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Care pathway of women with interval breast cancer in 2016, based on medico-administrative data

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INTRODUCTION

Breast cancer is the top-ranking cancer in women in terms of incidence and mortality worldwide [1]. In Mainland France, its incidence has been on the rise since 2010, reaching 58,500 new cases in 2018 (33,800 between 50 and 74 years) [2].

An organised screening programme (OSP, clinical examination and mammogram every two years) was set up throughout the country in 2004. In line with European guidelines [3], it is aimed at women aged from 50 to 74 years at an "average risk" of developing breast cancer, i.e. non-symptomatic and having no risk factors other than age. The rate of cancers detected was 7.5 ‰ of women taking part in the screening programme, representing 38,905 cases of invasive cancer and ductal carcinoma in situ detected in 2015-2016 [4]. Despite performance indicators demonstrating the quality of the programme [5], uptake among the French population remains below the proposed thresholds (70%) [6] with an uptake rate of merely 49.9% in 2017 [4], with a downward trend in this rate since 2015 - 2016.

Some cancers are diagnosed before the date of the next scheduled OS mammogram. These so-called "interval" cancers (IC) [6] are observed in all OSP, but they remain inadequately described in the international literature. They consist either of true negatives (not present at the time of the OS mammogram, developed subsequently), or false negatives (present at the time of the OS mammogram but not detected) due to a reading or technical error. The images obtained at the time of diagnosis are compared to the images from the prior screening in order to distinguish the 2 types of IC [7]. Out of 100 cases of IC, 50 to 60 cancers would be true negatives[8], [9], 15 to 20 cancers would be false negatives due to a technical error (positioning error, poor image quality or cancer outside standard film) [8], [9] and 25 to 35 cancers would be false negatives due to a reading error [8]. Cancers diagnosed during follow-up of a potentially benign lesion known as "ACR3" in the OSP mammogram (as per the BIRADS classification [10]), or of other types of benign lesions (atypical hyperplasia, etc.), are not considered as IC.

Of all the participants in the OSP, the estimated IC rate at 24 months in France (0.71‰-1.6‰) is consistent with the international literature - 1.1‰-1.8‰) [11]–[18]. A study conducted in 11 French departments over the 2004-2010 period estimated that 17% of all breast cancers detected after carrying out an OSP mammogram were ICs [19]. This rate was 17.2% in another study on 5 French departments from 2002 to 2005 [18].

One-third of cases of IC are diagnosed in the first year following the OSP mammogram [13]. Conventionally, cases of IC are symptomatic, although they may be detected at a subclinical stage, which is enabled by free access in France to mammography outside the OSP. Cases of IC would

appear to be more aggressive at the time of diagnosis and have a poorer prognosis than cancers screened through the OSP [18, 20–23] with a greater proportion of lymph node and metastatic involvement. The studies disagree as to the impact on survival [23–29].

The European guidelines are to monitor IC frequency in order to steer the quality of the OS programme and improve radiologist training.

In a previous study [30] we showed that women whose cancer was diagnosed following a mammogram performed in the context of the OSP had less advanced cancer and less aggressive treatments. However, the study did not distinguish IC which could affect the differences between these two groups. We therefore designed the present study to address that limit. Thus, after classifying cases of breast cancer according to diagnosis modalities using an algorithm based on French medico-administrative data, the study described the care pathways of women whose breast cancer was an IC (whatever the reason was), and compared them to those of women whose cancer was diagnosed through the OSP or outside the OSP (personalised screening or screening based on clinical signs).

MATERIALS AND METHODS

Data source and data

The study was conducted using data from the French administrative healthcare database (SNDS), medico-administrative data covering the entire French population [31]. It contains information from public and private healthcare facilities (PMSI), non-hospital care consumption, and death certificates in France.

The care consumption over the 2014-2017 period of the women included was retrieved, on one hand, to obtain all breast imaging tests (mammograms, ultrasound, MRI and CT scans of the breast) carried out in the 24 months prior to diagnosis, and, on the other, chart their care pathways (breast conservative surgery (BCS) or mastectomy, chemotherapy, radiotherapy) over the 12 months following the first anticancer treatment.

Study population selection

Cases of breast cancer in 2016 were identified based on medical, surgical, obstetric (MCO) hospital admissions mentioning an ICD-10 code of "malignant neoplasm of breast" (C50) or "carcinoma in situ of breast" (D05) as the primary (DP), associated (DAS) or connected (DR) diagnosis, and long-term disease scheme (LTD) for breast in 2016 (Supplementary Table S1). The following subjects were excluded (figure 1): (1) subjects with a breast cancer code or previous history of breast cancer

between 2005 and 2015 in order to select incident cases of breast cancer or (2) another cancer between 2005 and 2017 in order to be sure that treatment (chemotherapy, radiotherapy) is for breast cancer, (3) subjects having had no anticancer treatment in the 12 months post-diagnosis in order to select women with treated cancers, and (4) subjects having had no breast imaging in the 24 months prior to diagnosis. Women with a liver, bone, lung or brain cancer in 2016-2017 were retained, as these could have been metastases of liver, bone, lung or brain cancer miscoded as primary tumours. In fine we selected 28,159 women aged 50 to 74 years at the time of diagnosis, the age targeted by the organised screening program.

Date and stage of diagnosis

Because the date of breast cancer diagnosis was not available in the SNDS, this was defined as (1) the date of the latest breast biopsy or breast aspiration carried out in the 6 months prior to the first cancer treatment (surgery, chemotherapy, radiotherapy, hormone therapy or palliative cares), (2) otherwise if no biopsy and aspiration as the date of the latest breast imaging carried out in the 6 months prior to the first cancer treatment, (3) otherwise if no imaging, it was attributed using the mean interval observed between the latest biopsy and the first cancer treatment among women having had a biopsy. When a lymph node involvement code appeared within 6 months following the date of diagnosis, the cancers were automatically considered as invasive with lymph node involvement (N+), otherwise they were considered as N-. A similar approach was applied for the metastatic stage: M+ in the presence of at least one metastatic code (Supplementary Table S2) within 6 months post-diagnosis, otherwise M- ([31]).

Identification of diagnosis process group

As the SNDS does not provide any imaging results or the diagnosis method, an IC identification algorithm was developed to distinguish between three diagnosis process groups: OSP group, IC group and PSCS group (personalised screening or screening based on clinical signs).

The combination of a CCAM code QEQK004 (bilateral screening mammogram) and an OSP-specific "prevention" exemption code, was used to differentiate OSP mammograms. Cancers treated within 3 months following the OSP mammogram were automatically classified as OSP cancers.

After this interval, in order to differentiate between OSP and IC and account for BIRADS guidelines for ACR3 lesion follow-up [10], [32], an algorithm was created based on imaging tests (mammograms, ultrasound, CT and MRI scans) conducted between the latest OSP mammogram and the breast cancer diagnosis. These tests were grouped into 60-day sequences, the OSP mammogram marking the start of the first sequence. The last two test sequences were considered as a single sequence when they

were at an interval of less than 30 days. Women with a single sequence were also classified as OSP cancers.

In the absence of information on the presence of an ACR3 lesion, subjects with a series of diagnosis procedures as per BIRADS guidelines were classified as OSP. These were cancers diagnosed following a second sequence of tests conducted 5 to 7 months after the OSP mammogram, optionally followed by a third sequence of tests conducted at 11 to 13 months, optionally followed by a fourth sequence conducted at 22 to 24 months.

For women who had two sequences in the first 4 months, there were two distinct profiles. Schematically, the first consists of women having undergone a first sequence of not more than 60 days followed by a second sequence within 60 days following the end of the first sequence. The second consists of women having undergone a very short first sequence (conventionally a single mammogram or a mammogram combined with an ultrasound scan on the same day), followed by a second sequence between 60 and 120 days. In view of the positioning of the sequences over time (Supplementary Fig. S3), and despite not following the guidelines, the first group was considered as a matter of principle as cancers identified within the framework of the OSP programme, and the second as IC.

Women having had no OSP mammogram in the 24 months prior to diagnosis were classified in the PSCS group.

Statistical analyses

The data were processed on the SNDS portal using SAS Guide software. WPS software, particularly reading the computer languages SAS, SQL and R, was used to create visual representations of care pathways (R version 3.4.2). As this was a population study including all women from France according to the inclusion criteria, statistical tests lack legitimacy and differences were considered according to their clinical significance.

Data protection regulation

This study falls within the scope of the Commission nationale de l'informatique et des libertés (CNIL) (French data protection authority) authorisation decree dated 26 December 2016 No. 2016-1871

RESULTS

Study population

Among the 160,869 subjects with at least one breast cancer diagnosis code in 2016, 28,159 women made up the study population (figure 1) including 11,761 women who had not had an OSP mammogram in the 24 months prior to diagnosis (PSCS group) and 16,398 women who had at least one OSP mammogram in the 24 months prior to diagnosis.

The OSP, IC and PSCS groups represented 46.0%, 12.2% and 41.8% of women, respectively.

Among the 16,398 women having had at least one OSP mammogram, 12,965 women (79.1%) were classified in the OSP group and 3,433 women (20.9%) in the IC group. This IC percentage varied slightly with age (table 1). Among the women with 2 sequences and an interval of 2 to 4 months between the OSP mammogram and the start of the second sequence, 409 were classified as OSP and 733 as IC.

Diagnosis groups

In the case of OSP cancers, 84.6% were cancers treated within 3 months following the OSP mammogram, 9.8% had been diagnosed following a single test sequence, and 5.0% following a second sequence. Only 0.6% of OSP cancers were diagnosed following 3 test sequences conducted within intervals compatible with ACR3 lesion follow-up. In all, 15.4% of women with OSP cancer had a series of sequences compatible with ACR3 lesion follow-up.

IC were mostly diagnosed among women having 2 sequences and an interval between the OSP mammogram and the start of the second sequence of less than 5 months (17.7%) or more than 7 months (66.2%), then to a lesser degree among women having 3 (13.7%) or 4 test sequences (2.3%) (figure 2). In this way, 39.5% of IC were diagnosed during the first year following the OSP mammogram, and 60.5% during the second year.

IC presented with lymph node involvement (18.7%) and/or metastatic involvement from the outset (3.7%) more often, versus 15.8% and 2.4% in the OSP group. For its part, the PSCS group presented with a similar rate of lymph node involvement (18.2%) and a greater rate of metastatic involvement (6.9%) compared to the IC group. The differences are observed in each age group (table 2), but there is less of a predominance of metastatic cancers in the PSCS group among women aged 50-55 years.

Treatment and care pathways

Compared to the OSP group, women with localised invasive cancer in the IC group had fewer BCS-radiotherapy type pathways (48% versus 63%), more surgery-chemotherapy-radiotherapy type pathways (20% versus 16%), more neoadjuvant chemotherapy (10% versus 4%), and a similar rate of BCS- mastectomy conversion (5% versus 4%, figure 3).

Among the women with metastatic cancer, 64% of the IC group had been treated with breast excision, as opposed to 75% and 59% of the OSP and PSCS groups, respectively. The IC group was treated to a lesser extent with mastectomy (37% versus 39% and 53% in the OSP and PSCS groups), and to a greater extent with neoadjuvant chemotherapy (27% versus 16% and 19%). In the case of women not having undergone breast excision, the IC group had received more chemotherapy than the OSP group (28% versus 19% and 37%). Compared to the OSP group, women with metastatic cancer in the IC group had fewer BCS-radiotherapy type pathways (4% versus 13%) and BCS-chemotherapy-radiotherapy type pathways (19% versus 32%), and more chemotherapy-radiotherapy type pathways (16% versus 9%). The women from the PSCS group showed the same differences, to a more pronounced degree. Fewer women with metastatic cancer had been treated with hormone therapy than other women with invasive cancer, in particular the women from the IC group (54% versus 62% and 59% in the OSP and PSCS groups) (table 3).

The pathways with hormone therapy showed that this type of therapy was not specific to certain types of pathway, and that few women were treated with hormone therapy only. The proportion of treatment with hormone therapy is lower for IC group than for the other groups regardless of the stage at the time of diagnosis.

Overall, the IC group underwent conserving surgery as a first-line treatment less frequently than the OSP group, but more than the PSCS group. The BCS - mastectomy differential was more pronounced among women with cancer in situ (19% versus 12% and 9% in the OSP and PSCS groups) or metastatic cancer (8% versus 3% and 2% in the OSP and PSCS groups). Also, the proportion of complex pathways was greater in the IC group compared to the OSP group, and comparable between the IC and PSCS groups (figure 3). The care pathways of the IC group were closer to those of the PSCS group, without being identical however, with a greater mastectomy and chemotherapy rate than in the OSP group.

DISCUSSION

This study included 28,159 women aged from 50 to 74 years at the time of breast cancer diagnosis in 2016, 12,965 (46%) through the OSP, 3433 (12%) with an IC, and 11,761 (42%) outside the screening programme. In this population, the algorithm identified 20.9% IC cases among the cancers diagnosed after carrying out an OSP mammogram. The IC were diagnosed at a slightly more advanced stage at the time of diagnosis than the OSP group. The findings of this study supplement a previous study [30] which did not distinguish IC and could affect the differences between the OSP and non OSP groups. The present study highlights that these differences persist after isolating the IC from these two groups.

A high, but probably overestimated, rate of IC

The IC group includes all diagnoses made outside BIRADS guidelines: new investigation due to the onset of clinical signs, choice by doctor and patient to carry out a personalised screening mammogram in the period following the OSP mammogram, follow-up of a lesion other than ACR3, but also atypical ACR3 lesion follow-up, etc. The imaging reports which would allow us to ascertain the findings and the context are not available to us. Therefore, non-adherence to guidelines may have resulted in classification errors and in particular in an overestimation of the IC rate. This probably explains the IC rate presented in this study which seems higher than those reported in other studies (approximately 17%) [19], [33].

According to an internal assessment at Santé publique France (unpublished data), only 26.6% of women with an ACR3 lesion (detected in the OSP mammogram) underwent a first follow-up mammogram between 5 and 7 months. In addition, 41.4% of these women had this first follow-up after 7 months, including 10.5% specifically between 11 and 14 months. In this study, 9.1% of the women from the study population with multiple sequences underwent a second sequence between 11 and 14 months after the initial OSP mammogram. Furthermore, although the practice is not clearly acknowledged, follow-up at 3-4 months may be proposed in the case of an ACR3 lesion with sonographic mass indicating suspected triple-negative cancer.

Finally, MRI access may be more difficult and restricted in some French regions and the 60-day interval may not be observed, classifying MRI scans in the following sequence. However, this bias remains minimal as breast MRI scans represented 8% of all imaging tests conducted in the study population.

Conversely, women with IC diagnosed within 5 to 7 months or 11-14 months following the negative OSP mammogram, and following the standard ACR3 lesion follow-up schedule may have been incorrectly classified in the OSP group.

IC cases exhibit an intermediate care pathway profile

The IC group exhibited an intermediate profile in terms of treatments and care pathways compared to the OSP and PSCS groups. Overall, women with IC had more complex pathways than women with OSP cancer, but they were treated with primary surgery and BCS more frequently than the women of the PSCS group. On the other hand, they were treated less frequently with hormone therapy than the OSP group, possibly reflecting a higher proportion of hormono-resistant- cancers among the IC group.

The higher rates of primary BCS, and of surgical conversion (BCS followed by mastectomy), and the scale of primary surgery among those with metastatic involvement from the outset suggest that some IC would be cancers of small size tending to be less symptomatic at the time of diagnosis, and could explain some of the differences observed. Furthermore, the intermediate nature of the care

pathways probably reflects an intermediate distribution of prognostic factors among IC compared to OSP and PSCS cancers. Further studies describe IC cases as more aggressive at the time of diagnosis and as having a poorer prognosis than cancers detected through the OSP programme [18, 20–23].

A study on a nationwide scale based on medico-administrative data

Because the SNDS does not provide direct information about the circumstances of cancer diagnosis, an IC identification algorithm based on the imaging procedures and date of completion was developed to classify women as OSP group, IC group and PSCS group. An approach using a population-based cancer registry to identify cases would be more robust but registries cover local areas not necessarily representative of the whole France. The main advantage of our study was having access to the SNDS, the national medico-administrative database recording all outpatient and inpatient care consumption for the entire French population [30]. Defosse et al [34] demonstrated by comparing to the medical record, that 98% of pathways were correctly reconstructed in terms of status sequencing, and 94% of pathways were faithful to the truth within 3 days in terms of intervals, demonstrating the ability of this base to describe care pathways. This provides an additional tool to improve knowledge on a nationwide scale. However, some shortcomings in terms of quality may remain, particularly in relation to the information used to determine the stage at the time of diagnosis[31]. In this way, we observed an underestimation of the cases of cancer in situ (incorrectly classified as invasive); localised (N-) invasive cancers treated with neoadjuvant chemotherapy which were probably cancers in which lymph node involvement was not coded. Metastatic cancers may have been incorrectly classified as non-metastatic due to the lack of coding of the metastases within 6 months post-diagnosis. However, on the face of it, these errors are the same for the three groups, OSP, IC and PSCS, and do not modify the comparisons.

The first study on this scale, our analysis includes over 28,000 women with incident breast cancer and with no previous history of cancers (all types combined) between 2005 and 2015. The aim is to study a population with primary cancer (therefore having had no treatment for a recurrence of breast cancer or other cancers), without seeking to recalculate cancer incidence.

It compares the care pathway of women with IC to those of women with different diagnosis circumstances. The national approach makes it possible to retrieve all treatments administered for cancer throughout the country, regardless of the treatment or care setting, and take all geographic or socioeconomic diversities into consideration.

CONCLUSION

The analysis of care pathways on a national scale based on medico-administrative data confirms that women whose cancer was diagnosed following a mammogram performed in the context of the OSP had less aggressive treatments, and that women with IC had intermediate care pathways compared to other women with breast cancer outside the OSP programme.

The findings of this study will help women concerned by the breast cancer OSP programme be better informed, in order to allow them to make an informed choice. In addition, women should be aware that some cancers can occur between two screening mammograms and should remain vigilant for the appearance of symptoms.

Studies on IC characteristics should be continued to provide public authorities with the means to adapt the national breast cancer OSP, and offer personalised follow-up to women liable to develop IC.

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Figure legends :

Figure 1: Flow chart for selection of the population study from the SNDS

Figure 2: Algorithm for identifying the 3 groups, OSP, IC and PSCS group, according to imaging procedures and their date of completion (1 sequence = 60 days)

Figure 3 : Care pathways (breast conservative surgery, mastectomy, chemotherapy and radiotherapy) by stage at diagnosis for the 3 groups : OSP, IC and PSCS group.

DP/DAS/DR diagnosis codes for breast cancers in 2016

(PMSI MCO or LTD)

N=160 869

Exclusion :

Breast cancer history prior to 2016 (N= 91 312)

Other cancer history prior to 2016 (N= 6 282)

Other cancer (except liver, bones, lung, brain) in 2016-2017 (N= 2926)

Stay chaining anomaly (N= 41)

Incident cases without no cancer history

N= 60 308

Exclusion :

Male or unknown sex (N= 807)

Or No anticancer treatment found in 2016 (N= 10 453)

Or No breast imaging within 24 months of diagnosis (N= 4 622)

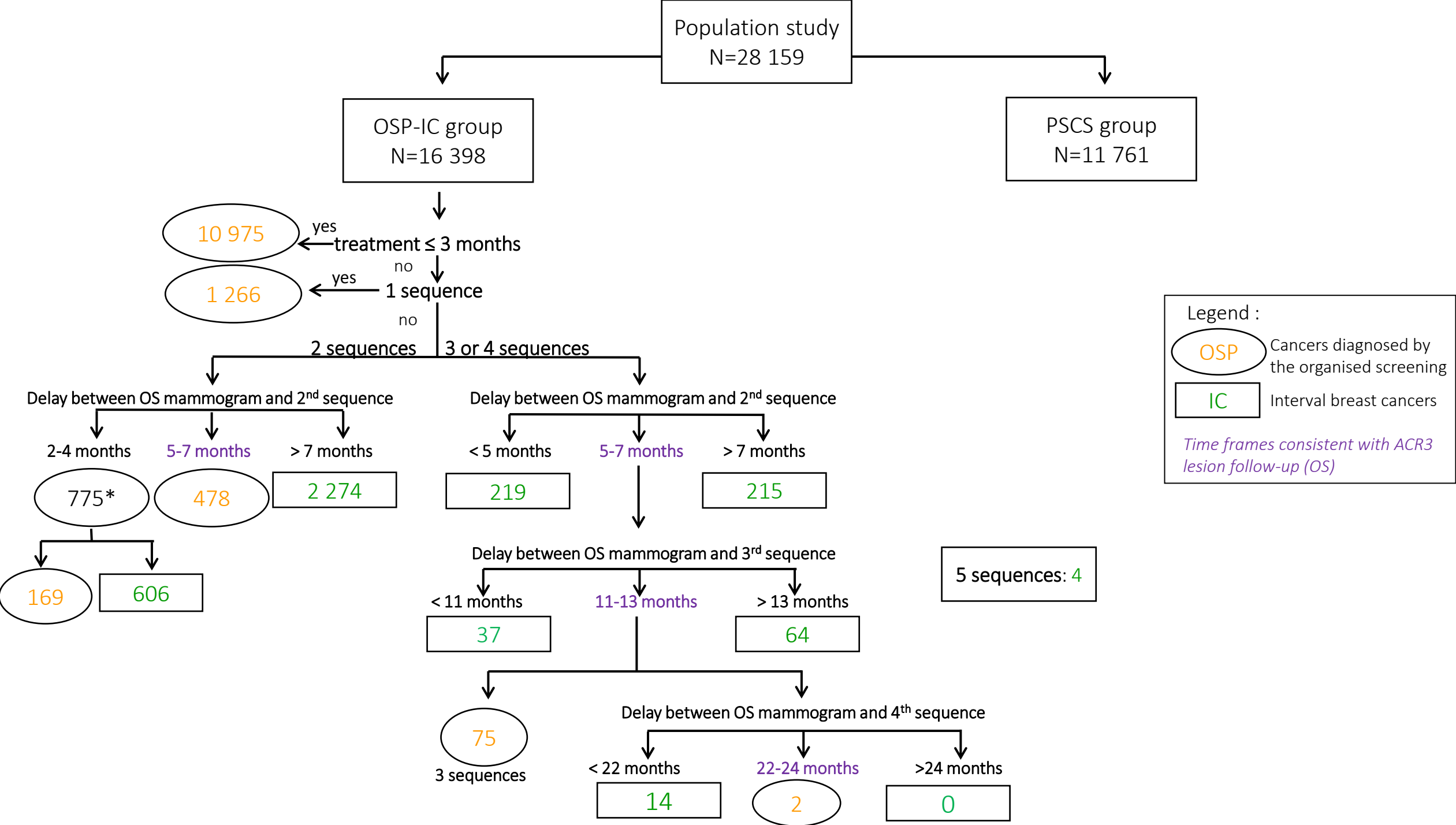
Or Age at diagnosis < 50 years or > 74 years (N= 30 358)

Population study

N= 28 159

At least one OSP
mammogram
OSP-IC group
N= 16 398

No OSP
mammogram
PSCS group
N= 11 761



Legend :

- OSP** (orange oval): Cancers diagnosed by the organised screening
- IC** (green box): Interval breast cancers

Time frames consistent with ACR3 lesion follow-up (OS)

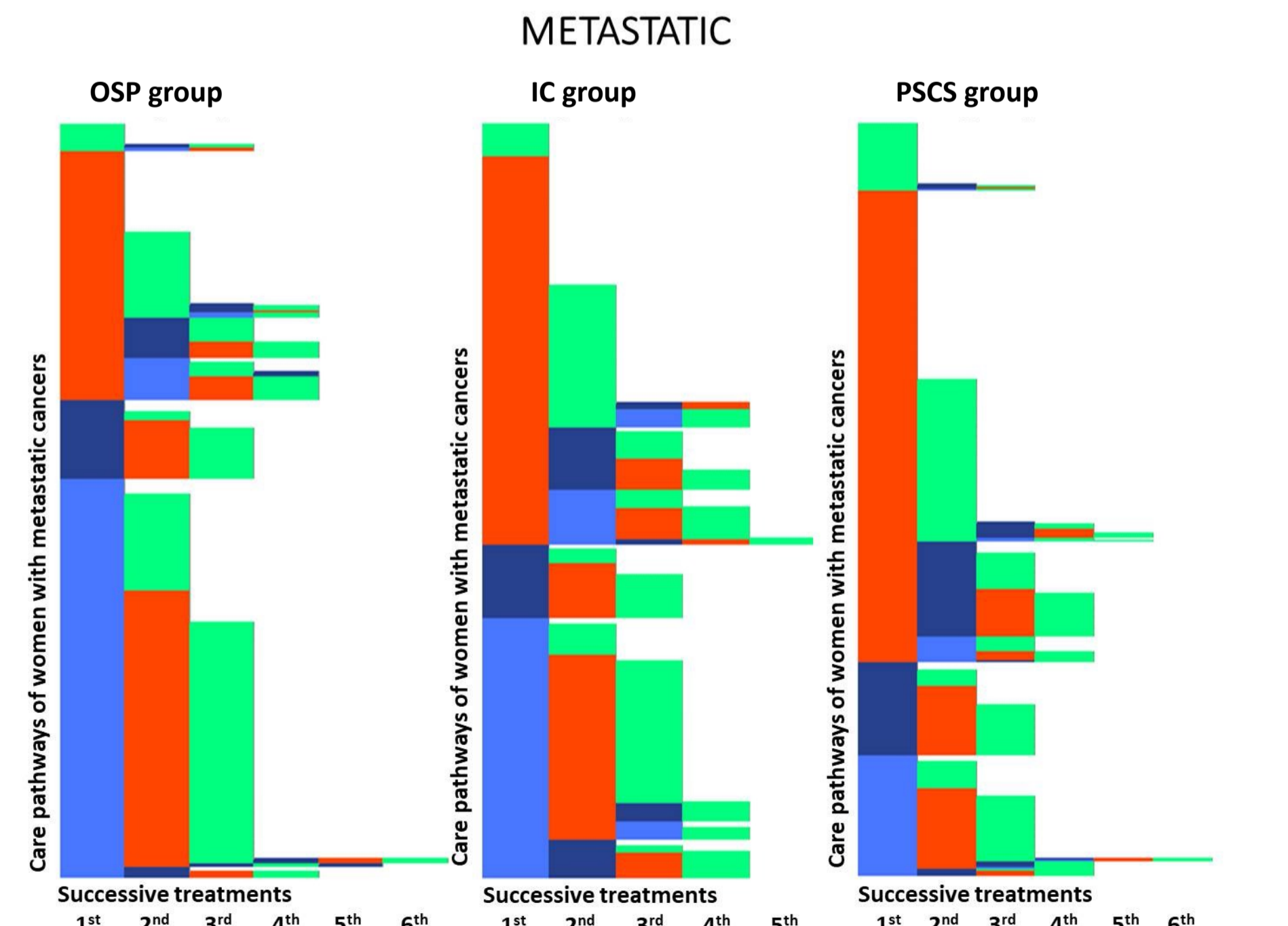
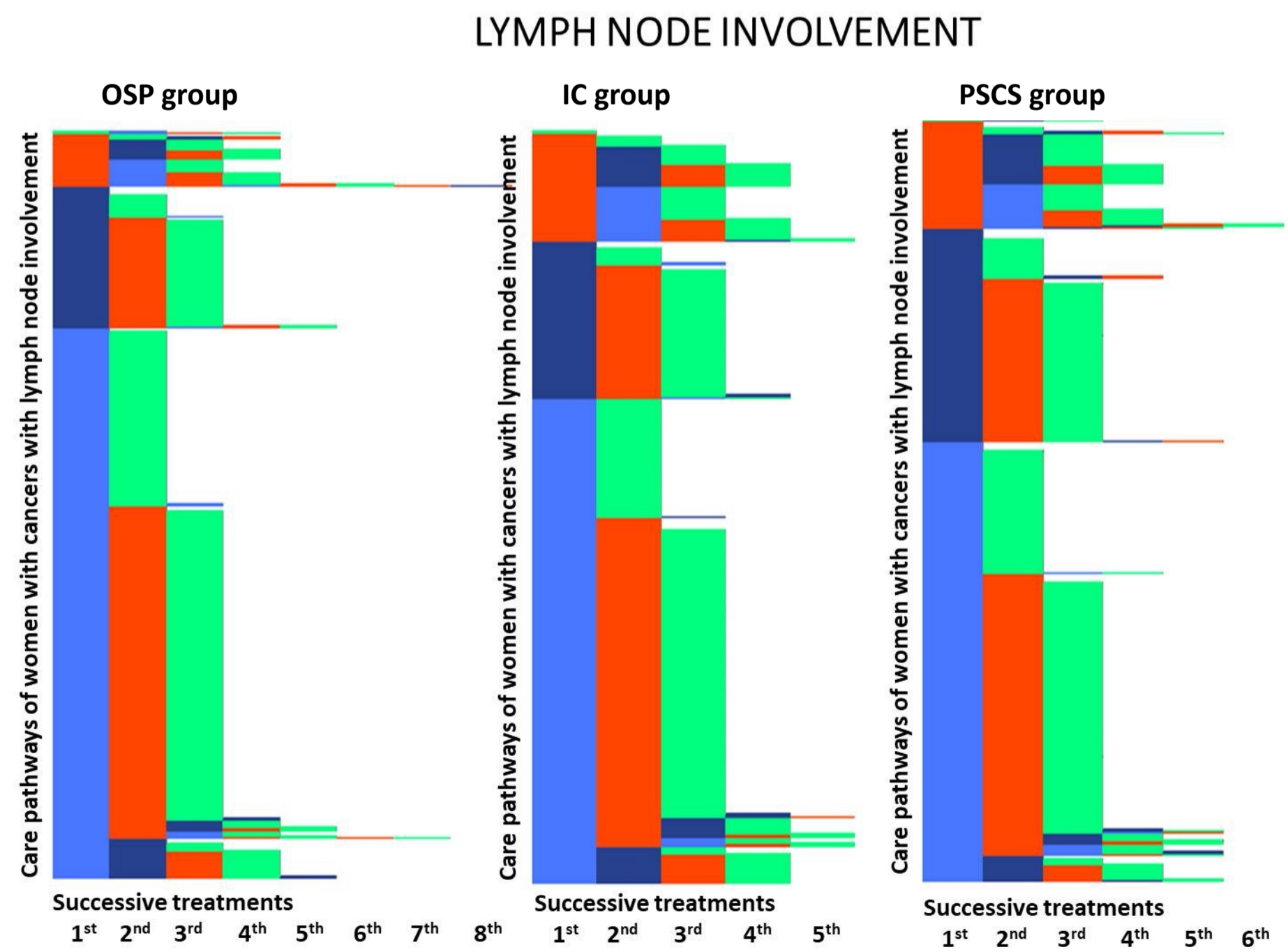
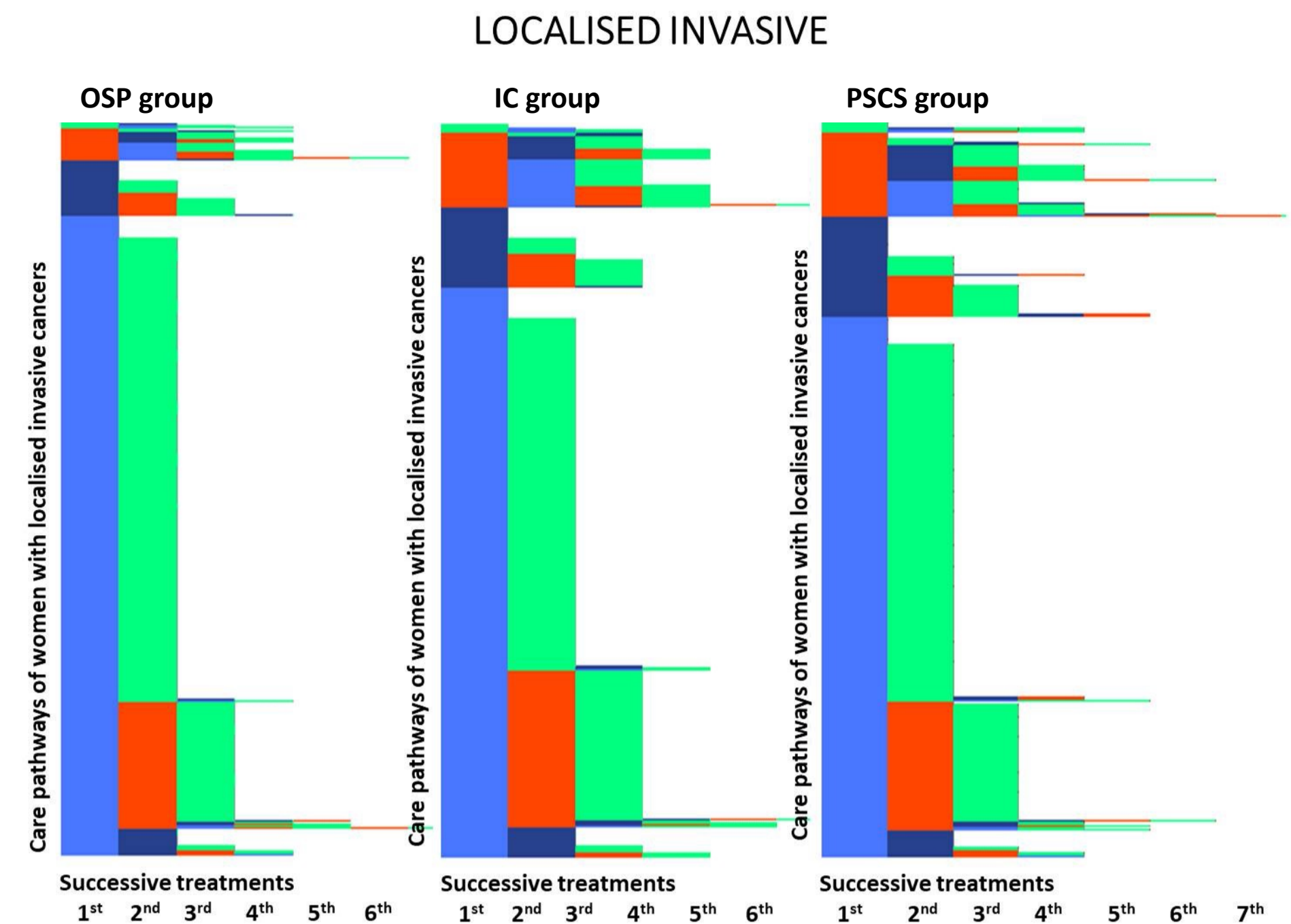
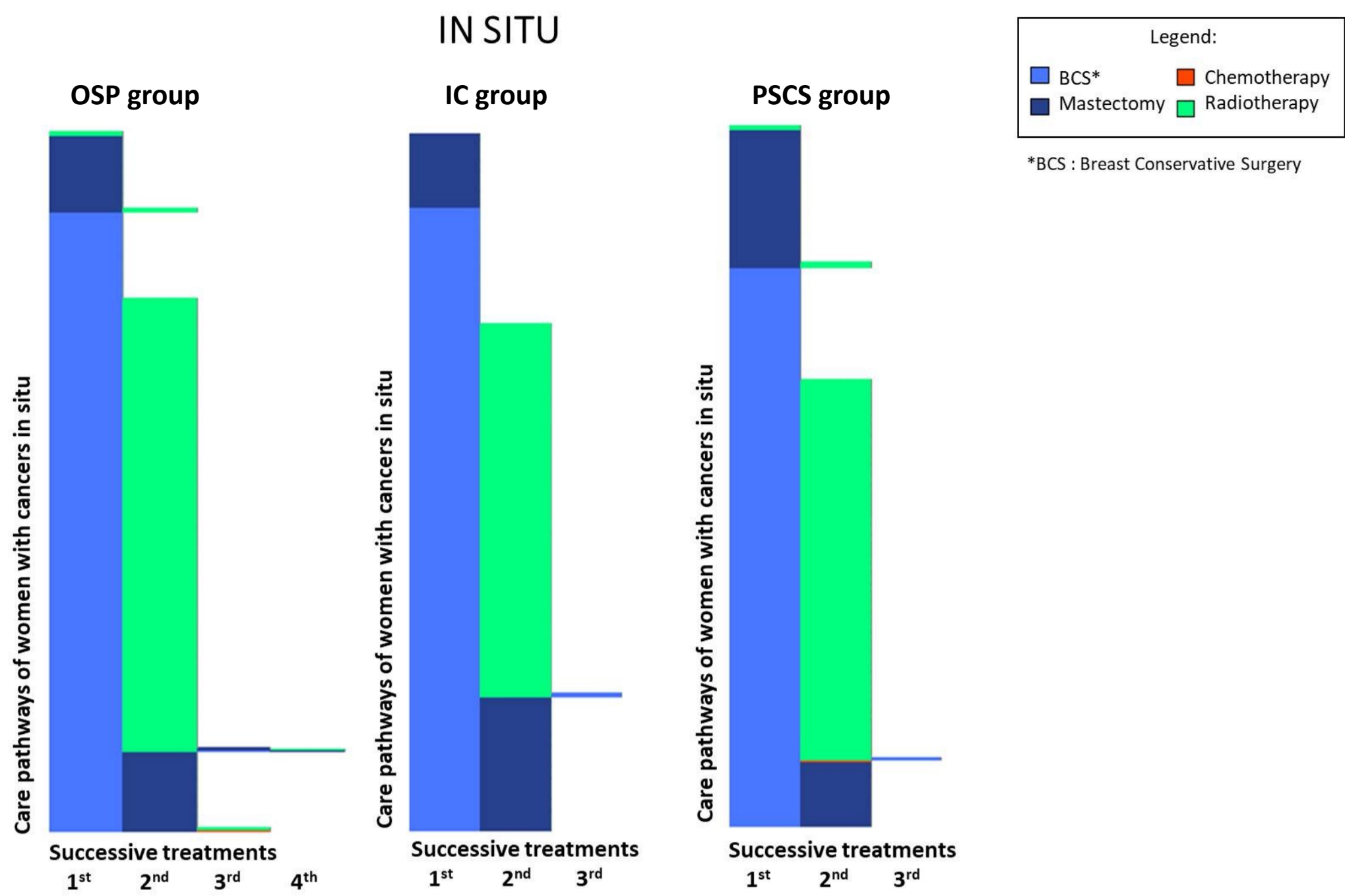


Table 1: Description of the study population by group and age class

Age	OS group	IC group	PSCS group	IC/total	IS/(OS+PSCS)
Middle age (confident interval)	62.3 (6.9)	62.4 (6.8)	61.4 (7.3)	-	-
50-55 years	2 764	720	3 220	10.7%	20.7%
56-60 years	2 414	668	2 173	12.7%	21.7%
61-65 years	2 948	758	2 302	12.6%	20.5%
66-70 years	3 122	833	2 571	12.8%	21.1%
71-74 years	1 717	454	1 495	12.4%	20.9%
Total	12 965	3 433	11 761	12.2%	20.9%

Table 2 : Group by age class and stage of diagnosis

Age	OS group n=12 965 (46.0%)	IC group n=3 433 (12.2%)	PSCS group n=11 761(41.8%)
50-55 years			
In situ	194 (7.0%)	34 (4.7%)	172 (5.3%)
Localised invasive	2 031 (73.5%)	518 (71.9%)	2 239 (69.5%)
With lymph node involvement	479 (17.3%)	136 (18.9%)	653 (20.3%)
Metastatic	60 (2.2%)	32 (4.5%)	156 (4.9%)
Total	2 764 (100%)	720 (100%)	3 220 (100%)
56-60 years			
In situ	144 (6.0%)	37 (5.5%)	88 (4.1%)
Localised invasive	1 793 (74.3%)	478 (71.6%)	1 474 (67.8%)
With lymph node involvement	428 (17.7%)	132 (19.8%)	421 (19.4%)
Metastatic	49 (2.0%)	21 (3.1%)	190 (8.7%)
Total	2 414 (100%)	668 (100%)	2 173 (100%)
61-65 years			
In situ	167 (5.7%)	34 (4.5%)	82 (3.6%)
Localised invasive	2 254 (76.4%)	552 (72.8%)	1 649 (71.6%)
With lymph node involvement	463 (15.7%)	147 (19.4%)	391 (17.0%)
Metastatic	64 (2.2%)	25 (3.3%)	180 (7.8%)
Total	2 948 (100%)	758 (100%)	2 302 (100%)
66-70 years			
In situ	165 (5.3%)	43 (5.2%)	96 (3.7%)
Localised invasive	2 425 (77.7%)	619 (74.3%)	1 876 (73.0%)
With lymph node involvement	442 (14.1%)	142 (17.2%)	420 (16.3%)
Metastatic	90 (2.9%)	28 (3.3%)	179 (7.0%)
Total	3 122 (100%)	833 (100%)	2 571 (100%)
71-74 years			
In situ	75 (4.4%)	25 (5.5%)	43 (2.9%)
Localised invasive	1 359 (79.1%)	325 (71.6%)	1 093 (73.1%)
With lymph node involvement	235 (13.7%)	83 (18.3%)	254 (17.0%)
Metastatic	48 (2.8%)	21 (4.6%)	105 (7.0%)
Total	1 717 (100%)	454 (100%)	1 495 (100%)
Total			
In situ	745 (5.8%)	173 (5.0%)	481 (4.1%)

Localised invasive	9 862 (76.1%)	2 492 (72.6%)	8 331 (70.8%)
With lymph node involvement	2 047 (15.8%)	641 (18.7%)	2 139 (18.2%)
Metastatic	311 (2.4%)	127 (3.7%)	810 (6.9%)

Table 3: Therapy by stage of diagnosis and group

	Cancers in situ			Localised invasive cancers			Cancers with lymph node involvement			Metastatic cancers		
	OS (N =878)	IC (N =107)	PSCS (N =360)	OS (N =10778)	IC (N =1723)	PSCS (N =10171)	OS (N =2229)	IC (N =454)	PSCS (N =2845)	OS (N =480)	IC (N =124)	PSCS (N =1175)
Surgery	876 (100%)	107 (100%)	627 (100%)	14 662 (99%)	1 700 (99%)	9 899 (97%)	2 214 (99%)	449 (99%)	2 812 (99%)	360 (75%)	79 (64%)	623 (53%)
BCS Mastectomy	679 (78%) 197 (22%)	74 (69%) 33 (31%)	462 (74%) 165 (26%)	9 174 (86%) 1 488 (14%)	1 391 (82%) 309 (18%)	7 754 (78%) 2 145 (22%)	1 515 (68%) 699 (32%)	270 (60%) 179 (40%)	1 561 (56%) 1 251 (44%)	221 (61%) 139 (39%)	50 (63%) 29 (37%)	291 (47%) 332 (53%)
Radiotherapy	585 (67%)	50 (47%)	380 (60%)	9 555 (89%)	1 515 (88%)	8 579 (84%)	2 105 (94%)	436 (96%)	2 262 (94%)	359 (75%)	83 (67%)	752 (64%)
Chemotherapy	3 (0%)	0 (0%)	1 (0%)	2 824 (26%)	622 (36%)	3 726 (37%)	1 722 (77%)	380 (84%)	2 322 (82%)	385 (80%)	101 (81%)	960 (82%)
neoadjuvant	1 (0%)	0 (0%)	0 (0%)	439 (4%)	151 (9%)	908 (9%)	279 (13%)	100 (22%)	585 (21%)	77 (16%)	33 (27%)	226 (19%)
adjuvant	2 (0%)	0 (0%)	1 (0%)	2 599 (24%)	534 (31%)	3 143 (31%)	1 569 (70%)	318 (70%)	1 973 (69%)	257 (54%)	50 (40%)	416 (35%)
without surgery	0 (0%)	0 (0%)	0 (0%)	41 (0%)	10 (1%)	112 (1%)	14 (1%)	5 (1%)	28 (1%)	91 (19%)	35 (28%)	434 (37%)
Hormone Therapy	59 (7%)	5 (5%)	42 (7%)	7 988 (74%)	1 158 (67%)	7 111 (70%)	1 854 (84%)	337 (74%)	2 222 (78%)	299 (62%)	67 (54%)	696 (59%)
Palliative care	0 (0%)	0 (0%)	0 (0%)	6 (0%)	3 (0%)	21 (0%)	5 (0%)	1 (0%)	8 (0%)	65 (14%)	17 (14%)	191 (16%)