

- 19 Huang L, Wang W, Li H, Xu B, Yang H. A descriptive study on diagnosis delays and factors impacting accessibility to diagnosis among TB patients in floating population in Shanghai. *J. Chin. Antituberc* 2007;29:127–9.
- 20 Demissie M, Lindtjorn B, Berhane Y. Patient and health service delay in the diagnosis of pulmonary tuberculosis in Ethiopia. *BMC Public Health* 2002;2:23.
- 21 Mirsaedi SM, Tabarsi P, Mohajer K, et al. A Long delay from the first symptom to definite diagnosis of pulmonary tuberculosis. *Arch Iranian Med* 2007;2:190–3.
- 22 Sagbakken M, Frich JC, Bjune GA. Perception and management of tuberculosis symptoms in Addis Ababa, Ethiopia. *Qual Health Res* 2008;10:1356–66.
- 23 Hino P, Bertolozzi MR, Takahashi RF, Egry EY. Health needs according to the perception of people with pulmonary tuberculosis. *Rev Esc Enferm USP* 2012;6:1438–45.
- 24 Gelaw M, Genebo T, Dejene A, et al. Attitude and social consequences of tuberculosis in Addis Ababa, Ethiopia. *East Afr Med J* 2001;7:382–8.
- 25 Courtwright A, Turner AN. Tuberculosis and stigmatization: pathways and interventions. *Public Health Rep* 2010;4:34–42.
- 26 Gilani SI, Khurram M. Perception of tuberculosis in Pakistan: findings of a nation-wide survey. *J Pak Med Assoc* 2012;2:116–20.
- 27 Przybylski G, Dabrowska A, Golda R, et al. The analysis of smoking tobacco of patients with tuberculosis—data from ten years observation in Regional Center of Pulmonology in Bydgoszcz. *Przegl Lek* 2012;10:953–7.
- 28 Wang X, Liu F, Dong B. Study-on the defecation rate of double infection among patients with AIDS and TB and its influencing factors. *Mod Prevent Med* 2007;23:4457–8,4460.

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European Journal of Public Health, Vol. 24, No. 5, 761–767

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 doi:10.1093/eurpub/ckt131 Advance Access published on 12 September 2013

Delays in diagnosis and treatment of breast cancer: a multinational analysis

Jacek Jassem¹, Vahit Ozmen², Florin Bacanu³, Monika Drobnienė⁴, Janis Eglitis⁵, Kuntegowdanahalli C. Lakshmaiah⁶, Zsuzsanna Kahan⁷, Jozef Mardiak⁸, Tadeusz Pieńkowski⁹, Tatiana Semiglazova¹⁰, Ljiljana Stamatovic¹¹, Constanta Timcheva¹², Suzana Vasovic¹¹, Damir Urbanec¹³, Piotr Zaborek¹⁴

1 Department of Oncology and Radiotherapy, Medical University of Gdansk, Gdansk, Poland

2 Department of Surgery, Istanbul University, Istanbul, Turkey

3 Department of Clinical Oncology, Sf Maria Hospital, Bucharest, Romania

4 Radiotherapy and Drug Therapy Center, Institute of Oncology, Vilnius University, Vilnius, Lithuania

5 Department of Breast Surgery, Oncology Centre of Latvia, Riga East University Hospital, Riga, Latvia

6 Department of Medical Oncology, Kidwai Memorial Institute of Oncology, India

7 Department of Oncotherapy, University of Szeged, Szeged, Hungary

8 2nd Department of Oncology, National Cancer Institute and Medical School of Comenius University, Bratislava, Slovak Republic

9 Department of Oncology and Surgery, Medical Centre of Postgraduate Education, Otwock, Poland

10 Department of Medical Oncology, Petrov Research Institute of Oncology, St. Petersburg, Russia

11 Department of Medical Oncology, Institute of Oncology and Radiology, Belgrade, Serbia

12 Department of Chemotherapy, Specialized Hospital for Active Treatment in Oncology, Sofia, Bulgaria

13 Department of Medical Oncology, Clinic of Oncology, Zagreb University Hospital Centre, Zagreb, Croatia

14 Collegium of World Economy, Warsaw School of Economics, Warsaw, Poland

Correspondence: Jacek Jassem, Medical University of Gdańsk, ul. Dębinki 7, 80-211 Gdańsk, Poland, Tel: +48 58 349 22 70, Fax: +48 58 349 22 10, e-mail: jjassem@gumed.edu.pl

Background: Reducing treatment delay improves outcomes in breast cancer. The aim of this study was to determine factors influencing patient- and system-related delays in commencing breast cancer treatment in different countries. **Methods:** A total of 6588 female breast cancer patients from 12 countries were surveyed. Total delay time was determined as the sum of the patient-related delay time (time between onset of the first symptoms and the first medical visit) and system-related delay time (time between the first medical visit and the start of therapy). **Results:** The average patient-related delay time and total delay time were 4.7 (range: 3.4–6.2) weeks and 14.4 (range: 11.5–29.4) weeks, respectively. Longer patient-related delay times were associated with distrust and disregard, and shorter patient-related delay times were associated with fear of breast cancer, practicing self-examination, higher education level, being employed, having support from friends and family and living in big cities. The average system-related delay time was 11.1 (range: 8.3–24.7) weeks. Cancer diagnosis made by an oncologist versus another physician, higher education level, older age, family history of female cancers and having a breast lump as the first cancer sign were associated with shorter system-related delay times. Longer patient-related delay times and higher levels of distrust and disregard were predictors of longer system-related delay times. **Conclusions:** The delay in diagnosis and treatment of breast cancer remains a serious problem. Several psychological and behavioural patient attributes strongly determine both patient-related delay time and system-related delay time, but their strength is different in particular countries.

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Introduction

Breast cancer (BC) is one of the most common causes of cancer deaths in women. Within the past decade, BC mortality has been

decreasing in developed countries.¹ In contrast, owing to lack of organized population-based screening programmes, lower BC awareness and poorer infrastructure, this has not been achieved in many low- and middle-income countries.^{2,3} Consequently, the BC

burden will remain a major health problem globally within the next decades.

Delays in diagnosis and treatment of BC may seriously impact survival.^{4,5} Treatment of BCs diagnosed at a later stage is also associated with higher morbidity, due to more aggressive and disfiguring approaches, and is more expensive. Thus, reducing these delays is believed to be of high importance. The delay in cancer care delivery may be categorized into patient-, physician- and system-related factors.⁶ Although factors associated with a delay in BC care have been well described,⁷ the data on their relative impact and on mitigation strategies are scarce. Most of the studies performed so far have dealt with patient-related delays, whereas few addressed system-related delays.⁸ The aim of the present study was to analyse the differences in time to diagnosis and treatment initiation in BC patients across a number of low- and middle-income countries, and to identify factors related to delays.

Methods

Patients

This study is based on a questionnaire survey conducted in 2011 in 12 countries. The countries were selected to represent a wide spectrum of different socioeconomic, geographical and cultural settings. The target population was defined as female BC patients undergoing treatment within 6 months preceding the survey, which for most countries spanned a period of 2–3 months in 2011. The selection of respondents followed the cluster sampling technique, conducted separately in each country. Considering the number of BC patients treated in 2010, a pre-specified number of oncology centres (ranging from 4 in Slovakia to 13 in Turkey) were randomly selected for the survey.

Questionnaire

The basic study questionnaire (originally developed in English) was translated into local languages, and the survey was conducted by a trained nurse or an oncologist during routine medical visits. Data collected from the survey were not verified with the patient medical records. The first part of the survey included patient demographics (age, education and place of residence) and the second part included the circumstances in which BC signs or symptoms were first presented to a medical doctor (MD), the type of signs or symptoms of BC first noticed by the patient, additional signs or symptoms detected by the patient before the first visit to an MD and the time elapsed before examination by an MD for BC signs or symptoms. Additional questions included the ownership status of the medical unit where the patient was first seen by an MD (public vs. private), factors potentially influencing the patient's decision of seeing an MD after the first signs or symptoms of BC and the time elapsed from registering for the first medical examination due to BC signs or symptoms to the start of therapy. Prevalence and availability of mammography screening programmes were measured by two variables on the questionnaire: reception of an invitation for a free-of-charge mammography and participation in a free-of-charge mammography. To achieve shorter interview times and alleviate problems with non-responded items, a close-ended question format with pre-defined answers was used instead of open-ended questions (Appendix 1). In the subsequent analysis, the midpoints of selected time categories were used to develop delay times and to compute averages.

This survey did not fulfil the criteria of a medical experiment and thus did not require ethics committee approval.

Outcome variables

The main outcome variables of the study included patient-related delay time (PDT), system-related delay time (SDT) and total delay

time (TDT). PDT was defined as the time between the onset of first symptoms and the first medical visit (this analysis included only patients with self-detected cancers). SDT was the time between the first medical visit and the start of therapy. TDT was determined using eight individual scales, including one pertaining to PDT and seven related to subsequent steps in a typical diagnostic process, and was the sum of PDT and SDT (in patients with BC detected during a medical visit or by mammography, PDT was considered zero). Each scale contained eight categories identifying possible delay times from 'less than 1 week' to 'more than 12 weeks'. All time-pertaining variables were continuous in nature. However, to facilitate measuring process and increase reply rate, they were structured as categorical characteristics. The resultant items displayed the features of interval-type scales, and allowed calculating arithmetic averages and performing expanded statistical analysis including parametric tests and regression models.⁹

Statistical methods

The results were analysed using the Statistical Package for the Social Sciences (SPSS, version 20). For continuous variables, data distribution was assessed visually (based on graphs) and by using the common descriptive statistics including mean, standard error and skewness coefficient. Some of the continuous variables (e.g. age, PDT) were also presented as the interval, and not ordinal-scale variables. The chi-square independence test, degrees of freedom (df), *P*-value and value of Cramer's *V* coefficient were used to compare categorical variables, considering the country as a separate variable. The PDT and SDT means in particular countries were compared using one-way analysis of variance and post-hoc tests (Games–Howell). If the distribution of a dependent variable was strongly deviating from normal, logarithmic transformation (log₁₀) was performed.

Two separate multivariate linear regression analyses were performed to create the best models for predicting PDT and SDT values. The first step in the regression analysis was data preparation that involved transforming several multicategory attributes into dichotomous variables (Appendix 2). The second step was a principal component factor analysis of 14 items included in item Q.7 of the questionnaire (statements that apply to feelings and behaviour from the onset of BC symptoms until the final diagnosis). With factor analysis, by extracting a set of more general, latent variables, we reduced the number of items for measuring patients' psychological and behavioural circumstances from 14 to 5 (data available at request). Multiple regression was first conducted in a stepwise manner, using the Ordinary Least Squares method. This approach allowed for the selection of a limited set of statistically significant predictors out of variables found to be relevant in earlier analyses (18 for PDT and 17 for SDT). To evaluate the impact of the country on PDT and SDT, a multilevel analysis was performed.

These models were developed for the whole database and separately for each country, and were presented as unstandardized and standardized coefficients, *t*-values and *p*-values. The questionnaire used in India contained two items less in question Q.7, which precluded calculation of scores for five psychological and behavioural components extracted through factor analysis.

Results

Demographic characteristics

Due to the assistance of the trained medical personnel administering the survey, virtually all questionnaires were adequately completed and were eligible for analysis. No detailed data were collected on the proportion of patients who refused participation in the survey, as their number was considered negligible. A total of 6588 female BC patients from 12 countries were surveyed (table 1). In most

Table 1 The characteristics of the study participants

Country ^a (n)	BGR (644)	HUN (350)	IND (268)	LVA (156)	LTU (458)	POL (1000)	ROU (319)	RUS (1059)	SVK (253)	SRB (800)	TUR (1031)	HRV (250)	Total (6588)
Contribution % ^b	9.8	5.3	4.1	2.4	7.0	15	4.8	16	3.8	12	16	3.8	100
Age (%)													
<30	1.4	1.4	4.1	2.6	0.9	1.1	0.6	1.6	2.4	1.6	2.1	2.0	1.7
30–39	12.2	5.4	18.0	3.2	6.5	9.9	10.3	9.7	9.5	8.5	13.4	9.2	10.1
40–49	26.5	19.1	43.6	17.3	24.6	19.7	22.9	28.5	26.1	19.9	31.8	25.3	25.5
50–59	29.7	32.6	21.8	27.6	26.1	37.4	33.2	33.8	34.4	26.6	29.0	28.9	30.9
60–69	25.2	28.9	10.9	23.1	29.0	25.1	24.8	19.6	22.5	25.8	15.9	23.3	22.5
≥70	4.9	12.6	1.5	26.3	12.9	6.8	8.2	6.7	5.1	17.5	7.8	11.2	9.2
Education (%)													
Primary	9.9	14.9	39.8	9.7	9.2	8.3	33.2	5.2	7.1	26.3	52.8	12.9	20.1
Technical secondary	25.0	21.4	29.9	5.2	28.9	16.7	18.2	13.2	16.6	8.2	2.5	49.2	16.3
Full secondary	28.5	40.3	23.4	45.8	34.0	48.8	32.6	40.8	42.7	40.1	23.6	14.9	35.7
Tertiary	36.5	23.4	6.9	39.4	27.9	26.2	16	40.7	33.6	25.4	21.1	23.0	27.9
Place of living (%)													
Hamlet or village	11.0	13.7	31.9	18.2	20.1	20.8	14.7	15.3	26.4	24.8	5.5	17.3	16.8
Town <50K inhabitants	18.5	20.6	25.1	15.6	20.8	21.8	15.4	9.4	26.8	13.6	10.2	25.3	16.5
Town >50K–100K	21.2	28.9	17.5	27.3	9.9	14.2	20.1	6.7	22.4	17.9	8.5	13.7	14.7
Town >100K–500K	20.4	21.1	11.8	3.2	37.1	15.5	40.1	15.4	13.6	13.4	16.0	1.2	17.7
Town >500K	29.0	15.7	13.7	35.7	12.1	27.7	9.7	53.3	10.8	30.3	59.7	42.6	34.2
Getting an invitation to screening mammography (%)													
Does not apply/no answer	41.9	38.6	58.2	39.7	30.8	45.7	98.1	34.3	39.1	100	55.1	30.8	52.2
Yes	10.7	43.7	1.1	44.2	27.7	54.3	1.9	19.9	38.7	–	9.0	42.8	22.4
No	47.4	17.7	40.7	16.0	41.5	–	–	45.8	22.1	–	35.9	26.4	25.3
Participation in screening mammography (only patients who received invitation) (%)													
Yes	46.4	83.7	33.3	62.8	81.9	21.6	12.2	64.6	85.1	–	72.0	59.2	45.8
No, mammography performed within the past 2 years	20.8	11.1	14.8	12.8	7.7	78.4	0.6	14.0	8.8	–	11.8	27.2	32.3
No, invitation or mammography not performed for some other reason	32.8	5.2	51.9	24.4	10.3	–	87.1	21.4	6.1	–	16.1	13.6	22.0

a: Country: Bulgaria (BGR), Hungary (HUN), India (IND), Latvia (LVA), Lithuania (LTU), Poland (POL), Romania (ROU), Russia (RUS), Slovakia (SVK), Serbia (SRB), Turkey (TUR) and Croatia (HRV).

b: Due to rounding of original figures to one decimal place, the sums of percentages may not add up to 100%.

countries, the majority of patients were aged 40–69 years, with most responders in the 50–59-year age category. There were substantial differences between countries with regard to respondents' education level and place of residence (both $P < 0.001$).

BC detection

The highest proportion of patients with self-detected symptoms were in Romania (93%) and Serbia (81%), and the lowest in Hungary (48%) and Poland (56%) (figure 1). Countries with the highest proportions of BC detected by mammography included Hungary (35%) and Poland (34%). The circumstances in which BC signs or symptoms were first noticed differed significantly between particular countries ($P < 0.001$). The most common first sign of BC detected by self-examination was a breast lump (>65% in all countries). Less frequent symptoms included breast pain, nipple or skin changes and nipple discharge (figure 2).

The availability of free mammography screening programmes varied between countries ($P < 0.001$). Of 2218 patients who received invitation for a mammography screening, 1015 (46%) actually underwent the examination; 716 (32%) did not respond, as they had already been examined within 2 years preceding the invitation and 487 (22%) did not participate in the screening for other reasons.

Patient-related delay time

The respondents who had found BC signs or symptoms themselves were inquired about the time elapsed from detecting the first sign or symptom to receiving medical advice from an oncologist or another MD. The mean PDT for all countries was 4.7 weeks, with a range between 3.4 weeks in Hungary and 6.2 weeks in Latvia (table 2). Based on the multivariate regression model, longer PDTs were associated with patients' distrust in the healthcare system and

successful therapy and with disregard or trivialization of discovered symptoms. Overall, patients who regularly practiced breast self-examination, experienced higher levels of fear of disease, had at least a secondary education, were employed, were influenced by family members or friends or lived in towns with a population larger than 100 000 tended to have shorter PDT (table 3). Other pertinent demographic characteristics such as age, education and income level were also considered as potential independent variables in the regression equation, but did not add considerably to the predictive capacity of the model.

Multilevel regression analysis showed that among all predictors of PDT, particular countries differed significantly with regard to the impact of distrust, disregard and self-examination (chi-square, reflecting change in -2 log likelihood from the baseline to the outcome model, was 97.1; $df = 4$; $P < 0.001$). On the other hand, the fixed term and some other predictors included in the regression model (i.e. at least secondary education, living in a town of more than 100 000 inhabitants, being employed, having fear of disease and having support from family and friends) did not show systematic inter-country variations.

To establish country-specific regression coefficients, multiple regression equations were constructed for each country, and proved to be significant, although at a different level of explained variance in PDT (data not shown).

The results of country-specific regression models suggested that the most universal predictors of PDT were distrust and disregard. These factors were significant in all countries and almost always most strongly affected PDT (the single exception was Lithuania, where practicing breast self-examination was the strongest factor). Other predictors identified in many countries were self-examination and fear (data not shown). The countries with the highest regression coefficients for distrust were Serbia (2.09), Romania (2.07) and

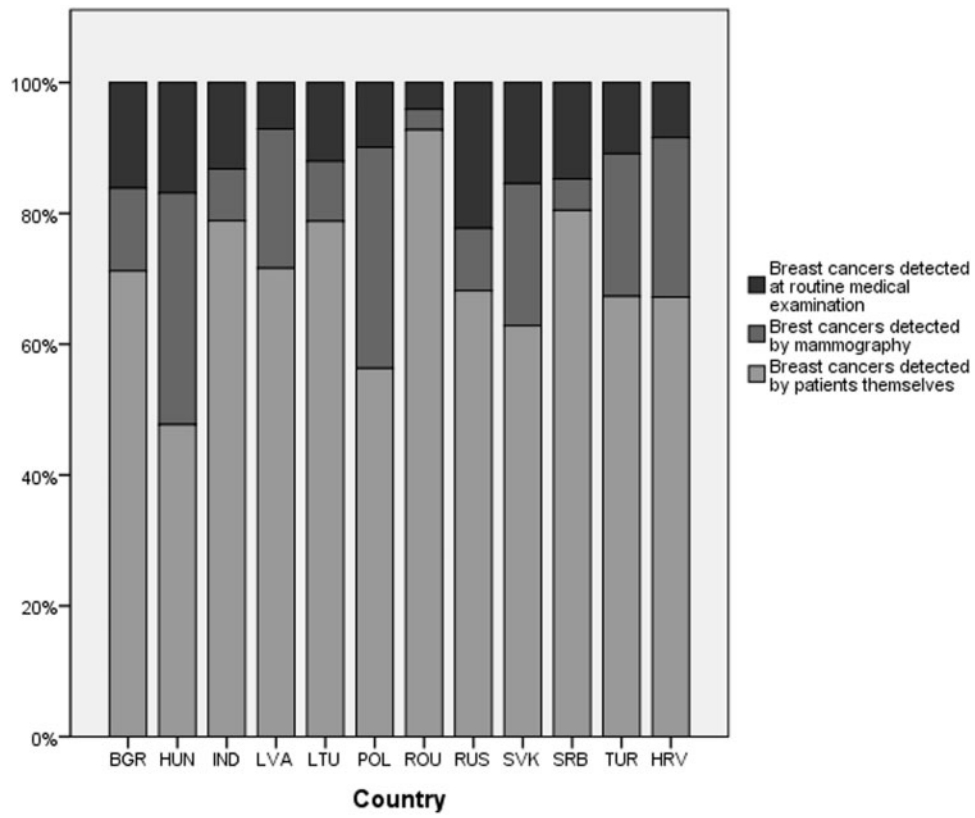


Figure 1 Circumstances of breast cancer detection

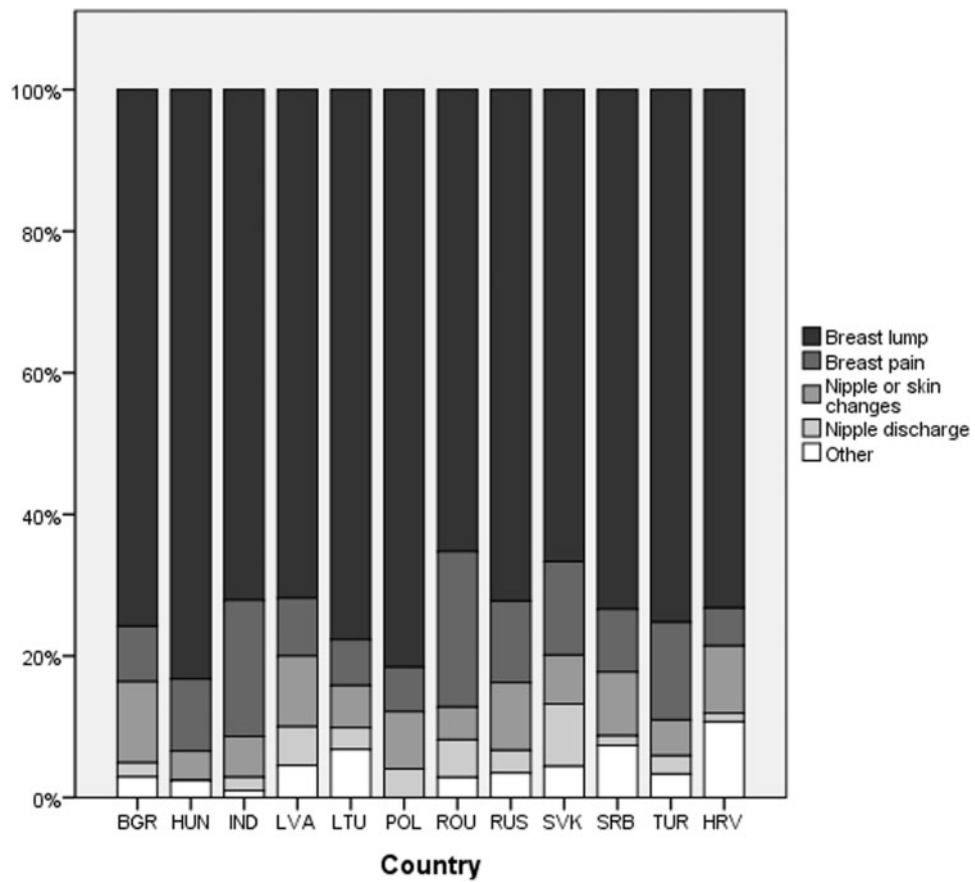


Figure 2 First symptoms of breast cancer noticed by patients

Croatia (1.73). Disregard was the strongest predictor of delay in Croatia (2.04), Latvia (1.72) and Slovakia (1.51), and the weakest in Hungary (0.61) and Lithuania (0.86). Unexpectedly, the reversed pattern of relationship was found in Romania (-1.36), indicating that a higher level of disregard and/or trivialization of discovered symptoms corresponded with a shorter PDT. Practicing self-examination was the strongest factor related to shorter PDT in Lithuania (-1.31), Russia (-1.14) and Slovakia (-1.08), and the weakest in Turkey (-0.48) and Serbia (-0.35). This factor was also an insignificant element of the regression model in Latvia, Croatia, Romania and Bulgaria.

System-related delay time

The mean SDT for all countries was 11.1 weeks, with the country-specific means varying from 8.3 weeks for Lithuania to 24.7 weeks for India (table 2).

In multiple regression analysis, the following variables were correlated with shorter SDT: being diagnosed by an oncologist versus another MD, having at least a secondary education, being older than 60 years, having a family history of female cancers and having a breast lump, as opposed to other symptoms. PDTs longer than 4 weeks, higher levels of distrust in the healthcare system and

disregard for the diagnosis were the most strongly correlated with longer SDT (table 4). Due to strong asymmetry of the output variable and some problems with heteroscedasticity, logarithmic transformation of original SDT values was performed to increase reliability of confidence intervals and test results. The coefficients presented in table 4 should be interpreted as exponents of 10 (base of the transformation logarithm) and considered as factors by which the length of SDT will change when the given predictor increases by 1 U (the results of these operations are shown in the last two columns of table 4). Multilevel analysis showed differences between particular countries regarding the correlations with a PDT of >4 weeks, distrust in the healthcare system and disregard of BC signs ($\chi^2=300.6$; $df=4$; $P<0.001$). The results of country-specific regression models suggested that the most universal predictors of SDT were distrust, disregard and PDT. PDT had the highest impact on SDT in Croatia (0.50) and Romania (0.30), and had no significant impact in Latvia, Lithuania and Slovakia. Disregard was the strongest correlate of SDT in Bulgaria (0.07) and Russia (0.06), with no significant correlation in Slovakia, Latvia and Poland. Distrust was the most potent determinant of SDT in Hungary (0.15) and Bulgaria (0.09), and had no considerable effect in Slovakia, Romania, Serbia, Croatia and Turkey.

Table 2 Patient-related delay time (PDT), system-related delay time (SDT) and total delay time (TDT) by country (weeks)

Country ^a	N	Mean PDT (SE)	Skewness	N	Mean SDT (SE)	Skewness	N	Mean TDT (SE)	Skewness
BGR	448	4.83 (0.22)	0.82	644	12.51 (0.53)	2.91	644	15.87 (0.62)	2.66
HUN	167	3.44 (0.30)	1.56	350	14.47 (0.59)	1.96	350	16.12 (0.66)	2.06
IND	207	6.10 (0.33)	0.40	268	24.69 (1.22)	1.26	268	29.41 (1.37)	1.09
LVA	111	6.17 (0.47)	0.37	156	13.14 (0.72)	2.01	156	17.53 (0.89)	1.47
LTU	368	4.85 (0.25)	0.79	458	8.27 (0.37)	2.50	458	12.16 (0.45)	1.94
POL	557	3.61 (0.17)	1.42	1000	9.49 (0.22)	1.70	1000	11.50 (0.25)	1.58
ROU	271	6.02 (0.28)	0.30	319	20.42 (0.75)	1.11	319	25.54 (0.92)	0.89
RUS	718	4.81 (0.17)	0.84	1059	12.42 (0.37)	2.46	1059	15.68 (0.43)	2.14
SVK	154	4.00 (0.35)	1.14	253	10.72 (0.50)	1.83	253	13.15 (0.60)	1.80
SRB	663	4.47 (0.19)	0.89	800	9.16 (0.27)	2.20	800	12.86 (0.38)	1.56
TUR	694	4.84 (0.18)	0.81	1031	10.49 (0.32)	2.70	1031	13.75 (0.38)	2.40
HRV	167	4.88 (0.39)	0.73	248	10.23 (0.65)	2.33	248	13.51 (0.85)	2.03
Total	4525	4.71 (0.07)	0.84	6586	11.86 (0.14)	2.58	6586	15.10 (0.16)	2.27

a: Country: Bulgaria (BGR), Hungary (HUN), India (IND), Latvia (LVA), Lithuania (LTU), Poland (POL), Romania (ROU), Russia (RUS), Slovakia (SVK), Serbia (SRB), Turkey (TUR) and Croatia (HRV).
SE, standard error.

Table 3 Factors influencing PDT (multivariate regression model)

Model	Coefficients ^a			t	Significant
	Unstandardized coefficients		Standardized coefficients		
	B	Standard error	Beta ^b		
(Constant)	5.67	0.15	-	37.3	<0.001
Distrust	1.25	0.07	0.26	17.9	<0.001
Disregard	1.16	0.07	0.25	17.0	<0.001
Self-examination	-0.63	0.07	-0.13	-8.9	<0.001
Fear	-0.38	0.07	-0.08	-5.6	<0.001
Education level (at least secondary)	-0.48	0.16	-0.05	-3.2	0.002
Job status (employed)	-0.54	0.16	-0.05	-3.4	0.001
Support of family and friends	-0.18	0.07	-0.04	-2.6	0.008
Place of living: >100 000 inhabitants	-0.36	0.14	-0.04	-2.6	0.010

a: Dependent variable: Patient delay.

b: The absolute values of standardized betas indicate which predictors had the strongest impact on the target variable; thus the most important variables are psychological and behavioural factors, including in order of importance: DISTRUST, DISREGARD, SELF EXAMINATION and FEAR.

Table 4 Factors influencing SDT (multivariate regression model)

Model	Coefficients ^a			Significance tests		Transformed B coefficients	
	Unstandardized coefficients		Standardized coefficients Beta	t	P-values	10 [^] B	Average % change in SDT with 1 U change in predictor
	B	SE					
Intercept	0.85	0.03		33.3	<0.001	–	–
PDT more vs. less than 4 weeks	0.15	0.01	0.21	12.8	<0.001	1.43	43%
Distrust	0.05	0.01	0.15	9.3	<0.001	1.13	13%
Oncologist vs. other MD	–0.08	0.01	–0.10	–6.3	<0.001	0.82	–18%
Ownership status of medical unit where patient was first diagnosed (1-private; 2-public)	0.04	0.01	0.05	3.3	0.001	1.10	10%
Support of family and friends	0.02	0.01	0.04	2.8	0.005	1.04	4%
Disregard	0.02	0.01	0.04	2.7	0.006	1.04	4%
At least secondary education	–0.03	0.01	–0.05	–2.9	0.004	0.92	–8%
Age ≥60 years	–0.04	0.01	–0.05	–3.0	0.003	0.92	–8%
Self-examination	0.01	0.01	0.03	2.1	0.039	1.03	3%
Participation in mammography	0.04	0.02	0.03	2.0	0.042	1.08	8%

a: Dependent variable: Log 10 SDT.
PDT, patient delay time.

TDT and its correlation with indicators of cancer advancement

The mean TDT was 14.3 weeks, with a wide range from 11.5 weeks in Poland to 29.4 weeks in India ($P < 0.001$; table 2). A strong association ($P < 0.001$) was found between TDT and indicators of cancer advancement at diagnosis (tumour size, nodal spread and distant metastases). The mean TDT in the subset of patients with breast tumours of 2–4 cm and >4 cm was 15.5 and 20.1 weeks, respectively (Supplementary table S1). Likewise, the mean TDT in patients with and without nodal spread was 13.2 and 14.8 weeks, respectively, and with and without distant metastases was, 18.3 and 14.2 weeks, respectively.

Discussion

Several studies reported increased morbidity and mortality related to delays in BC diagnosis and treatment.^{4–7} In a systematic review including 87 studies (101 954 patients), delays in the range of 3–6 months between the onset of symptoms and the start of treatment had a significantly adverse impact on survival.⁸ Our study, including more than 6500 patients from 12 countries, is the largest single analysis of factors influencing delay in diagnosis and treatment of BC. Notably, the mean TDT in our study was 15 weeks, and only in six countries, this period was shorter. We did not determine an acceptable TDT, but clearly it should be kept to a minimum. Indeed, in the current study, three indicators of tumour advancement (tumour size, nodal involvement and dissemination) were strongly associated with TDT.

In a group of 2212 Danish patients with various malignancies, BC was among those with the shortest TDT (median 9.2 weeks).¹⁰ The mean TDT of 14.3 weeks in our survey was longer than in the aforementioned study, with a wide range between particular countries. In a study including 100 patients with locally advanced BC, the average time lapse before diagnosis was higher for rural compared with urban patients (9.6 vs. 7.7 weeks, respectively).¹¹ However, large differences between particular countries shown in our study cannot be attributed to substantial distinctions in place of residence and education level.¹² In another recent study, 17% of patients in the USA had a delayed BC diagnosis, defined as an interval >3 months between the patient's first breast-related problem that prompted seeking of medical care and the BC diagnosis.¹² In that study, delayed BC diagnosis was associated with younger age, minority race and self-identification of BC symptoms compared with identification via an abnormal

mammogram, whereas women living with two or more household members had lower odds of a delay in BC diagnosis. In our study, factors influencing PDT, SDT and TDT were investigated separately; however, in many countries, PDT significantly impacted TDT.

Nationwide screening mammography programmes allow detection of early, non-palpable BC. The proportion of patients with self-diagnosed symptoms of cancer may therefore be inversely related to the prevalence and availability of mammography screening. In our study, India, Romania and Serbia apparently did not have such programmes available, and a small percentage of respondents reporting otherwise may be ascribed to misunderstanding the question. Of note, in our study, India and Romania had the longest SDT and TDT.

In our study, the mean PDT for all countries was 4.7 weeks (3.4–6.2 weeks). In a study from Malaysia, the median times to consultation (corresponding respectively to PDT and TDT in our study) were 2 and 5.5 months, respectively.¹³

In previous studies, the negative attitude toward BC treatment was associated with delayed diagnosis,¹² and increased levels of fear with seeking cancer care earlier.¹⁴ Multivariate regression of the current analysis indicated that distrust and disregard were the most universal predictors of a longer PDT, whereas practicing breast self-examination was associated with a shorter PDT. However, the impact of distrust in the healthcare system and disregard of BC signs on PDT was weak. Systematic approach and susceptibility to the influence of authority may affect greater confidence in the healthcare system, therefore causing fewer attempts to speed up the procedure. Similarly, it cannot be excluded that a family that calms the patient can reduce the level of determination. This result may be the subject of further studies. Breast self-examination has been shown to be ineffective as a screening tool.^{15,16} However, this habit may be considered a surrogate of increased BC awareness and thus might have positively impacted PDT in our study. Partridge *et al.*¹⁷ indicated that older age is not an independent predictor of PDT and is modestly associated with a more advanced stage of disease at diagnosis.

The mean SDT in our study was 11.1 weeks and accounted for a substantial part of the TDT. Delayed BC diagnosis and start of treatment is influenced by patterns of healthcare utilization and the effectiveness of primary care services. In the study by Carter and Reilly,¹⁸ early-stage BC patients were three times more likely to have received a clinical breast examination compared with their locally advanced BC counterparts. Physician-related delay in the diagnosis of BC is a common occurrence, and

patients with normal mammograms are more likely to have longer delay.¹⁹ In our study, the first examination being performed by an oncologist, as compared with another MD, and being diagnosed in a private, compared with public, unit were associated with shorter SDT.

We are aware of some limitations of this study. First, our analysis was based exclusively on the data collected from patient questionnaires, which were not verified with the patient medical records. Thus, some information might have been imprecise. Second, the survey was conducted by a trained medical personnel, thus the anonymity of the answers was not maintained. In consequence, the data provided might have been biased, for example due to a shame on disclosure of all information, and this might have differed in various cultural environments of particular countries. We were also unable to verify the level of understanding of particular questions and potential respective differences in particular countries.

In conclusion, the delay in medical advice and diagnosis of BC remains a serious problem. Several factors, mainly related to psychological and behavioural patient attributes, appear to correlate with delay in diagnosis and treatment of BC, but their impact differs between particular countries. Other variables, for example related to the differences in national healthcare systems (not addressed in detail in this study), might also have a considerable impact on the time to the initiation of BC therapy. Breast health awareness and education may positively impact early detection, diagnosis and treatment. The knowledge of these issues may allow identifying groups of women with an increased risk of a delay and building programmes that promote timely access to care. Clearly, additional research considering specific socioeconomic and cultural settings of particular populations may further elucidate this question.

Supplementary data

Supplementary data are available at *EURPUB* online.

Acknowledgements

The authors thank Proper Medical Writing (Infrared Group s.c.) for the language assistance provided in the preparation of this article.

Funding

This study was supported by a grant from Roche Poland.

Conflicts of interest: None declared.

Key points

- Psychological and behavioural patient attributes strongly contribute to delays in BC diagnosis and treatment.

- The impact of these factors is significantly different in particular countries.
- Identifying groups of women with an increased risk of delay may allow designing preventive strategies.

References

- 1 Ferlay J, Shin HR, Bray F, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010;127:2893–17.
- 2 Shyyan R, Masood S, Badwe RA, et al., for the Global Summit Diagnosis and Pathology Panel. Breast cancer in limited-resource countries: diagnosis and pathology. *Breast J* 2006;12(Suppl. 1):S27–37.
- 3 Ozmen V. Breast cancer in Turkey and in the world. *J Breast Health* 2008;4:6–12.
- 4 Smith EC, Ziogas A, Anton-Culver H. Delay in surgical treatment and survival after breast cancer diagnosis in young women by race. *JAMA Surg* 2013;24:1–8.
- 5 Hansen RP, Vedsted P, Sokolowski I, et al. General practitioner characteristics and delay in cancer diagnosis. A population-based cohort study. *BMC Fam Pract* 2011; 12:100.
- 6 Burgess C, Hunter MS, Ramirez AJ. A qualitative study of delay among women reporting symptoms of breast cancer. *Br J Gen Pract* 2001;51:967–71.
- 7 Caplan LS, Helzlsouer KJ. Delay in breast cancer: a review of the literature. *Public Health Rev* 1993;20:187–214.
- 8 Richards MA, Smith P, Ramirez AJ, et al. The influence on survival of delay in the presentation and treatment of symptomatic breast cancer. *Br J Cancer* 1999;79: 858–64.
- 9 Abbot ML, McKinney J. *Understanding and Applying Research Design*. Canada: Willey and Sons, Inc, 2013: 74–7.
- 10 Hansen RP, Vedsted P, Sokolowski I, et al. Time intervals from first symptom to treatment of cancer: a cohort study of 2212 newly diagnosed cancer patients. *BMC Health Serv Res* 2011;11:284.
- 11 Chintamani, Tuteja A, Khandelwal R, et al. Patient and provider delays in breast cancer patients attending a tertiary care centre: a prospective study. *JRSM Short Rep* 2011;2:76.
- 12 Stuver SO, Zhu J, Simchowitz B, et al. Identifying women at risk of delayed breast cancer diagnosis. *Jt Comm J Qual Patient Saf* 2011;37:568–75.
- 13 Norsa'adah B, Rampal KG, Rahmah MA, et al. Diagnosis delay of breast cancer and its associated factors in Malaysian women. *BMC Cancer* 2011;11:141.
- 14 Dubayova T, van Dijk JP, Nagyova I, et al. The impact of the intensity of fear on patient's delay regarding health care seeking behavior: a systematic review. *Int J Public Health* 2010;55:459–68.
- 15 Thomas DB, Gao DL, Ray RM, et al. Randomized trial of breast self-examination in Shanghai: final results. *J Natl Cancer Inst* 2002;94:1445–57.
- 16 Semiglazov VF, Manikhas AG, Moiseenko VM, et al. Results of a prospective randomized investigation [Russia (St.Petersburg)/WHO] to evaluate the significance of self-examination for the early detection of breast cancer. *Vopr Onkol* 2003; 49:434–41.
- 17 Partridge AH, Hughes ME, Ottesen RA, et al. The effect of age on delay in diagnosis and stage of breast cancer. *Oncologist* 2012;17:775–82.
- 18 Carter TI, Reilly JJ. Missed opportunities: clinical antecedents in the diagnosis of advanced breast cancer. *Ann Surg Oncol* 2012;19:2782–5.
- 19 Tartter PI, Pace D, Frost M, Bernstein JL. Delay in diagnosis of breast cancer. *Ann Surg* 1999;229:91–6.