Delay of medical care for symptomatic breast cancer: A literature review

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Abstract

The purpose of this paper is to organize and summarize existing information on delayed medical attention for women with breast cancer and identify research needs in this area. This review is organized in six parts: origins and permanence of the message "do not delay" medical attention for potential cancer symptoms; definition and classification of breast cancer delay; impact of delay on breast cancer prognosis; factors related to breast cancer delay and the ways these have been studied; the study of breast cancer delay in Mexico; and directions for future research in developing countries, with a special focus on Mexico. We point out the need of a more integral study of delay that takes into account socio-structural and health services factors, in order to find modifiable factors towards which political actions should be directed to improve breast cancer medical attention in underdeveloped countries.

Key words: Breast neoplasms; delay; lag-time; duration of symptoms; survival; sick role; health service accessibility; health services research; review; Mexico

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Resumen

El objetivo de esta revisión es integrar información disponible con respecto al retraso en la atención médica del cáncer de mama e identificar necesidades de investigación en este tema. La revisión consta de seis apartados: origen del mensaje "no retrasar" ante la aparición de síntomas de cáncer; definición y clasificación del retraso en la atención del cáncer de mama; impacto del retraso sobre el pronóstico de la enfermedad; factores asociados con el retraso; la investigación del retraso en la atención del cáncer de mama en México; y necesidades de investigación en este tema. Se señala la necesidad de estudiar el retraso en la atención del cáncer de mama de forma más integral, tomando en cuenta características socio-estructurales y de servicios de salud, para identificar factores modificables hacia los cuales dirigir esfuerzos para mejorar la atención de esta enfermedad en países en vías de desarrollo.

Palabras clave: neoplasias de la mama; duración de síntomas; oportunidad del diagnóstico; retraso en la atención; supervivencia; rol del enfermo; accesibilidad a los servicios de salud; investigación en servicios de salud; revisión; México

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The majority of breast cancer deaths occur in developing countries.[1] Mortality reductions achieved in the last decades in developed countries have not been achieved in developing countries mainly because of a lack of access to early medical attention.[2] Most cancer in low- and middle-income countries (LMC) are detected at later stages than in high-income countries.[3] It is commonly assumed that this late diagnosis is due to the population's lack of information and to deficient coverage of screening programs. However, there are very few research studies on the reasons behind delayed medical attention for breast cancer in women in underdeveloped countries.

The purpose of this review is to organize, summarize and critically assess existing information on delayed medical attention for women with breast cancer and identify research needs in this area for LMC.

A literature review was conducted of studies on breast cancer delay published in English or Spanish language journals between 1950 and 2008. Searches were made using PubMed and Scielo electronic databases for the following terms, in English and Spanish: breast cancer delay, delay and breast carcinoma, delay and breast neoplasms, breast cancer experience, breast cancer and help seeking behavior. References from relevant studies were also used to trace other studies. Only literature on delay for breast cancer, and not other cancers, was included since factors influencing delay differ between different types of cancer.[4-7]

Information from 96 studies is summarized in this review. Selected studies were analyzed in order to respond to specific objectives. Results are presented in six parts, each of which corresponds to one of these objectives: I) understand the origins of the message "do not delay when you discover breast cancer signs or symptoms"; II) review the different definitions and classifications of delay used; III) analyze what is known to date regarding the impact of delay on prognosis; IV) identify factors related to delay and the most relevant methodological features of studies analyzing them; V) critically analyze available information on delay in Mexico; and thus VI) identify research needs on this topic in LMC, with a special focus in Mexico.

Origin and permanence of the message "do not delay"

While there is now scientific evidence that timely treatment of breast cancer is decisive for survival,[8] this information was in the "public domain" for almost a century before the evidence existed. Since the beginning of the 20th century, women have been urged to seek medical attention as soon as they discover any lump or change in the breast.[9]

Since the creation of the "radical mastectomy" surgical technique developed by William Halsted in the late 19th century, a widespread belief originated among surgeons about surgery being able to "*cure*" patients if done "in time".[9] Halsted himself wrote: "a cure for breast cancer is not only possible, but, if operated upon early, quite probable."[10] For over 70 years, research has thrown results in both directions, supporting and rejecting an association between delay and survival. Despite the controversy, the prevailing message among doctors, researchers and lay people since the beginning of the 20th century has been *do not delay medical attention when discovering cancer symptoms*. Nevertheless, this controversy could have contributed to hinder recognition of the importance of research on factors that could explain delay. Before we further discuss this issue, we will review the most accepted definition and classification of delay.

Breast cancer delay: definition and classification

Total delay in cancer is defined as more than three months between symptom discovery by the patient and the beginning of medical treatment. Longer delays are associated with reduced survival.[8] Studies done in different countries have estimated total breast cancer delay to range from 17%[11] in a population sample of the Saarland region in Germany to up to 42.5%[12] in a regional hospital sample in Tehran, Iran. Total delay is usually divided into *patient delay* and *provider delay*.

a) Patient delay

The first study on cancer delay where these two types of delay are described was done by Pack and Gallo in 1938. They defined "*undue patient delay*" as "three months or more elapsed time between discovery of symptoms and a visit to a physician."[13] This first definition has been surprisingly preserved for 70 years in most studies of *patient delay*, even though the time threshold was established arbitrarily.

b) Provider delay

Provider delay refers to a prolonged period of time between the initial medical consultation and the beginning of definitive treatment. It is also known as *system* or *doctor* delay. Pack and Gallo defined one month as "adequate time for the physician to take appropriate action."[13] This too was arbitrarily established. Although

other researchers have used it, variability of the period of time used to define *provider delay* has been greater than that of *patient delay*.

Provider delay has been further divided by some authors into *diagnosis delay*, time between the first clinical consultation and cancer diagnosis, and *treatment delay*, time between diagnosis and beginning of treatment.[14-17] Less frequently it has been divided into *referral* or *general practitioner delay*, time elapsed between first consultation to a primary care service and referral to a hospital, and *hospital delay*, time from referral to beginning of definitive cancer treatment.[18,19]

The impact of breast cancer delay on prognosis

In this section we argue that delay adversely affects survival due to disease progression. Study results regarding the relation between delay and the most important known prognostic factors are discussed. Table I summarizes general characteristics and results of these studies.

a) Impact of breast cancer delay on survival

This association was taken for granted during at least a century,[9] but it was proved in 1999.[8] Prior to this, various studies yielded contradictory findings. Differences in conclusions between studies may be due to: 1) differing sample characteristics (including patients in all clinical stages or only patients with operable cancer), 2) differences in the delay interval studied (patient, diagnostic, treatment, provider, total delay or different combinations) and 3) differences in time periods used to define delay (e.g. 1, 2, 3, 6 months, etc.).

In general, studies that found an inverse association between delay and survival times measured delay considering the time interval between symptom discovery and first consultation: either *patient delay*,[20.-24] *total delay*[25-27] or *hybrids of patient delay* with *subtypes of provider delay*.[27-29] Studies where no association was found only included women with operable tumors.[30,31] As it will be discussed more thoroughly later on, evidence suggests that delay affects survival via the progression of cancer. Hence, a possible explanation for the negative findings of these studies is that for patients within a same clinical stage duration of symptoms has no impact on survival, as other studies have shown.[23,25,27]

The association between *provider delay* and survival has been more controversial. Some authors have reported no association[19,31] while others have found an inverse association between *diagnosis delay* and survival time.[20] Furthermore, others have found a direct association which might seem paradoxical, i.e. the greater the *provider delay*, the longer the survival.[24] This has been explained as the ability of health providers to identify more advanced cases, with a probable short time of survival, and speed up the beginning of treatment. Studies in support of this argument have found that small tumors[24,32] and early clinical stage[33] are associated with delay, probably because diagnosis of early disease is more challenging for physicians.

In 1999, Richards and colleagues strongly contributed to clarify the controversial relationship between *total delay* and survival. Their meta-analysis of observational studies published between 1907 and 1996 demonstrated that women with total delays of more than three months have shorter survival times than women who start treatment within three months of symptom discovery.[8] This study is the strongest evidence available to date, but has some limitations. Studies with different operational definitions of delay had to be included as well as studies that used different survival measures, although, in an attempt to make a more valid comparison, the authors subdivided studies into three different categories according to the type of survival measure used. Another limitation was that very few of the included studies considered the potential confounding effect of "lead-time bias" regarding the association between delay and survival, as the authors well recognize. Lead-time bias can occur when survival is only measured from the time of diagnosis instead of symptom discovery. As the time interval between symptom discovery and diagnosis confirmation increases, survival time is expected to be reduced. Therefore, if survival time is estimated from diagnosis confirmation the effect of delay on survival could be attributed to this lead-time effect. In order to reduce this bias, patients with delays of more than six months were excluded from the meta-analysis and comparisons were only done between patients with delays of three to six months and patients with delays of less than three months.[8] In an attempt to control for this bias in later original research, these same authors measured survival both from the confirmation of diagnosis and symptom discovery. They found a significant relation between delay and both ways of measuring survival.[27]

These findings might be taken with skepticism by clinicians, as breast cancer can disseminate early in the course of disease.[34] It has recently been shown that even cells from ductal carcinoma in situ can metastasize.[35] This could make us wonder how important could a delay of three to six months in the clinical phase of the disease actually be. While for many patients, delays between three and six months would probably not have an impact on five-year survival,[8] it has been well

Table I

STUDIES OF BREAST CANCER DELAY AND ITS EFFECT ON PROGNOSTIC FACTORS

Ref.	*Year*	*Country*	*Delay Type*	*Operational definitions of delay*	*DV*	*n*	*Patient characteristics*	*A*
(30)	1957	USA	TD	Symptom discovery to beginning of treatment. (Months: <2, 2-6, >6)	N OS	1281	BC patients who had radical mastectomy	X X
(20)	1962	USA	PD	Symptom discovery to 1st medical consultation. (<6 d,<28 d, <6 m,<12 m)	CS OS	3623	Patients with different cancers (644 BC)	√(D) √(I)
			DD	1st medical consultation to diagnosis confirmation. (<6 d, <28 d; < 6 m)	CS OS			√(D) √(I)
(31)	1975	USA	PD	Symptom discovery to 1st medical consultation. (Months: <1, 1-3, >3)	OS	237	BC patients who had radical mastectomy	X
			SD	1st medical consultation to beginning of treatment. (Months: <1, > 1)				X
(48)	1977	USA	TD	Symptom discovery to beginning of treatment. (Months: ≤1, 1.1-3, 3.1-9, >9)	T N	1539	BC patients with operable disease (stages I & II)	√(D) √(D)
(28)	1980	Canada	PD + DD	Symptom discovery to diagnosis confirmation. (Months: ≤1 , 2-11, ≥ 12)	CS OS	1591	BC patients diagnosed in 1945, 1950,1955,1960, 1965,1970,1975	√(D) √(I)
(21)	1983	USA	PD	Symptom discovery to 1st medical consultation. (Months: <3, 3-11, ≥12)	OS	1497	BC patients treated at 1 (1976-1977) & 15 NY hospitals (1975-1979)	√(I)
(71)	1983	USA	PD + RD	Symptom discovery to arrival at hospital. (Months: ≤1, 1 to <3, 3 to <6, ≥6)	T	569	BC patients treated at 1 hospital (1967-1978)	X
(29)	1983	USA	PD + RD	Symptom discovery to arrival at hospital. (Quantitative variable: months)	OS	185	BC patients treated at 1 hospital between 1957 and 1965.	√(I)
(51)	1983	USA	DD	Normal interpretation of mammogram to cancer biopsy.	N	165	Women with breast lumps & normal mammogram	√(D)
(22)	1984	Israel	PD	Patient perception of delay between symptom discovery and diagnosis (yes/no)	CS OS	2299	Patients with different types of cancer (412 BC)	√(D) √(I)
(25)	1985	USA	TD	Symptom discovery to beginning of treatment. (Months:< 3, 3-6, > 6)	CS OS	685	BC patients treated at one hospital between 1962 and 1969	√(D) √(I)
(23)	1985	USA	PD	Symptom discovery to 1st medical consultation. (Months: 3-6, ≥ 7)	OS CS	4518	BC patients treated at MD Anderson Center (1949-1968)	√(I) √(D)
(40)	1986	Italy	PD + DD	Symptom discovery to diagnosis confirmation. (Months: ≤3, 4-6, > 6)	CS T N	1110	BC patients seen at 63 Italian public hospitals (1983-1984)	√(D) √(D) √(D)
(26)	1990	Italy	TD	Symptom discovery to beginning of treatment. (Days: < 30, 31-90, 91- 180, 181 - 365, > 365.)	OS T N	189	BC patients treated at two hospitals in Rome between (1982-1988)	√(I) √(D) √(D)
(42)	1990	USA	PD + DD	Symptom discovery to diagnosis confirmation. (Weeks: 0-2, 3-12, > 12)	CS T	1055	Cancer patients, residents of New Mexico, ≥ 65 years old (1984-1986)	√(D) X
(24)	1994	Denmark	PD	Symptom discovery to 1st medical consultation. (> 60 days)	OS T	7608	BC patients registered at the Danish BC Cooperative Group between 1977 & 1982	√(I) √(D) √(D) √(D)
			SD	1st medical consultation to surgery. (> 60 days)	N			√(I) X
(41)	1998	UK	PD	Symptom discovery to 1st medical consultation. (≥ 12 weeks)	CS T	185	BC patients with symptoms, treated at one hospital (1992 & 1994)	√(D) √(D)
(27)	1999	UK	TD	Symptom discovery to beginning of treatment. (Weeks: <12, 12-26, >12)	T CS OS	2964	BC patients treated at one hospital between 1975 & 1990	√(D) √(D) √(I)
(15)	1999	USA	DD	1st medical consultation to diagnosis confirmation. (Months: < 3, ≥ 3)	CS T N	606	BC patients who received medical attention at one of the authors' office	X √(D) X
(19)	1999	UK	TD	Patient referral to beginning of treatment. (Days: <30, 30-59, 60-89,>90)	OS	36222	BC patients identified at Yorkshire Cancer Registry (1976 -1995)	X
(8)	1999	UK	TD	Symptom discovery to beginning of treatment. (Months: < 3, ≥ 3)	CS OS	87	Studies published between 1907 & 1996 (87 studies, 101,954 patients)	√(D) √ (I)
(45)	2001	Germany	PD + DD	Symptom discovery to diagnosis confirmation. (Months: 0-1, 1-3, > 3)	CS	380	Residents of Saarland region, with BC diagnosed by any means	X
(11)	2002	Germany	PD	Symptom discovery to 1st medical consultation. (Months: 1-3, > 3)	CS	280	Residents of the Saarland region, diagnosed with symptomatic BC	√(D)
(49)	2002	Canada	DD	Abnormal mammogram to cancer diagnosis confirmation. (Weeks: ≤4, 4-12, >12 to 20, >20 to 52, >52 to 104, >104)	T N	4465	BC patients diagnosed within three years of abnormal mammogram in five Canada provinces	√(D) √(D)
(43)	2003	Iran	PD	Symptom discovery to 1st medical consultation. (Months: ≤ 3, > 3)	CS T	190	BC patients that received medical attention at 2 hospitals in Tehran	√(D) √(D)
(44)	2006	USA	DD	1st medical consultation to diagnosis confirmation. (Quantitative variable: months)	CS T N	40	BC patients seen at 1 hospital (1995 – 2005), with diagnosis delay of more than three months	X X X
(39)	2006	UK	PD	Symptom discovery to 1st medical consultation. (Weeks: < 12, ≥ 12)	CS	69	BC patients ≥65 years, diagnosed at two London hospitals (2002 - 2003)	√(D)

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Abbreviations. TD= total delay, PD= patient delay, SD= system delay or provider delay, DD= diagnosis delay, RD= referral delay, TD= treatment delay, d= days, w= weeks, m= months, DV= Dependent variables, OS= overall survival, CS= clinical stage, T= tumor size, N= lymph node involvement, BC= Breast Cancer, A= Association: I= inverse association, D= direct association

documented that as delay time increases, so does the probability of clinical progression,[25] which has shown to negatively affect survival.[25,36] Even though breast cancer's natural history is unpredictably heterogeneous,[34,37] most studies have shown a reduction in mortality with earlier diagnosis.[38] Therefore, as long as this disease can not be prevented, efforts should be kept in direction of early and adequate diagnosis and treatment.

b) Impact of breast cancer delay on clinical stage

Most studies have found that the longer the delay, the more likely a woman is diagnosed in advanced stages (Table I). Studies that have considered *total delay* or *patient delay* as independent variables (using the most accepted operational definitions) have consistently confirmed this association.[11,20,22,23,25-28,39-43] The meta-analysis performed by the London group[8] also found 13 published studies that confirm this same result.

Few studies have not confirmed the relation between delay and clinical stage.[15,44,45] In one such study, the time threshold used to define *diagnosis delay* was too broad (more than three months between first consultation to the physician and diagnosis confirmation).[15] It is noteworthy that the authors revised records of their own patients which is a great threat to validity. Another study where no association was found between *doctor delay* and clinical stage[44] included a very small sample of women with delay, which impeded comparisons with women without delay. An additional study with negative findings between *patient delay* and clinical stage included patients diagnosed with breast cancer detected by any means (mammography screening, clinical breast examination or patient symptom discovery).[45] In a latter publication these same authors reported a positive association between *patient delay* and clinical stage when analyzing only symptomatic women.[11] In light of this evidence, and given that clinical stage has proven to affect survival,[23,25,29,36,46] the most likely explanation for the association between delay and survival is that delay influences disease progression which in turn affects survival. Other study findings that support this hypothesis have reported the association between delay and survival to disappear when controlling for clinical stage.[23,25,27]

c) Impact of breast cancer delay on tumor size

Tumor size is one of the most important prognostic factors in breast cancer.[7] After clinical stage, it is the prognostic factor that has most consistently been associated with delay.[15,24,26-28,40-43,48,49] The longer the delay, the greater the tumor size at diagnosis. This is another indicator of delay's effect on disease progression.

d) Impact of breast cancer delay on lymph node involvement

Involvement of regional lymph nodes is another important prognostic factor in breast cancer.[47] Some authors have found a significant association between *total delay* and regional lymph node involvement.[26,48] Among studies where *patient delay* was measured, two found a significant association[24,40] while another did not.[50] In the latter only patients in clinical stage I and II were included, who by definition are patients with little or no lymph node involvement. No relationship has been found between *provider delay* and lymph node involvement.[15,44] However, an association was found in a study that documented time elapsed between an abnormal mammogram and diagnosis confirmation of breast cancer,[49] and another where time between a normal mammogram interpretation for a clinically detectable breast lump and a diagnostic biopsy was considered.[51]

e) Impact of breast cancer delay on quality of life

Breast cancer delay is not only associated with a reduced survival time. Given that the longer the delay, the more likely for the patient to present with large tumors and regional lymph node involvement, delay conveys a greater risk of needing more aggressive treatments. Hence, the longer the delay, the more likely it is for a woman to require mastectomy instead of conservative surgery as well as more toxic or extended adjuvant treatment.[52] Patients diagnosed with advanced disease have also shown to have important psychological morbidity.[53] Both these aspects strongly impact the patient's quality of life.

Factors related to breast cancer delay

Different factors have been pointed out in relation to *patient* and *provider delay*. In this section we discuss the most important factors studied in relation to patient delay and provider delay and the methodological features of these studies.

a) Factors related to patient delay

As shown in Table II, according to the systematic review done by Ramirez *et al*,[54] the only socio-demographic factors that seemed to be strongly associated with *patient de-*

Table II

FACTORS RELATED TO PATIENT DELAY IN SEEKING MEDICAL ATTENTION FOR BREAST CANCER

Factors	*Qualitative studies*	*Quantitative studies*	
		Association	*No association*
Socio-demographic factors			
Marital status: single		(5) (11) (12) (28) (43) (**54**)[§] (56)	(4) (7) (110) (32) (41) (50) (57) (60) (111) (112) (113)
Advanced age		(11) (24) (32) (**54**)[§] (68) (114)	(5) (7) (28) (41) (55) (57) (58) (60) (111) (110) (115)
Residence in rural areas		(12) (116)	(32)
African or Hispanic ethnicity (in countries where the majority of the population is non-Hispanic white)		(5) (23) (62) (63) (110) (54, *113*)[‡]	(4) (29) (60) (57)
Low education		(12) (43) (**54**)[‡] (110) (115)	(4) (7) (50) (55) (58)
Low socioeconomic level	(98)	(7) (12) (60) (62) (68) (*113*) (116)	(4) (5) (28) (**54**) (55) (57) (111) (110) (115)
Accessibility barriers	(67) (77)	(111)	(4) (55)
Lack of health insurance		(58) (111)	(4) (110)
Activities that compete with health problem (e.g.: labor, vacations, caring for an ill family member or for young children, household activities, etc.)	(6) (**59**) (66) (67) (75) (77) (82) (98)	(112) (*113*)	(115)
Adversity / life crisis in last year			(50) (112) (117)
Knowledge and beliefs			
Lack of cancer knowledge	(66) (67) (69) (79)	(12) (61) (68) (65)	(4) (**54**) (55) (70) (71) (112) (116)
Previous experiences with family members or friends that had cancer	(6) (**59**) (66) (67) (74) (75) (76)	(12) (43) (68)	(41) (**54**) (57) (115)
Psychological factors			
Fatalism	(66) (67) (81) (80) (82)	(61) (111) (112)	
Denial	(66) (67) (81) (80) (118)	(68) (112)	(**54**) (119)
Rationalization / suppression	(66) (67) (79) (80)	(68) (116)	
Anxiety / cancer worry		(115)	(**54**) (110) (116)
Fear of cancer confirmation	(**59**) (66) (67) (69) (74) (77) (78)	(57) (111) (112)	(41)
Fear of mastectomy	(66) (67) (76) (78)	(68) (81) (111) (112) (*113*)	(115)
Fear of adverse effects on relationship with partner (interference with sexuality, partner's abandonment)	(67) (78) (82)		
Fear to treatment's adverse effects	(**59**) (75) (76)	(39) (111)	(115)
Fear or lack of trust in doctors and hospitals in general	(66) (67) (82)	(68) (112)	
Embarrassment of being examined by a doctor	(**59**) (66) (67) (78) (82)	(68) (111) (112)	
Low risk perception of cancer	(79) (82) (83)	(61)	(39)
Characteristics of symptoms / signs			
Breast symptoms other than a lump	(**59**) (75)	(18) (21) (39) (41) (57) (*113*)	(32) (115) (116)
Absence of pain	(**59**)	(68)	(115)
Initial interpretation of symptoms as "not serious"	(**59**) (66) (69) (74) (75) (78) (79) (83)	(11) (**54**)[‡] (57) (68) (111) (112) (*113*) (115)	
Social network and social support			
Not talking to anyone about symptoms	(6) (78)	(39) (41) (**54**)[‡] (116)	(58) (115)
Lack of social support			(4) (**54**) (58)
Health service utilization habits			
No breast cancer screening habits	(67) (81)	(32) (46) (50) (*113*) (120)	(41) (**54**) (55)
Past experiences of health service utilization for other health problems		(4) (11) (12) (39) (111) (*113*) (115) (116)	(**54**)
Lack of a regular physician	(98)	(11) (12) (111) (110)	
Use of alternative medicine	(78) (81) (82)	(68) (113)	

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* References highlighted in bold indicate meta-analysis studies when placed in the Quantitative studies columns and meta-synthesis when placed under Qualitative studies. References in italics are reviews *without* meta-analysis. Remaining references correspond to original research studies

‡ Moderate evidence according to Ramírez et al's meta analysis (data are suggestive of an effect, with at least two studies in support of the direction of the effect, but conclusions could be affected by a new study with a large sample)

§ Strong evidence (a substantially greater proportion of studies point to one direction than one would expect to happen by chance)

lay up to 1999 were the patient's single *marital status* and advanced *age*. However, subsequent studies have continued to come up with contradictory results.[5,7,11,12,32,43,50,55-58] There seems to be consensus regarding the influence on delay of presenting *breast symptoms different from a lump*[18,21,39,41,57,59] and the patient's *initial interpretation of her symptoms as "not serious."*[11,54,57,59] Though not conclusive, other factors that seem to be of great importance are low *education* and *ethnicity* other than non-Hispanic white (in countries where the majority of the population is Caucasian).[54] Several studies report a reduced survival time of Hispanic-American and African-American patients[23,46,60] as well as breast cancer diagnosis at more advanced clinical stages[23,46,61-63] in comparison to non-Hispanic white American patients.

The association between *socioeconomic status* (SES) and delay has not been firmly demonstrated. Nevertheless, it can not be ruled out since the different ways this variable has been measured are not comparable between studies. SES is most likely related to delay as it is a "powerful determinant of possessing particular health enhancing resources."[64] Many of the factors that have shown to be related to delay are likely to be associated with a low SES, e.g. belonging to an ethnic minority, low education, rural residence, lack of health insurance, access barriers to care and activities that compete with medical attention.

It is noteworthy that despite the fact that some studies have documented an inverse relation between *cancer-related knowledge* and delay,[12,61,65-69] this has not been proven in the majority of quantitative studies.[54] Health professionals have been compared with lay people and no differences in delay have been found.[70,71] This lack of relation between knowledge and practice has also been documented for other illness behaviors.[72,73]

The patient's *knowledge of other people with cancer* has emerged in several qualitative studies as a relevant factor influencing help seeking behavior.[6,59,74-76] Nevertheless, results about this association have been controversial in quantitative studies.[12,41,43,54,57] Once more, the way this variable is operationalized and measured is inconsistent between studies, making it difficult to reach conclusions.

Among the psychological factors that have been studied in relation to delay, *fear* deserves a special comment. Fear has been shown to have a curvilinear association with patient delay; it can either accelerate seeking of medical attention[76-79] or it can cause delay.[59,74-76,78,79] The mechanisms that determine one patient with fear to act one way or the other have still not been elucidated. In addition, different kinds of fears have been measured using different instruments, which further complicates comparisons between studies.

We identified a lack of high quality quantitative studies that measure the role of certain relevant factors found in qualitative studies, such as: *fatalism*,[66,67,80-82] *denial*,[66,67,80,81,83] *rationalization/ suppression*,[66,67,79,80] *embarrassment of being examined by a doctor*,[59,66,67,78] and *risk perception*.[79,82,83] It is interesting to highlight that studies on breast cancer risk perception have shown that the majority of women underestimate their personal risk to develop breast cancer,[83-85] which might exert an important influence on early detection practices and on delayed medical attention for breast symptoms. Finally, we detected very few studies on the role of *social networks* and *social support* in breast cancer delay.

b) Factors related to provider delay

Table III summarizes factors in relation to *provider delay*. As can be observed when comparing between Tables II and III, this type of delay has been a lot less studied than patient delay. We believe this is a reflection of two trends: 1) the minimization of socio-medical and health services research that competes with the overwhelming advances in biomedical knowledge and technology and 2) the fact that the medical model has traditionally attributed health problems and lack of their medical attention to the affected individuals, thus blaming the "victim,"[86] which causes social problems to be reduced to individual behaviors without consideration of the influence exerted by the socio-structural factors and inequity that lead to a differential distribution of disease, access to health services and quality of care.

Among the most studied factors in relation to *provider delay* we again find characteristics of the patient: *young age*[5,7,32,54,87] and having *breast symptoms other than a tumor*,[54,87,88] both of which make the physician's diagnosis more difficult; having African or Hispanic *ethnicity* in countries where the majority of the population is Caucasian[14,17,54,57,89] and *low socioeconomic status*.[5,57,87,90] While there seems to be consensus regarding young age and presenting symptoms different from a breast lump, the relation of provider delay with ethnicity and SES is still controversial. They have both been deficiently measured in order to understand how they intervene with timely medical attention through availability, accessibility and acceptability of health services. Nevertheless, the way these variables have been conceptualized allocate delay responsibility on the patient as an individual instead of dealing with the much more complex problem of understanding the ways in which health systems are inequitable with minorities and with the poor.

Even though health services are considered as important actors in the study of delay, the few investigations that address *provider delay* reduce the problem to

Table III
FACTORS RELATED TO PROVIDER DELAY IN MEDICAL ATTENTION FOR BREAST CANCER

Factors	*Qualitative studies*	*Quantitative studies*	
		Association	*No association*
Patient and symptom characteristics			
Patient's young age		(5) (16) (19) (24) (32) (51) (**54**)[§] (87) (88) (121) (89) (113)	(7) (15) (57) (90)
Patient's African or Hispanic ethnicity (in countries where the majority of the population is non-Hispanic white)		(14) (17) (**54**)[‡]	(15) (57) (121) (89)
Low socioeconomic level		(5) (90)	(57) (87)
Breast signs or symptoms other than a lump		(18) (41) (**54**)[§] (87) (88) (121) (89) (*113*)	
Early clinical stage or small tumor size		(24) (32) (33)	
Quality of health services			
Medical errors in diagnosis	(6) (67)	(14) (15) (18) (51) (56) (88) (90) (89) (92) (91) (112) (*113*)	(**54**)
Administrative barriers to health care	(97)	(89) (112)	
Far distance from residence to cancer centers			(87)

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* References highlighted in bold indicate meta-analysis studies when placed in the Quantitative studies columns and meta-synthesis when placed under Qualitative studies. References in italics are reviews *without* meta-analysis. Remaining references correspond to original research studies

‡ Moderate evidence according to Ramírez et al's meta analysis (data are suggestive of an effect, with at least 2 studies in support of the direction of the effect, but conclusions could be affected by a new study with a large sample)

§ Strong evidence (a substantially greater proportion of studies point to one direction than one would expect to happen by chance)

estimation of delay time intervals and to finding whose fault it was; if it isn't the patient, then the doctors are the ones usually blamed. This is reflected in the most common remaining variables studied in relation to provider delay (Table III), *medical errors*, manifested either as the primary care physician's failure to suspect cancer at initial visit[18,56,89] or as false negative interpretations of mammography[14,15,51,88,90-92] or biopsy.[88,90] The study of the real problems of health services accessibility and quality at a health system level –which can have an effect, for example, on breast cancer delayed medical attention– is practically non-existent.[93]

c) Methodological features of studies on factors related to delay

Knowledge of factors associated with breast cancer delay that have been studied helps to understand how the study of delay has been constructed. Nevertheless, research strategies and methods also constitute a determinant factor in the advance of scientific knowledge. It is therefore also necessary to explore the methodological evolution of research studies on delay to more comprehensively understand past achievements and constraints to be overcome in future research.

Table IV presents general characteristics of studies that analyzed the factors listed in Tables II and III. As it can be observed, the majority of studies use quantitative methods which aren't very helpful for a deep understanding of the underlying reasons why women delay seeking medical attention and the health services obstacles they are confronted with.

Among quantitative studies, the following issues called our attention: 1) There is an evident *lack of population based studies* which accounts for the lack of information on women with breast cancer that *never* reach health services for medical attention; 2) Since a prospective study on delay is unethical, all *studies are retrospective*, which implies certain limitations. The most mentioned limitation throughout studies on delay is *recall bias*, i.e. women might report wrong dates and delay time because they don't remember well. Nonetheless, it has been shown that usually women do recall quite well the beginning of their symptoms.[41,94] Another limitation of retrospective studies is that patients may report less delay than they really experimented in an effort to please the interviewer with "an adequate answer"; 3) Some studies used *self-administered questionnaires* which have the disadvantage of lower participation rates, specially if it is a postal questionnaire,[95] and the threat of selection bias. People who participate in this type of survey are usually more interested in their own health, fact that is probably linked with timely medical care seeking, in comparison to people that do not bother to answer the questionnaire;

Table IV

CHARACTERISTICS OF STUDIES THAT ANALYZE FACTORS IN RELATION TO BREAST CANCER DELAY

Ref.	*Year*	*Country*	*Dependent variables*	*Source of information*	*n*	*Patients*	*Data analysis‡*
(111)	1950	USA	PD= symptom discovery to 1st consultation. (> 3 m)	Semistructured interviews	329	Random sample of people with cancer symptoms seen at one hospital	Bivariate analysis.
(80)	1951	USA	PD= Patient postpones medical consultation. (NS)	In depth interviews	NS	Cancer patients referred for psychiatry consultation in one hospital.	Defensive maneuvers theory
(70)	1953	USA	PD= symptom discovery to 1st consultation. (>3 m)	Medical records	229	Doctors with cancer seen at one hospital. (Compared with 2000 lay patients) *9 doctors with BC	Bivariate analysis
(68)	1954	USA	PD= Delay caused by the patient. (NS)	Semistructured interviews + personality tests	100	Random sample of cancer patients attended at one hospital (50 with Delay and 50 without Delay)	Bivariate analysis
(66)	1955	UK	PD= symptom discovery to 1st consultation. (≥ 3 m)	Interviews + IQ instrument	314	Cancer patients (breast, cervix, oral cavity or skin) attended at one hospital	Descriptive
(116)	1957	USA	PD= symptom discovery to 1st consultation. (≥ 3 m)	Interviews	727	People with potential cancer symptoms seen at NY clinics	Bivariate & stratified analysis.
(60)	1959	USA	PD= symptom discovery to 1st consultation. (>1 m)	Medical records	633	BC ♀ treated at 1 hospital (1943 - 1951)	Bivariate analysis
(67)	1964	USA	PD= symptom discovery to 1st consultation. (>2 m)	Interviews	150	♀ with breast symptoms referred to one hospital	Psycho-analytic theory
(115)	1968	UK	PD= symptom discovery to 1st consultation. (>1 m)	Structured interviews + self-administered questionnaires	83	♀ hospitalized for operation of breast tumors (benign or malignant)	Bivariate analysis
(112)	1974	UK	PD= symptom discovery to 1st consultation. (> 3 m)	Psychiatric interviews + psychological tests	160	♀ hospitalized for breast lump biopsy; (69 cancers; 91 benign)	Bivariate analysis
(28)	1980	Canada	Delay= symptom discovery to BC final diagnosis. (> 1 m)	Medical records	1591	BC patients diagnosed in 1945, 1950, 1955, 1960, 1965, 1970 &1975	Bivariate analysis
(120)	1981	USA	DD= symptom discovery to 1st consultation. (>2 to ≤6, >6 m)	Structured interviews	2092	BC ♀ diagnosed in 14 hospitals of Georgia (1975 ♀ 1979)	Bivariate analysis
(18)	1981	UK	PD= symptom discovery to 1st consultation. (≤1w, ≤3m, ≤6m) GPD= 1st consultation to treatment referral. (≤2w, ≤3m) HD= referral to treatment. (NS)	Structured interviews + Medical records	145	BC ♀ diagnosed in four public hospitals of Northwestern England.	Bivariate analysis
(71)	1983	USA	Delay= symptom discovery to arrival at 3rd level hospital. (1 to < 3, 3 to < 6 , ≥ 6 m)	Medical records	569	BC ♀ operated at one hospital (1967 – 1978). * 27/569 health professionals	Bivariate analysis
(21)	1983	USA	PD= symptom discovery to 1st medical consultation. (≥ 3 m)	Structured interviews + Medical records	664	BC patients seen in 15 Brooklyn hospitals (1975 – 1979)	Bivariate analysis
(29)	1983	USA	TD= symptom discovery to arrival at hospital. (Quantitative variable: months)	Structured interviews + Medical records	185	BC ♀ admitted to a hospital between 1957 & 1965. (29/185 African-American)	Bivariate analysis
(51)	1983	USA	DD= normal mammogram to BC biopsy. (NS)	Medical records	165	s+ with palpable breast masses & normal mammograms	Bivariate analysis
(119)	1984	UK	Delay= symptom discovery to 1st consultation. (1 to <5 w, 5 to <12 w, > 12 w to <6 m, > 6 m)	Structured interviews + psychological tests	24	Hospitalized BC ♀ who had breast surgery.	Bivariate analysis
(23)	1985	USA	PD= symptom discovery to 1st consultation. (3-6 m, ≥ 7 m)	Medical records	4518	BC ♀ treated at MD Anderson Cancer Center (1949 – 1968)	Bivariate analysis
(46)	1988	USA	PD= symptom discovery to 1st consultation. (> 2 m)	Structured interviews + Medical records	2083	BC ♀ diagnosed at 14 hospitals of Georgia (1975-1979)	Bivariate analysis.
(4)	1988	USA	PD= symptom discovery to 1st consultation. (3 to 12, > 12 w)	Structured interviews	800	New Mexico ≥ 65 old residents with cancer (1984-1986). *194 BC cases	Bivariate analysis.
(63)	1992	USA	Symptom duration= symptom discovery to 1st consultation. (Quantitative variable: days)	Structured interviews + Medical records	735	BC ♀ residents of Atlanta, New Orleans & San Francisco (1985–86) (Afro-Americans & whites matched by age and geographic area)	Multivariate analysis
(62)	1992	USA	DD= symptom discovery to final BC diagnosis.	Cancer registry of Los Angeles	23567	BC Los Angeles residents (1977 – 1985)	Multivariate analysis
(113)	1993	USA	PD= symptom discovery to 1st consultation. (≥3 m) SD= 1st beginning consultation to treatment. (> 1 m)	Literature review	101	Delay studies published in English between 1975 and 1993	Critical review
(110)	1993	USA	PD= symptom discovery to 1st consultation. (Quantitative variable: days)	Semistructured interviews + psychological tests	106	♀ with self-discovered breast symptoms referred to two teaching hospitals	Multivariate analysis
(24)	1994	Denmark	PD= symptom discovery to 1st consultation. (>60 d) DD= 1st medical consultation to surgery or biopsy. (>60 d)	National database – (DBCG) Danish BC Cooperative Group	7608	BC patients registered in the DBCG between 1977 and 1982	Multivariate analysis

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(121)	1995	USA	SD= 1st medical consultation to BC final diagnosis. (Quantitative variable: days)	Structured interviews + Medical records (NCI Black/white Cancer Survival Study)	996	Cohort of African-American and white BC patients residents of Atlanta, New Orleans and San Francisco (1985 -1986). * 519 African-Americans & 477 white Americans	Multivariate analysis
(77)	1995	USA	Delay= symptom discovery to 1st contact with health services –personal or by phone. (> 3 m)	In depth interviews	138	♀ with self-discovered breast symptoms referred to two teaching hospitals	Content analysis
(89)	1996	USA	SD= 1st medical consultation to final BC diagnosis. (>4 m)	Structured interviews + Medical records (NCI Black/white Cancer Survival Study)	367	Cohort of African-American and white BC patients residents of Atlanta, New Orleans and San Francisco , who experienced system delay (1985 -1986)	Bivariate analysis
(118)	1997	USA	PD= symptom discovery to 1st consultation. (> 3 m)	Case descriptions	5	Cancer patients with psychiatric problems & delay or no adherence	Psychiatricde-scription
(114)	1998	UK	Concealed cancer= patient with breast lump that doesn´t seek medical help. (≥ 6 m)	Medical records	170	BC ♀ between 1988 and 1992 in one general hospital	Bivariate analysis
(41)	1998	UK	PD= symptom discovery and 1st consultation (≥ 3 m) GPD= failure to refer patient to a 3rd level hospital after 1st visit.	Semistructured interviews	185	Two series: 1) Cohort of BC ♀ aged < 60 (141); 2) Case control: patients aged ≥ 60, inoperable cancers matched with operable tumors	Multivariate analysis
(78)	1998	USA	Women's opinions about actions they would take if they discovered a breast symptom.	Focus groups	80	Voluntary ♀ with no cancer recruited in communitarian organizations other than health care services.	Narrative analysis
(61)	1998	USA	Advanced BC clinical stage= patients with BC stages III & IV.	Structured interviews + Medical records	954	Cases: 540 BC ♀ diagnosed at one hospital (1985 – 1992). Controls: 414 ♀ matched by age, race & residence.	Multivariate analysis
(54)	1999	UK	PD= symptom discovery and 1st consultation. (≥ 3 m) SD= 1st medical consultation to treatment. (≥ 3 m)	Critical and systematic review of the literature	23	Cohort or case-control studies, published after 1960, with samples of only patients with BC, with validated measure of the involved factor, & that described a discrete interval of delay (23 out of 101 original studies)	No meta-analysis. Strength of evidence estimated for each factor.
(19)	1999	UK	SD= 1st medical consultation to treatment. (30-59, 60-89, >90d)	Yorkshire Cancer Registry	36222	BC patients diagnosed between 1976 and 1995	Multivariate analysis
(15)	1999	USA	DD= 1st consultation to BC final diagnosis. (≥ 3 m)	Medical records	606	BC patients seen at the office of one of the authors	Bivariate analysis
(117)	2000	UK	PD= symptom discovery to 1st consultation. (≥ 12 w)	Semistructured interviews + adverse life events & psychiatric tests	185	2 series: 1) Cohort of BC ♀ aged < 60 (141); 2) Case control: patients aged ≥ 60, inoperable cancers matched with operable tumors	Bivariate analysis
(14)	2000	USA	Diagnosis interval= abnormal mammogram to BC diagnosis. (> 60 d) Treatment interval= final diagnosis to treatment. (>30 d)	National Breast and Cervical Cancer Early Detection Program (NBCCEDP)	1659	NBCCEDP participants with BC detected through screening mammography or clinical breast examination	Bivariate analysis
(82)	2000	USA	Women's opinions about actions they would take if they discovered a breast symptom.	Focus groups	45	Voluntary Chinese-American ♀ with no cancer recruited in community organizations (no health services).	Content analysis
(88)	2000	UK	HD= 1st consultation to BC diagnosis. (QV: m)	Medical records	1004	BC ♀ in one hospital between 1988 and 1997	Bivariate analysis
(57)	2000	UK	PD= symptom discovery to 1st consultation. (QV: d) SD= 1st medical consultation to 1st consultation with specialist. (QV: d)	Semistructured interviews + Medical records	692	♀ with breast symptoms referred to one hospital between 1996 and 1997	Multivariate analysis
(56)	2000	Thailand	PD= symptom discovery to 1st consultation. (QV: w) SD= 1st medical consultation to hospital admission. (QV: w)	Structured interviews + Medical records	94	BC patients treated at the only university hospital in the Southern Region of Thailand	Multivariate analysis
(75)	2001	UK	Women's narratives about their experiences from symptom discovery to treatment.	Semistructured interviews	46	BC ♀ diagnosed at one hospital in previous two months	Framework method of analysis.
(69)	2001	Netherlands	Women's experiences from symptom discovery to seeking for medical attention.	In-depth interviews	23	Patients with self-discovered cancer symptoms (breast, melanoma, colon and testicular)	Andersen's PD theory

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(79)	2001	Nether-lands	Women's experiences from symptom discovery to seeking for medical attention.	In- depth interviews	33	23 patients with self-discovered cancer symptoms & 10 General Practitioners	Content analysis
(32)	2001	Italy	PD= symptom discovery to 1st consultation. (≥ 1, ≥ 3 m) DD= 1st consultation to hospital admission. (≥1, ≥3 m)	Semistructured questionnaires	644	♀ with operable BC, operated at the National Cancer Institute of Naples	Multivariate analysis
(11)	2002	Germa-ny	PD= symptom discovery to 1st consultation. (1-3, ≥ 3 m)	VERDI study database + Structured interviews	380	Saarland region residents, with symptomatic BC (1996-1998)	Multivariate analysis
(122)	2002	USA	Self-reported likelihood of patient delay= probability of patient delay for BC symptoms.	Self-administered questio-nnaires	699	Voluntary ♀ without cancer recruited in communitarian organizations other than health care services	Multivariate analysis
(91)	2002	USA	DD= physician action that completed an episode of care without diagnosing cancer of which there was a sign.	Medical records of patients seen by 1 surgeon (one of the authors)	454	BC patients referred to a single surgeon (between 1992 and 1999 (454 cancers in 436 patients)	Multivariate analysis
(123)	2003	Germa-ny	SD= 1st consultation to treatment. (1-3, ≥ 3 m)	VERDI study database + Structured interviews	380	Saarland region residents, with symptomatic BC (1996-1998)	Multivariate analysis
(65)	2003	Nether-lands	Intention to seek medical attention for cancer symptoms.	Postal self-administered questionnaires	534	Convenience sample: controls of a longitudinal study of asymptomatic Dutch adults recruited in 1999	Multivariate analysis
(74)	2003	Hong Kong	Illness experience of BC women from symptom discovery to recovery.	Semistructured interviews	17	Chinese ♀ treated for non-metastatic BC in one public breast medical center	Phenomenological analysis
(6)	2003	UK	PD= symptom discovery to 1st consultation.	Semistructured interviews + focus groups	33	Cancer patients diagnosed in previous two years	Content analysis
(43)	2003	Iran	PD= symptom discovery to 1st consultation. (> 12 w)	Structured interviews + Medical records	190	BC ♀ treated at two hospitals in Tehran	Multivariate analysis
(55)	2003	Mexico	Early Clinical Stage: women with BC stage I. SD= 1st consultation to beginning of treatment. (> 3 m)	Structured interviews	40	BC ♀ treated at breast clinic. Cases: stage I patients (10); Controls: stage II, III & IV patients (30)	Multivariate analysis
(16)	2004	UK	DD= 1st medical consultation to final BC diagnosis. (> 2 m)	Medical records	72	BC ♀with diagnosis delay seen at one hospital (1988-1999)	Bivariate analysis
(92)	2004	Nether-lands	DD= abnormal screening mammography to final BC diagnosis. (> 3 m)	Medical records	770	BC ♀ diagnosed after abnormal screening mammogram at two units of national screening program	Bivariate analysis
(17)	2004	USA	SD= 1st medical consultation to treatment.	Structured interviews + Medical records	831	BC ♀, residents of Atlanta. (251 African-Americans & 580 whites)	Multivariate analysis
(87)	2004	UK	SD= 1st medical consultation to treatment.	Medical records	1097	BC ♀ identified through Scottish Cancer Registry (1997-1998)	Multivariate analysis
(50)	2004	Norway	PD= Definition not specified. (≥ 1 m)	Semistructured interviews + psychological tests	96	BC ♀ stages I & II treated at one hospital	Multivariate analysis
(12)	2005	Iran	PD= symptom discovery to 1st consultation. (> 1 m)	Structured interviews	200	BC ♀ with stage IIB, III or IV seen at referral hospital of Tehran.	Bivariate analysis
(83)	2005	USA	Medical seeking behavior of women who experienced breast symptoms.	In depth interviews	11	♀ with previous experiences of breast symptoms	Heuristic analysis
(81)	2005	USA	Locally advanced BC = clinical stages III and IV at arrival to 3rd level hospital.	Semistructured interviews + psychological tests	35	BC ♀ seen at university hospital. (11 early stage & 11 late stage); & 13 patients' husbands	Descriptive analysis
(5)	2005	UK	PD = Definition not specified	Self-administered postal questionnaires	65192	Cancer patients (data extracted from 1999 -2000 National Survey of NHS Patients)	Multivariate analysis
(59)	2005	UK	Cancer patients' experiences from symptom discovery to 1st medical consultation.	Meta-synthesis	32	Qualitative studies related to cancer help seeking experience, published in English between 1985 & 2004	Meta-synthesis
(97)	2006	Canada	Patient perceptions of impeding and facilitating events in cancer care continuum.	Structured questionnaire + semistructured interview	120	♀ with BC receiving adjuvant radiotherapy between 2002 & 2003 at a university hospital	Content analysis. Andersen's PD theory
(39)	2006	UK	PD = symptom discovery to 1st medical consultation. (≥ 12 w)	Semistructured interviews	69	Consecutive series of 100 _ ≥ 65 years old with BC diagnosed between 2002 and 2003 in two London hospitals	Quant:bivariate/ Qual: framework method
(76)	2006	USA	PD = symptom discovery to 1st medical consultation. (≥ 3 m)	In-depth interviews	28	Voluntary ♀ with breast symptoms recruited in community organizations other than health care services	Heuristic analysis
(98)	2007	Canada	Women's descriptions of path--ways from detection of breast abnormality to treatment.	Semistructured interviews	35	♀ recently operated for symptomatic BC	Critical ethnography

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(90)	2007	Canada	DD= 1st diagnostic procedure to final BC diagnosis. (> 5 w)	Structured interviews + Medical records	696	♀ with BC stages I, II and III who were receiving treatment	Multivariate analysis
(58)	2007	Colombia	Advanced BC= clinical stages III and IV at diagnosis.	Semistructured interviews + self-administered questionnaires	102	Cases: advanced BC. Controls: early BC (stage I & II)	Multivariate analysis
(7)	2008	Denmark	PD= symptom discovery to 1st consultation.	Self-administered postal questionnaires answered by: GPs (medical care events) & Patients (socioeconomic data)	1892	Cancer patients residents of Aarhus County, identified through County Health Service Registry (2004 -2005) (291 BC cases)	Multivariate analysis
			DD= 1st medical consultation to 1st procedure of diagnosis.				
			SD= 1st procedure of diagnosis to beginning of treatment.				
(33)	2008	Spain	Interval from diagnosis to treatment= 1st diagnostic test to beginning of treatment.	Medical records	1023	Cancer patients diagnosed in 22 public hospitals of Barcelona (266 BC cases)	Multivariate analysis

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* White rows: quantitative studies; gray rows: qualitative studies. Abbreviations: BC= breast cancer; NS= not specified, TD= total delay, PD= patient delay, SD= system delay or provider delay, DD= diagnosis delay, GPD= general practitioner delay, RD= referral delay, TD= treatment delay, HD= hospital delay; d= days, w= weeks, m= months, QV= quantitative variable (where not specified delay was given categorical values which are indicated in parenthesis).

‡ Information in this column refers to type of analysis used to conclude regarding the association between delay and factors listed in Tables II and III. Some studies might have included additional types of analysis for other variables

♀ = women

4) The use of clinical records and population registries has the limitation of the quality of information and that only the available data can be used. Furthermore, delay has been shown to be underestimated when calculated based on information obtained from medical records;[94] 5) The lack of validation of instruments that measure delay is a problem common to most studies; and 6) Operational definitions used differ tremendously (Table IV) and this impedes comparison of results and meta-analysis that allow for more valid conclusions about the relationship between different factors and delay.

Among the qualitative studies reviewed, the most common flaw was the absence of theoretical analyses. The majority are merely descriptive. Nevertheless, there are interesting studies where different theories are used in an attempt to explain the reasoning of women who delay seeking medical attention. Most of them use psychological theories: psychoanalysis,[67,80] Leventhal's self-regulation theory,[96] Leventhal's theory of fear and danger control,[69] Ajzen's theory of planned behavior,[96] Gollwitzer's theory of implementation of intentions,[96] Merton & Kitt's theory of reference group behavior,[68] Andersen & Cacioppo's theory of total patient delay[69,97] and heuristic analysis.[73,83] Among the social theories that have been used are Beck & Rosenstock's health belief model,[69] Bordieu's social capital theory[98] and anthropological theories related to meaning construction such as those developed by Taylor, Lipowski and Kleinman.[74]

Breast cancer delayed medical attention in Mexico

Even though in Mexico about 50% of breast cancer patients are diagnosed at stages III and IV,[99] research on the reasons behind delayed medical attention of breast cancer is practically non-existent. Only one published study done in Mexico was found,[55] with several methodological limitations. It was done in Mexico City, in a military health services clinic that offers specialized services for women. It included only 40 patients, among which there was patient delay in 14 (35%) and provider delay greater than three months in 21 (52.5%). This study reports the association of certain factors with clinical stage, which was considered as the dependent variable that reflected delay. It was interesting that they considered indicators of accessibility but the small sample size did not allow for significant findings.

We currently have preliminary results of a research project that aims to measure and explain patient and provider delay of women seen in several hospitals in Mexico City. The first phase is qualitative, based on in-depth interviews of women with symptoms highly suggestive of breast cancer who arrive for the first time to the Breast Tumors Department of the Mexican National Cancer Institute. This institution is a concentration hospital that offers specialized cancer care for uninsured patients. The initial results of this study phase show that

the most determinant factors in the conformation of different help seeking trajectories are women's socio-cultural characteristics, especially poverty, characteristics of their social networks, the kinds of social support they are able to get, accessibility to health services and medical errors in primary and secondary levels of care.[100]

Directions for future research in developing countries

Mortality rates for breast cancer have been steadily decreasing by 1-2% per year since the 1990s in Europe and the United States of America,[101] which has been attributed mainly to screening mammography and improvements in systemic therapy.[102] In contrast, in resource-limited countries, breast cancer mortality rates have remained the same.[101] Some of the barriers to improve medical care for breast cancer in underdeveloped countries are lack of cancer knowledge among the general population, socioeconomic and cultural barriers, health service organizational problems, and resource constraints,[103] as well as low quality of health services frequently used by people with low SES who lack formal employment, economic stability and health insurance. Improvements accomplished in breast cancer mortality rates in developed countries are most likely a consequence of a combination of scientific research, increased population awareness of the problem and political will. In the end, a health system is not only the Ministry of Health or the personal medical services offered, but the collection of social subsystems that interact to comprise it.[104]

In many LMC, including most of Latin American countries, emphasis in breast cancer policies and programs is currently being directed towards screening mammography,[105] despite the fact that it is still controversial as to whether it does "more good than harm."[106] Moreover, establishing a national screening program implies not only the cost of mammography equipment but also its equitable distribution as well as training and distribution of technical personnel for its execution and interpretation. Making this great expenditure on the availability of a screening test –of which the impact on mortality is still controversial– in countries where universal supply of accessible and high quality health services for breast cancer is still not available seems unfounded. Before developing mammography screening programs, efforts should be directed to develop and implement appropriate treatment guidelines and provide access to diagnostic and treatment services.[105,107]

In Mexico, treatment expenditures for many previously uninsured women with breast cancer have been covered since 2007[108] thanks to the creation of the program "Seguro Popular de Salud" (Popular Health Insurance). This is a program that subsidizes an explicit system of health interventions financed with contributions by federal and state governments and by affiliated families.[109] While recognizing this as a very relevant effort to overcome treatment coverage problems that existed for this population, there are still multiple barriers that impede breast cancer patients to be timely diagnosed and treated.

Identification of factors related to delay of diagnosis and treatment in the context of underdeveloped countries, including Mexico, is greatly needed. Only five of the breast cancer delay studies reviewed were done in developing countries: Thailand, Iran, Colombia and Mexico. The study of breast cancer delay considering specific socio-cultural and health systems characteristics would allow for the identification of specific factors toward which interventions should be directed. Many of these factors are difficult to modify since they are cultural or at the society's structural level; the challenge we face is finding modifiable mechanisms that can improve early medical attention of breast cancer in each country.

Conclusion

This paper identifies knowledge gaps and methodological inconsistencies found in international publications of breast cancer delay. Our purpose was to facilitate the identification of the most pressing research needs on the matter. There is a need for more comprehensive research that takes into account socio-structural and health services factors. Furthermore, research on delay should aim to identify locally modifiable factors in underdeveloped countries towards which equity oriented political programs can be directed to improve medical attention for breast cancer so that mortality rates can be reduced and patients' quality of life improved.

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