

## Family ties: young breast cancer patients and their children

Uwe Güth<sup>a,b</sup>, Dorothy Jane Huang<sup>b</sup>, Judith Alder<sup>c</sup>, Rebecca Moffat<sup>d,e</sup>

<sup>a</sup> Cantonal Hospital Winterthur, Department of Gynaecology and Obstetrics, Breast Centre “Senosuisse”, Winterthur

<sup>b</sup> University Hospital Basel (UHB), Women’s Hospital, Division for Gynaecology and Gynaecological Oncology, Basel

<sup>c</sup> University of Basel, Department of Psychology, Basel

<sup>d</sup> UHB, Women’s Hospital, Clinic for Gynaecological Endocrinology and Reproductive Medicine, Basel

<sup>e</sup> Fertsuisse, Centre for Reproductive Medicine, Olten

### Summary

**BACKGROUND:** This study assessed the interaction of “family ties” in a cohort of young breast cancer patients.

**METHODS:** Based on the Basel Breast Cancer Database, we analysed an unselected, consecutive cohort of patients who were  $\leq 40$  years at breast cancer diagnosis ( $n = 100$ ).

**RESULTS:** Sixty patients had children at the time of diagnosis (mean number of children: 1.03). Only four patients had desired children after BC therapy. The average age of the children at breast cancer diagnosis of their mother was 7.7 years. The mean age of the children whose mothers died of breast cancer at the time of their mother’s death was 13.1 years; these children ( $n = 37$ ) lived an average of 84.7 months with the illness of their mother.

Parity status was not a significant factor for compliance/persistence to adjuvant chemotherapy ( $p = 1.00$ ). Patients who had children were more likely to be compliant/persistent to endocrine therapy ( $p = 0.021$ ). Out of these patients, 41.2% rejected or discontinued endocrine therapy with the explicit intention to get pregnant.

**CONCLUSIONS:** Desire for children was an important factor in refusing endocrine therapy. This clearly highlights the enormous pressure that many young women face in this situation.

About a third of the children whose mothers were diagnosed with breast cancer experienced the palliative situation and the death of their mother. Since many of these children are confronted with a cancerous disease of their mothers during half of their childhood, special attention should be paid to age-appropriate support of a child in all phases of the mother’s disease.

**Key words:** breast cancer; parental cancer; parity; children; compliance; persistence

### Introduction

Children play an important role in the life of many young women. With regard to oncological diseases, there are two

general conditions which often pertain to young breast cancer (breast cancer) patients:

1. The trend in the Western world toward postponing child bearing to the late reproductive years [1], means that the number of childless women or those who have not completed childbearing at the time of breast cancer diagnosis will continue to increase. Breast cancer treatment will render many of the affected women infertile. Particularly women without children are distressed about their impaired family planning perspectives [2]. Therefore, fertility after breast cancer treatment and preservation of fertility at diagnosis are issues that are currently receiving significant attention [3, 4].
2. This increasing awareness regarding fertility preservation of young breast cancer patients eclipses the fact that many breast cancer patients already have children at the time of diagnosis. It cannot be sufficiently emphasised that breast cancer diagnosis not only severely affects a woman’s life, but also challenges the entire family system including the patient’s children.

In recent years, it has been increasingly recognised that psycho-oncological support should be available for the family and the children, especially since about a third of the children will develop relevant emotional or behavioural symptoms [5–7].

To our knowledge, this study is the first to provide an assessment of the interaction of “family ties” by analysing an unselected, consecutive cohort of young breast cancer patients and addressing the following issues:

- Parity status: How many patients had children at the time of breast cancer diagnosis?
- How many patients gave birth to children after breast cancer?
- How old were the patients’ children at the time of breast cancer diagnosis of their mother?
- For those women who died of breast cancer: how old were their children at time of death and how long did they live with the illness of their mother?

- We analysed whether having children influenced the patient's compliance and persistence to surgery and adjuvant breast cancer therapies.

## Patients and methods

This study is based on the data of the prospective relational Basel Breast Cancer Database (BBCD), which includes all newly diagnosed primary invasive breast cancer cases treated at the University Women's Hospital Basel, Switzerland since 1990. We analysed all patients who were diagnosed with invasive breast cancer between 1990 and 2007 and who were 40 years or younger at diagnosis ( $n = 100$ , 7.7% of all breast cancer patients in the above mentioned period). At the time of data analysis in 2013, we had complete data regarding breast cancer therapy and outcome in 97 of these patients.

### Compliance and persistence with surgery and adjuvant therapies ( $n = 98$ )

For this analysis, we excluded the two patients who already had distant metastatic disease at initial diagnosis. The treatment recommendations for all patients were based on the decision of the interdisciplinary tumour board of the University Hospital Basel. We had complete information regarding type of surgery for the entire cohort ( $n = 98$ ) and complete information regarding receipt of adjuvant chemotherapy, endocrine therapy and/or radiation for 95 patients. In this study, we defined "compliance" as the readiness to accept a proposed adjuvant treatment or drug regimen; in our particular case, to accept A) radiation, B) chemotherapy, and C) endocrine therapy. When the patients started the treatment, we used the term "persistence" for the further application of therapy or intake of the drug regimen. The reasons for modifying or discontinuing the medication were precisely recorded. According to previous studies on compliance and persistence with adjuvant endocrine therapy, we also interpreted nonpersistence with therapy not simply as the act of stopping medication, but rather as the manifestation of an intentional behaviour of the patient [8–11]. According to this principle, patients who had to

**Table 1:** Age, disease stage and outcome characteristics of young breast cancer patients ( $n = 100$ ).

Age at breast cancer diagnosis	Mean age (range)	35.9 (26–40)
	Age group: 26–30 years	10
	Age group: 31–35 years	29
	Age group: 36–40 years	61
TNM Stage*	Stage I	36
	Stage II	45
	Stage III	17
	Stage IV	2
Outcome	Alive, no evidence of breast cancer	64
	Alive with metastatic breast cancer	1
	Died of breast cancer	30
	Died of other disease	2
	Follow-up <3 months	3

\* Classification according to the AJCC/UICC TNM Classification, 7th edition.  
For 13 patients, who were treated with neoadjuvant therapy, the tumour stage after surgery (ypTNM) was considered.

stop therapy because of systemic breast cancer recurrence, i.e. for whom discontinuation of therapy was not a choice but was mandatory, were not defined as nonpersistent. During the period of observation, the recommendations for treatment concerning adjuvant endocrine therapy in young breast cancer patients changed. In the early 1990s, endocrine therapy had been comparatively rarely recommended. This changed during the mid-nineties. In order to have a homogenous cohort with regard to endocrine therapy, we restricted our analysis of compliance/persistence with endocrine therapy to those patients who were diagnosed since 1995.

### Statistical analysis

Data was analysed descriptively. To investigate age differences in women giving and those not giving birth after initial breast cancer treatment, Student's t-Test was used. To assess whether the fact that young breast cancer patients have children at the time of breast cancer diagnosis had an impact on compliance/persistence to therapy, we used the Fisher's exact test. In all statistical tests the level of significance was  $p < 0.05$ .

### Ethics approval

Data collection methods and study design were approved by the local Ethics Review Board.

**Table 2:** Parity and reproductive outcome of young breast cancer patients ( $n = 100$ ).

Parity at diagnosis	P0 (nullipara, woman has never given birth)	40
	P1 (woman who has delivered one viable infant)	29
	P2 (woman who has delivered two viable infants)	22
	P3 (woman who has delivered three viable infants)	6
	P4 (woman who has delivered four viable infants)	3
	Number of born children/children delivered	103
	Mean number of children	1.03
	Mean number of children in patients with children	1.7
	Mean maternal age at birth of first child (range)	27.9 (17–37)
No. of pregnancy-associated breast cancer*		6
Patients giving birth to a child after diagnosis of breast cancer (%)†		5 (5.2)
	P1	4
	P3	1
	Average age at diagnosis of breast cancer (range)	33 (30–39)
	Average maternal age at birth of child (range)	38.6 (36–43)
	Duration in months between breast cancer diagnosis and birth of child (range)	66.8 (14–117)
	Pregnancy after chemotherapy	3
	* Definition: Breast cancer diagnosed during pregnancy or within one year after giving birth. † Not considered: patients lost to follow-up after <3 months ( $n = 3$ ).	

## Results

The data on patients' age at diagnosis (mean: 35.9 years), disease stage and outcome are summarised in table 1. In this particular subgroup of young breast cancer patients ( $\leq 40$  years), 61% were 36 years or older at diagnosis.

### Patients and their children at the time of diagnosis (parity status)

Sixty percent of our cohort had children at the time of diagnosis (range: 1–4; table 2). The mean number of children was 1.03 per woman. The mean maternal age at birth of the first child was 27.9 years (range: 17–37 years).

### Patients who gave birth to children after breast cancer diagnosis and therapy

Five women gave birth to a child after breast cancer diagnosis and therapy (table 2). In four cases, the pregnancies were desired. These four women were childless at the time of breast cancer diagnosis. One pregnancy occurred after assisted reproduction (oocyte donation) and three women became pregnant spontaneously. Two patients had received adjuvant chemotherapy. In two cases, ongoing endocrine therapy was discontinued with the intention of getting pregnant (nonpersistence). One patient opted against endocrine therapy for this reason (noncompliance). The fourth

patient had no endocrine therapy because she had hormone receptor (HR)-negative disease. The patients who gave birth to a desired child were significantly younger at the time of breast cancer diagnosis than the other 96 patients of the cohort (31.5 years vs 36.0 years,  $p = 0.021$ ). The time between breast cancer diagnosis and birth was 32 months, 38 months, 77 months and 117 months, respectively. At the time of data analysis, all four women were alive with no evidence of disease.

In one case, the pregnancy was unintended and was diagnosed shortly after completion of oncological therapy (neoadjuvant chemotherapy, surgery, radiotherapy). At the time of breast cancer diagnosis, the patient was 39 years of age and already had two children. Ten months after she delivered her third child, distant metastases were diagnosed. Eight months later, she died of metastatic breast cancer.

### The impact of children (parity status) on compliance and persistence with adjuvant breast cancer therapy

Compliance and persistence with breast cancer therapy in the adjuvant situation are summarised in table 3.

#### Primary Surgery

Compliance with surgery was high. All patients ( $n = 98$ ) underwent surgery. Only two patients refused the recommended axillary lymph node dissection.

#### Adjuvant radiotherapy

Out of the 69 patients to whom radiotherapy was suggested, only three (4.3%) refused the recommended therapy and never began the treatment. Once radiation was initiated, all patients completed the therapy.

Owing to the low number of patients who did not follow the recommendations for primary surgery ( $n = 2$ ) and adjuvant radiation ( $n = 3$ ), we omitted an analysis regarding the impact of parity status on noncompliance with these therapies.

#### Adjuvant chemotherapy

Out of the 63 patients for whom chemotherapy was proposed, five (7.9%) did not follow this recommendation (noncompliance). Out of the 58 patients who started chemotherapy, in three cases (5.2%) the patients choose to stop the therapy prematurely (nonpersistence). Whether the patients had children or not was not a significant factor for compliance and persistence with chemotherapy ( $p = 1.00$ ). The main reasons for noncompliance and nonpersistence to therapy given by the patients are listed in table 4.

#### Adjuvant endocrine therapy

Out of the 43 patients to whom endocrine therapy was recommended, nine women (20.9%) refused this therapy, in spite of extensive counselling, and never began this treatment. Out of the 34 patients who initiated endocrine therapy, 21 (61.8%) fully completed the targeted therapy. Five patients (14.7%) ceased therapy as a result of breast cancer recurrence. Eight patients (23.5%) independently chose to end the endocrine therapy prematurely (nonpersistence). The main reasons for noncompliance and nonpersistence with therapy given by the patients are listed in table 4.

Patients who had children were more likely to be compliant and persistent with endocrine therapy ( $p = 0.021$ ). Out of

**Table 3:** Compliance and persistence with breast cancer therapy in the adjuvant situation.

		n (%)
Surgery, n = 98	Breast conserving therapy	63 (64.3)
	Mastectomy	35 (35.7)
	Surgical axillary staging (SLND or ALND)	97 (98.9)
	Noncompliance with recommended ALND	2 (2.0)
Adjuvant radiotherapy, n = 95	Therapy not indicated / not recommended	26
	Therapy recommended	69 (100)
	– Noncompliance	3 (4.3)
	Therapy started and completed	66 (95.7)
Adjuvant chemotherapy, n = 95	Therapy not indicated / not recommended	32
	Therapy recommended	63 (100)
	– Noncompliance	5 (7.9)
	Therapy started	58 (100)
	– Therapy completed	55 (94.8)
	– Nonpersistence	3 (5.2)
Adjuvant endocrine therapy (1995–2009), n = 66	Therapy not indicated (negative HR status)	20
	Therapy indicated (positive HR status)	46
	– Therapy not recommended	3
	Therapy recommended	43 (100)
	– Noncompliance	9 (20.9)
	Number of patients for persistence analysis	34 (100)
	Persistence	26 (76.5)
	– Therapy fully completed	21 (61.8)
	– Therapy discontinued owing to breast cancer recurrence	5 (14.7)
	Nonpersistence	8 (23.5)

ALND = axillary lymph node dissection; HR = hormone receptor; SLND = sentinel lymph node dissection

the 17 patients who were noncompliant or nonpersistent with endocrine therapy, seven patients (41.2%) rejected or discontinued the therapy with the explicit intention to get pregnant in the near future (table 4).

### The children of young breast cancer patients

The 60 patients with children at the time of breast cancer diagnosis had a total of 100 children (mean number: 1.7). The discrepancy between the total number of children in the parity analysis (n = 103) and the number of children analysed here (n = 100) is due to the fact that for three patients one child died before breast cancer diagnosis (and thus did not experience their mothers' disease).

The mean age of the children at the time of breast cancer diagnosis of their mothers was 7.7 years (range: 1 week to 18 years). Table 5 summarises the age distribution with regard to five childhood periods: baby/toddler: 21%, kindergarten age: 19%, primary school age: 35%, early teenage age: 19%, advanced teenage age: 6%.

Thirty patients died from metastatic breast cancer. Of these, 23 (76.7%) had a total of 37 children. At the time of death of their mother, these children had an average age of 13.1 years (range: 18 months to 26 years). When one analyses the total survival time of their mothers, these children lived approximately 7 years (average duration: 84.7 months, range: 21–209 months) with the illness of their mothers. When one analyses the time between diagnosis of distant metastatic disease and death (metastatic disease-survival), these children were confronted with on average 32.1 months (range 1–87 months) of the palliative situation.

## Discussion

### Parity status

In our study cohort, 60% of the young women who were diagnosed with breast cancer had children at the time of breast cancer diagnosis. The average number of children (1.03) was a little lower than in the general Swiss population (1.46) [12]. Of those patients who were childless, approximately 10% fulfilled their wish to have children after breast cancer diagnosis.

In accordance with other cohorts of young breast cancer patients analysed in the literature, the mean age of our cohort was, at least from the perspective of reproductive medicine, comparatively high [13–15]; 61% of the patients were  $\geq 36$  years old. The impact of age on fertility must be kept in mind because, even using modern assisted reproductive technologies, the live birth rate sharply declines with increasing maternal age; it drops from 32% at age 36 to 19% at age 40 and to 3% at age 44 [16].

Recently, we analysed how many young breast cancer patients are actually potential candidates for fertility preservation. Our assessment used an algorithm that considered not only the administration of potentially gonadotoxic chemotherapy but also “family ties”-factors such as family structure (number and age of children) and information indicating completed family planning (e.g. history of hysterectomy, tubal ligation or vasectomy of the partner) and found that approximately 25%–30% of young breast cancer

patients were actually true candidates for fertility preservation [17].

### The children of young breast cancer patients

The heterogeneity of the children's age distribution was considerable and points to the challenges a parental cancer diagnosis imposes on the family system. Being an affected mother of a toddler makes different demands from being the mother of a school aged child or adolescent regarding the importance of age-specific communication about the situation and the support for helping the child to cope with the situation. Yet several factors have been identified which mediate the coping response of the child, including the psy-

**Table 4:** Reasons for noncompliance and nonpersistence on adjuvant chemotherapy and endocrine therapy.

Adjuvant	Noncompliance	
chemotherapy recommended, n = 63	Reasons: – Lack of belief in the necessity or the benefit of the therapy / resistance against therapy / fear of therapy-related side effects.	3
	– Desire to get pregnant	2
	Therapy started	58
	Nonpersistence	3
	Reason: – Therapy-related side effects	3
	Adjuvant endocrine recommended, n = 43	Noncompliance
Reasons: – Lack of belief in the necessity or the benefit of the therapy / resistance against therapy.	7	
– Desire to get pregnant	2	
Therapy started	34	
Non-persistence	8	
Reasons: – Lack of belief in the necessity or the benefit of the therapy / resistance against therapy.	2	
– Desire to get pregnant / weight gain / menopausal symptoms.	1	
– Desire to get pregnant / menopausal symptoms.	2	
– Desire to get pregnant.	2	
– Menopausal symptoms.	1	

**Table 5:** The children of young breast cancer patients (n = 100).

Children's average age at diagnosis of their mothers' disease (range)	7.7 years (1 week–18 years)
– 0–3 years (baby, toddler)	21
– 4–6 years (kindergarten age)	19
– 7–10 years (primary school age)	35
– 11–15 years (young teenage age)	19
– 16–18 years (advanced teenage age)	6
Number of children whose mothers died of breast cancer (n = 23 patients)	37
Children's average age at the time of their mothers' death (range)	13.1 years (18 months–26 years)
– 0–6 years (%)	8 (21.6)
– 7–12 years (%)	8 (21.6)
– 13–17 years (%)	11 (29.7)
– $\geq 18$ years (%)	10 (27.0)

chological stability of the parents and level of family functioning [18–20]. Therefore, there is not only a need to offer age-appropriate support to children confronted with parental cancer; interventions should also focus on the improvement of parental and familial coping.

In addition, the data of the present study shows that 37% of the children, after an average period of 4 years after diagnosis, experience the illness of their mother progressing to an incurable disease and leading to their loss after a further 3 years. In total, these children are confronted for a median of 7 years with their mother's cancerous disease. This long period of time, which spans half of their childhood, clearly demonstrates that psycho-oncological support must change and adapt to the children's actual phase of development and personality. To exemplify this, an 8-year-old child who experiences its mother's first breast cancer diagnosis with surgery and adjuvant chemotherapy has completely different needs for coping with the situation compared with 7 years later, as a 15-year-old adolescent who is confronted with his/her mother dying from the disease. This palliative period is particularly sensitive for the entire family. The experience of physical deterioration of the mother, the ups and downs of palliative cancer treatment and preparation for end of life very often temporarily destabilises family systems.

#### **Impact of children on compliance and persistence with oncological therapy**

Children may affect the motivation for therapy in young breast cancer patients in two ways. On the one side, one could hypothesise that the fact that for young patients, having a child might have a positive impact on compliance with oncological therapies because these women feel a high level of responsibility towards their usually young children, and want to do everything possible to gain victory over cancer. If the disease progresses in spite of therapy, these women might be comforted by the fact that they had done everything possible to ensure that their children had a mother.

With regard to chemotherapy, approximately 13% of the patients refused the recommended therapy or did not complete it. Parity did not influence compliance and persistence with adjuvant chemotherapy. In contrast, parity did have a significant impact on compliance and persistence with endocrine therapy. Nevertheless, we do not interpret this as meaning that women with children are more motivated to accept and complete therapy. As mentioned above, children might affect the motivation for therapy in two ways. In our cohort, present children were not the deciding factor for choosing therapy, but rather the unborn children were the reason for declining therapy [21]. At more than 40%, a considerable number of the patients who refused or discontinued endocrine therapy did so with the explicit wish still to have children. These patients were fully aware of the impact of their decision on the outcome of a potentially life-threatening disease. This clearly highlights the enormous pressure that many young women face in this situation. From the four patients in our cohort who chose to have children after breast cancer therapy, three women discontinued ongoing endocrine therapy prematurely with the explicit intention to get pregnant. A further four patients

stopped therapy for the same reason, but have not yet become pregnant. Several studies demonstrated that noncompliance and nonpersistence were highest in young breast cancer patients [10, 22–24]. It was assumed that these women might not have adjusted to the diagnosis of breast cancer as well as older women and, therefore, were also less willing to accept or more likely to experience therapy-related side effects [25, 26]. The wish to have children, or at least to maintain fertility, seems to be an additional factor that influences the decision not to accept a recommended oncological therapy or to discontinue therapy prematurely. In recent years, the topic area of adherence/persistence to adjuvant endocrine therapy has increasingly become a focus of interest (overview in: [27]). However, most data available regarding persistence with adjuvant endocrine therapy are from studies including older breast cancer patients. A few observational studies also included younger patients, but this subgroup comprised a clear minority of the cohorts analysed [22, 23, 28, 29]. Studies focusing on women under 40 years of age are rare. Two studies aimed to examine persistence with adjuvant tamoxifen therapy using data from the French National Health Insurance System database [13, 14]. The authors reported a nonpersistence rate of 39.5% after 3 years [14]. Treatment interruptions were associated with a lack of understandable information about endocrine therapy, treatment side effects, loss of fear of cancer relapse and insufficient social support [13]. In contrast to our study, the authors found no association between nonpersistence and being childless [13, 14]. This might partly be explained by:

- a) A different study approach. The French study used pharmacy refill data. This might be a promising strategy to identify nonpersistence to therapy. However, patients who initially refused therapy and thus rejected any prescriptions are underrepresented in this system. Accordingly, the French study reports a noncompliance rate of 7% which is significantly lower than the 21% noncompliance rate in our cohort.
- b) Differences in the parity status. Although the median ages of the French cohort and our study cohort were comparable (36 vs 37 years), a considerably higher proportion of the French cohort had children at the time of breast cancer diagnosis (Huiart: 82.5% [14]; Basel cohort: 60%). These data mirror the fact that French women are on average 2 years younger than Swiss women at birth of their first child [12, 30]. Presumably, a larger proportion of patients in the French cohort had already completed child bearing at breast cancer diagnosis and thus were less prone to refuse or discontinue therapy for the sake of pregnancy.

#### **Conclusions**

Desire for children was an important factor in not accepting adjuvant endocrine therapy. These patients were fully aware of the impact of their decision on the outcome of a potentially life-threatening disease. This clearly highlights the enormous pressure that many young women face in this situation. Few women fulfil their wish to have children after receiving the diagnosis of breast cancer. About a third of the children whose mothers were diagnosed with breast cancer not only experienced the adjuvant therapy, but also

the palliative situation and the death of their mother. Since many children are confronted with a cancerous disease of their mothers during half of their childhood, special attention should be paid to age-appropriate support of a child in all phases of its mother's disease.

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**Correspondence:** Professor Uwe Güth, MD, Cantonal Hospital Winterthur, Department of Gynecology and Obstetrics, Breast Center "Senosuisse", Brauerstrasse 15, CH-8401 Winterthur, Switzerland, [uwe.gueth\[at\]junibas.ch](mailto:uwe.gueth[at]junibas.ch)

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