16].

General Objective

To evaluate the prognosis of breast cancer in relation with receptor status.

Specific objective

- 1) To see the age distribution among the participants.
- 2) To see the types of carcinomas among respondents.
- 3) To know the tumor stages and grades of the study subjects.
- 4) To assess the nodal and receptor status among the

study population.

2. Methodology

This was a prospective observational study which was carried out in the Department of Clinical Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh during the period from December 2011 to December 2021. In total 100 breast cancer patients of several stages and grades were enrolled in this study as study subjects. Proper written consents were taken from all the participants before data collection. Only female patients aged above 18 years, with histo-pathological diagnosed duct cell carcinoma, with good hepatic, renal and cardiac function and without any co-morbidity were included as the study population. Data were collected using the predesigned semi-structured questionnaire. As per the inclusion criteria of this study, only patients of >18 years' age range, with tumor stages I to IIIA, ECOG performance status 0-2 and cases with HPR-duct cell carcinoma were included. On the other hand, according to the exclusion criteria, patients with tumor stage IV, medically unfit cases and patients who showed unwillingness to participate in the study were excluded. The study coordinators performed random checks to verify data collection processes. Completed data forms were reviewed, edited and processed for computer data entry. Frequencies, percentages, and cross-tabulations were used for descriptive analysis. The data analysis was performed using Statistical Package for the Social Sciences (SPSS) Version 25.0. The significance level of 0.05 was considered for all tests.

Inclusion criteria:

1. Age >18 years
2. Tumor stages I to IIIA
3. ECOG performance status 0-2
4. HPR-Invasive Duct Cell Carcinoma and other varieties

Exclusion Criteria:

1. Patients' with tumor Stage IV
2. Medically unfit patients
3. Patients who showed unwillingness to participate in the study.

3. Result

In this study, among the study population (N=100), most of the patients (35%) belonged to the age group of 41-50 years, 28% were from 31-40 years age group, 17% were from under 30 years of age group and 20% of the patients age were more than 50 years. The majority of the patients (98%) had invasive breast carcinoma, one patient (1%) had lobular carcinoma and another one (1%) had medullary carcinoma. Most of the cases (60%) were with stage II, one-fourth of the cases (28%) were with stage I, and the rest 12% were with stage III carcinoma. Among total patients, most of the cases (59%) were with grade II carcinoma, 24% were with grade I carcinoma and 17% were with grade III carcinoma. (Auxiliary node) N₀ nodule status was found in 25% of patients, N₁ status was found in 62% of patients, and N₂

status was found in 13% of cases. In this study among total 100 cases, estrogen receptors were analyzed in 88 cases; among them in majority (86%), positive estrogen receptors were found whereas negative receptors were found in 14% cases. Progesterone receptors were analyzed in 85 cases; among them in majority (69%), positive progesterone receptors were found whereas negative receptors were found in 31% cases. HER 2 receptors were analyzed in 52 cases; among them in majority (67%), negative HER 2 receptors were found whereas positive receptors were found in 33% cases. In comparing the estrogen receptor status among participants, we did not find any significant correlation considering the stages or grades of carcinoma; the P values were >0.05 . In this study as final outcome, in majority of the cases (70%) no evidence of recurrence was found in either local or distant sites. Bone metastasis was found in 10% cases and death was occurred in 20% cases. In this study, highest death (12%) occurred in patients with ER-/PR-. In contrast, no death was seen in ER+/PR+ patients.

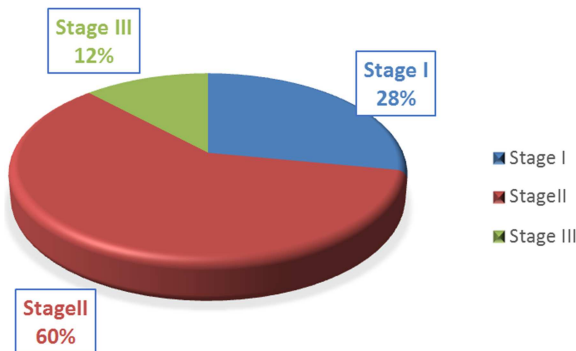


Figure 1. Tumor Stages Among Participants (N=100).

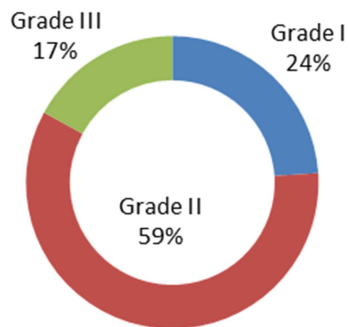


Figure 2. Tumor Grades Among Participants (N=100).

Table 1. Age Distribution of Participants (N=100).

Characteristics	N	%
<30	17	17%
31-40	28	28%
41-50	35	35%
>50	20	20%

Table 2. Types of Carcinomas Among Participants (N=100).

Characteristics	N	%
Invasive breast carcinoma	98	98%
Lobular breast carcinoma	1	1%
Medullary carcinoma	1	1%

Table 3. Nodal Status Among Participants (N=100).

Characteristics	N	%
N ₀	25	25%
N ₁	62	62%
N ₂	13	13%

Table 4. Receptor Status Among Participants (N=100).

Receptor status	n	%
Estrogen receptors		
Negative	12	14%
Positive	76	86%
Total	88	100%
Progesterone receptors		
Negative	26	31%
Positive	59	69%
Total	85	100%
HER 2 receptors		
Negative	35	67%
Positive	17	33%
Base	52	100%

Table 5. Comparison of Estrogen Receptor Status with Stage and Grade (N=100).

Variables	ER+	ER-	P value
Stages			
Stage 1	18	5	0.340
Stage 2	49	4	
Stage 3	9	2	
Stage 4	1	0	
Grades			
Grade I	13	6	0.496
Grade II	47	7	
Grade III	12	3	

Table 6. Outcomes Among the Participants (N=100).

Outcomes	N	%
No evidence of metastasis	70	70%
Bone metastasis	10	10%
Death	20	20%

Table 7. Prognosis of Breast Cancer in Relation with Receptor Status (N=100).

Receptor status	Bone metastasis (%)	Death (%)
ER+/PR+	1	0
ER+/PR-	2	1
ER-/PR+	3	7
ER-/PR-	4	12

4. Discussion

The aim of this study was to evaluate the receptor status of breast cancer patients and to evaluate the prognosis of breast cancer in relation with the receptor status. Breast cancer is the most common invasive cancer in women universally and it comprises 22.9% of invasive cancers in women [17]. The degree of breast carcinoma involves a sequence of processes starting with epithelial hyperplasia, which is followed by subsequent evolution to carcinoma in situ, invasive carcinoma, and finally into a metastatic disease [18]. In this current analysis, the majority of the patients (35%) belonged to the age group of 41-50 years. A similar study

demonstrated in Shanghai, China found that, most of the patients belonged between 55 to 64 years of age [19]. A cohort analysis found that, women aged 40 years or older had a greater risk of developing breast cancer compared to younger women [20]. On the other hand, a contradictory study showed a greater percentage of younger patients (76.9%) presented with ductal carcinoma as opposed to elder people (67.9%) [21]. In our study, the majority of the patients (98%) had invasive breast carcinoma, one patient (1%) had lobular carcinoma and another one (1%) had medullary carcinoma. A related article found that ductal carcinoma was the most frequently occurring tumour [17]. A study found that the survival rate from cancer was much higher in 40 or less than 40 years old compared to that of people whose age were more than 40 years old [22]. The American Cancer Society's found about 51,400 new cases of ductal carcinoma were diagnosed [23]. A study carried out in the USA found that, the proportions of ductal, ductal lobular and mucinous carcinomas increased while the proportions of tubular, inflammatory as well as medullary tumours decreased [24]. Another study found the prevalence of lobular carcinoma was higher compared to ductal carcinoma but despite the higher tumor burden at diagnosis, patients with lobular carcinoma received chemotherapy less frequently [25]. In this analysis, most of the patients (60.0%) were with stage 2 carcinoma and the majority of the patients (59%) were with grade II carcinoma. Another related article reported that, majority of patients had early-stage carcinoma [26]. According to another study, 5% were with stage 0, 27% were with stage 1, 44% were with stage 2, 21% were with stage 3, and 3% were with stage 4 breast cancers [27]. Another contradictory study found that, 78% of patients were with stage 1, 67% were with stage 2 and 40% were with stage 3 breast carcinoma [28]. In this recent analysis, estrogen was positive in around three-fourths of the patients; estrogen was negative in twelve patients and estrogen was not done in seventeen patients. In this study among total 100 cases, estrogen receptors were analyzed in 88 cases; among them in majority (86%), positive estrogen receptors were found whereas negative receptors were found in 14% cases. Progesterone receptors were analyzed in 85 cases; among them in majority (69%), positive progesterone receptors were found whereas negative receptors were found in 31% cases. HER 2 receptors were analyzed in 52 cases; among them in majority (67%), negative HER 2 receptors were found whereas positive receptors were found in 33% cases. Another article published in 2014 found that the majority of breast cancers showed overexpression of progesterone and estrogen receptors [29]. In another analysis, the author found that 19.5% of patients' estrogen status was positive and metastatic status was negative in 10.5% of patients [30]. In a study, it was reported that, the estrogen-negative or progesterone-positive subtype was rare and showed no significant reproducibility [31]. Another study of Turkey found that, HER-2 receptor positivity rates in invasive breast cancer were around one-fifth of the patients (21.8%) [27]. In this current analysis, in most of the patients (70%) there was no evidence of

recurrence, 10% had bone metastasis and 20% were dead. In this study, compared to women with ER+/PR+ tumors, women with ER+/PR-, ER-/PR+, or ER-/PR- tumors experienced higher risks of mortality and distant metastasis which was quite relatable to another study. [32]

5. Limitation of the Study

This was a single centered study with small sized samples. Moreover, the study was conducted at a 10 years period of time. So, the findings of this study may not reflect the exact scenario of the whole country.

6. Conclusion and Recommendation

This study concluded that, compared to women with ER+/PR+ tumors, women with ER+/PR-, ER-/PR+, or ER-/PR- tumors experienced higher risks of mortality and distant metastasis. Receptor status of breast cancer may be considered as potential indicator for proper management of patients with breast cancer. Initial diagnosis and treatment of breast cancers have a definite survival benefit. Evidence-based guidelines for treatment should continue to be trailed. Although great improvements in the stratification of breast cancer, the greatest difficulty found in clinical oncology are the heterogenic nature of tumor. The American Society of Clinical Oncology recommends estrogen and progesterone receptor testing for all new diagnosed cases of invasive breast cancer. For getting more specific results, we would like to recommend for conducting similar more studies in several places with larger sized samples.

Conflicts of Interest

The authors declare that they have no competing interests.

References

- [1] Ferlay J, Soerjomataram I, Ervik M, et al. GLOBOCAN 2012 v1. 0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer. globocan.iarc.fr/Default.aspx 2014; 2013.
- [2] Coleman R, Finkelstein DM, Barrios C, Martin M, Iwata H, Hegg R, Glaspy J, Periañez AM, Tonkin K, Deleu I, Sohn J. Adjuvant denosumab in early breast cancer (D-CARE): an international, multicentre, randomised, controlled, phase 3 trial. *The Lancet Oncology*. 2020 Jan 1; 21(1): 60-72.
- [3] American Cancer Society. Breast Cancer Facts & Figures 2017–2018. Atlanta: American Cancer Society I; 2018.
- [4] Breast Cancer. World Health Organization (WHO). [Available at: <https://www.who.int/news-room/fact-sheets/detail/breast-cancer>] [Last Accessed on: 12-12-2022].
- [5] Forazy MA. Healthcare. [Available at: <https://www.walshmedicalmedia.com/proceedings/incidence-of-breast-cancer-in-bangladesh->] [Last Accessed on: 16-11-2022].

- [6] Types of Breast Cancer. [Available at: Breastcancer.org. Donate] [Last Accessed on: 12-12-2022].
- [7] Abdulkareem IH, Zurmi IB. Review of hormonal treatment of breast cancer. *Nigerian journal of clinical practice*. 2012; 15(1).
- [8] Lin NU, Vanderplas A, Hughes ME, Theriault RL, Edge SB, Wong YN, Blayney DW, Niland JC, Winer EP, Weeks JC. Clinicopathologic features, patterns of recurrence, and survival among women with triple-negative breast cancer in the National Comprehensive Cancer Network. *Cancer*. 2012 Nov 15; 118(22): 5463-72.
- [9] Pauklin S, Sernández IV, Bachmann G, Ramiro AR, Petersen-Mahrt SK. Estrogen directly activates AID transcription and function. *Journal of Experimental Medicine*. 2009 Jan 16; 206(1): 99-111.
- [10] Trabert B, Sherman ME, Kannan N, Stanczyk FZ. Progesterone and breast cancer. *Endocrine reviews*. 2020 Apr; 41(2): 320-44.
- [11] Srivastava S, Koay EJ, Borowsky AD, De Marzo AM, Ghosh S, Wagner PD, Kramer BS. Cancer overdiagnosis: a biological challenge and clinical dilemma. *Nature Reviews Cancer*. 2019 Jun; 19(6): 349-58.
- [12] Cancer Grade. Breast Cancer New. [Available at: <https://breastcancernew.org/information-support/facing-breast-cancer/diagnosed-breast-cancer/cancer-grade>] [Last Accessed on: 16-11-2022].
- [13] Mukherjee D, Zhao J. The role of chemokine receptor CXCR4 in breast cancer metastasis. *American journal of cancer research*. 2013; 3(1): 46.
- [14] Ginsburg O, Yip CH, Brooks A, Cabanes A, Caleffi M, Dunstan Yataco JA, Gyawali B, McCormack V, McLaughlin de Anderson M, Mehrotra R, Mohar A. Breast cancer early detection: A phased approach to implementation. *Cancer*. 2020 May 15; 126: 2379-93.
- [15] Schüz J, Espina C, Villain P, Herrero R, Leon ME, Minozzi S, Romieu I, Segnan N, Wardle J, Wiseman M, Belardelli F. European Code against Cancer 4th Edition: 12 ways to reduce your cancer risk. *Cancer epidemiology*. 2015 Dec 1; 39: S1-0.
- [16] Ahuja R, Chauhan N, Saini S, Harsh M. Expression of Ki67 as a Prognostic Marker in Invasive Breast Carcinoma. *National Journal of Laboratory Medicine*. 2017.
- [17] Banin Hirata BK, Oda JM, Losi Guembarovski R, Ariza CB, Oliveira CE, Watanabe MA. Molecular markers for breast cancer: prediction on tumor behavior. *Disease markers*. 2014 Oct; 2014.
- [18] Yan B, Yang LM, Hao LP, Yang C, Quan L, Wang LH, Wu Z, Li XP, Gao YT, Sun Q, Yuan JM. Determinants of quality of life for breast cancer patients in Shanghai, China. *PloS one*. 2016 Apr 15; 11(4): e0153714.
- [19] Chen HL, Zhou MQ, Tian W, Meng KX, He HF. Effect of age on breast cancer patient prognoses: a population-based study using the SEER 18 database. *PloS one*. 2016 Oct 31; 11(10): e0165409.
- [20] Sariego J. Breast cancer in the young patient. *The American surgeon*. 2010 Dec; 76(12): 1397-400.
- [21] Liedtke C, Rody A, Gluz O, Baumann K, Beyer D, Kohls EB, Lausen K, Haker L, Holtrich U, Becker S, Karn T. The prognostic impact of age in different molecular subtypes of breast cancer. *Breast cancer research and treatment*. 2015 Aug; 152(3): 667-73.
- [22] Giaquinto AN, Sung H, Miller KD, Kramer JL, Newman LA, Minihan A, Jemal A, Siegel RL. Breast cancer statistics, 2022. *CA: A Cancer Journal for Clinicians*. 2022 Oct 3.
- [23] Li CI. Risk of mortality by histologic type of breast cancer in the United States. *Hormones and Cancer*. 2010 Jun; 1(3): 156-65.
- [24] Metzger - Filho O, Ferreira AR, Jeselsohn R, Barry WT, Dillon DA, Brock JE, Vaz - Luis I, Hughes ME, Winer EP, Lin NU. Mixed invasive ductal and lobular carcinoma of the breast: prognosis and the importance of histologic grade. *The oncologist*. 2019 Jul; 24(7): e441-9.
- [25] Nanda R, Liu MC, Yau C, Shatsky R, Pusztai L, Wallace A, Chien AJ, Forero-Torres A, Ellis E, Han H, Clark A. Effect of pembrolizumab plus neoadjuvant chemotherapy on pathologic complete response in women with early-stage breast cancer: an analysis of the ongoing phase 2 adaptively randomized I-SPY2 trial. *JAMA oncology*. 2020 May 1; 6(5): 676-84.
- [26] Özmen V. Breast cancer in Turkey: clinical and histopathological characteristics (analysis of 13,240 patients). *The journal of breast health*. 2014 Apr; 10(2): 98.
- [27] Giordano SH, Cohen DS, Buzdar AU, Perkins G, Hortobagyi GN. Breast carcinoma in men: a population - based study. *Cancer: Interdisciplinary International Journal of the American Cancer Society*. 2004 Jul 1; 101(1): 51-7.
- [28] Mougalian SS, Soulos PR, Killelea BK, Lannin DR, Abu - Khalaf MM, DiGiovanna MP, Sanft TB, Pusztai L, Gross CP, Chagpar AB. Use of neoadjuvant chemotherapy for patients with stage I to III breast cancer in the United States. *Cancer*. 2015 Aug 1; 121(15): 2544-52.
- [29] Yip CH, Rhodes A. Estrogen and progesterone receptors in breast cancer. *Future oncology*. 2014 Nov; 10(14): 2293-301.
- [30] Lower EE, Glass EL, Bradley DA, Blau R, Heffelfinger S. Impact of metastatic estrogen receptor and progesterone receptor status on survival. *Breast cancer research and treatment*. 2005 Mar; 90(1): 65-70.
- [31] Hefti MM, Hu R, Knoblauch NW, Collins LC, Haibe-Kains B, Tamimi RM, Beck AH. Estrogen receptor negative/progesterone receptor positive breast cancer is not a reproducible subtype. *Breast Cancer Research*. 2013 Aug; 15(4): 1-3.
- [32] Dunnwald LK, Rossing MA, Li CI. Hormone receptor status, tumor characteristics, and prognosis: a prospective cohort of breast cancer patients. *Breast cancer research*. 2007 Feb; 9: 1-0.