



## Original article

# The challenge of sustainability in healthcare systems: Frequency and cost of inappropriate patterns of breast cancer care (the E.Pic.A study)



Ilaria Massa <sup>a,\*</sup>, William Balzi <sup>b</sup>, Costanza Burattini <sup>a</sup>, Nicola Gentili <sup>c</sup>, Lauro Bucchi <sup>d</sup>, Oriana Nanni <sup>a</sup>, Davide Gallegati <sup>e</sup>, Andrea Pierini <sup>f</sup>, Dino Amadori Scientific Director <sup>g</sup>, Fabio Falcini <sup>d</sup>, Mattia Altini <sup>b</sup>

<sup>a</sup> Unit of Biostatistics and Clinical Trials, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, via P. Maroncelli 40, 47014 Meldola, FC, Italy

<sup>b</sup> Healthcare Administration, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, via P. Maroncelli 40, 47014 Meldola, FC, Italy

<sup>c</sup> IT Unit, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, via P. Maroncelli 40, 47014 Meldola, FC, Italy

<sup>d</sup> Romagna Tumor Registry, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, via P. Maroncelli 40, 47014 Meldola, FC, Italy

<sup>e</sup> Management and Accounting Unit, Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, via P. Maroncelli 40, 47014 Meldola, FC, Italy

<sup>f</sup> Market Access, Roche S.p.A., via G.B. Stucchi 110, 20900 Monza, MB, Italy

<sup>g</sup> Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, via P. Maroncelli 40, 47014 Meldola, FC, Italy

## ARTICLE INFO

## Article history:

Received 21 March 2017

Received in revised form

3 May 2017

Accepted 15 May 2017

## Keywords:

Breast cancer  
Real-world evidence  
Appropriateness  
Sustainability  
Healthcare systems

## ABSTRACT

**Objectives:** In a context of decreasing economic health resources and a rise in health needs, it is urgent to face this sustainability crisis through the analysis of healthcare expenditures. Wastages, deriving from inappropriate interventions, erode resources which could be reallocated to high-value activities. To identify these areas of wastages, we developed a method for combining and analyzing data from multiple sources. Here we report the preliminary results of a retrospective cohort study evaluating the performance of breast cancer (BC) care at IRST, an Italian cancer institute.

**Materials and methods:** Four data sources gathered in a real-world setting (a clinical database, two administrative databases and a cancer registry) were linked. Essential Key Performance Indexes (KPIs) in the pattern of BC diagnosis (KPI 1 and 2) and treatment (KPI 3 and 4) based on current guidelines were developed by a board of professionals. The costs of inappropriate examinations were associated with the diagnostic KPIs.

**Results:** We found that 2798 patients treated at IRST from January 2010 to June 2016 received a total of 2516 inappropriate examinations accounting for € 573,510.80. Linkage from multiple routine healthcare data sources is feasible: it allows the measurement of important KPIs specifically designed for BC care, and the identification of areas of low-value use of the resources.

**Conclusion:** If systematically applied, this method could help provide a complete picture of inappropriateness and waste, redirect these resources to higher-value interventions for patients, and fill the gap between proper use of the resources and the best clinical results.

© 2017 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## 1. Introduction

In developed countries, oncology represents an increasing burden on the healthcare budget. Major determinants of healthcare expenditures include the increase in cancer incidence, closely linked to population aging, and the use of new high-cost drugs and technologies, especially in patients with advanced disease. These innovations have led to an improvement in survival rate, but challenge the sustainability of health systems. It is estimated, for

\* Corresponding author.

E-mail addresses: [ilaria.massa@irst.emr.it](mailto:ilaria.massa@irst.emr.it) (I. Massa), [william.balzi@irst.emr.it](mailto:william.balzi@irst.emr.it) (W. Balzi), [costanza.burattini@irst.emr.it](mailto:costanza.burattini@irst.emr.it) (C. Burattini), [nicola.gentili@irst.emr.it](mailto:nicola.gentili@irst.emr.it) (N. Gentili), [lauro.bucchi@irst.emr.it](mailto:lauro.bucchi@irst.emr.it) (L. Bucchi), [oriana.nanni@irst.emr.it](mailto:oriana.nanni@irst.emr.it) (O. Nanni), [davide.gallegati@irst.emr.it](mailto:davide.gallegati@irst.emr.it) (D. Gallegati), [andrea.pierini@roche.com](mailto:andrea.pierini@roche.com) (A. Pierini), [dino.amadori@irst.emr.it](mailto:dino.amadori@irst.emr.it) (D. Amadori), [f.falcini@irst.emr.it](mailto:f.falcini@irst.emr.it) (F. Falcini), [mattia.altini@irst.emr.it](mailto:mattia.altini@irst.emr.it) (M. Altini).

### Abbreviations

BC	Breast Cancer
CH	Chemotherapy
EHR	Electronic Health Record
E.Pic.A.	Economic Appropriateness of an Integrated Care Pathway (Appropriatezza Economica del Percorso Integrato di Cura)
HDC	Hospital Discharge Card
IRST	Istituto Scientifico Romagnolo per lo studio e la cura dei Tumori
KPI	Key Performance Index
RTRo	Registro Tumori della Romagna
SA	Specialist Assistant

example, that in the USA the costs of cancer care will increase by an average of 20% per year in the period 1990–2020 [1,2].

Breast cancer (BC) is the most common cancer among women in western countries [3], and the second leading cause of cancer-related death [4]. It is a clinically complex condition, which requires a coordinated multidisciplinary approach and is susceptible to different treatment solutions due to its heterogeneity [5]. The increasing trend towards the centralization of BC care in multidisciplinary breast units has probably promoted a greater adherence to practice guidelines, but the patterns of care actually provided and the associated costs have seldom been evaluated [6].

The funding of the Italian health system will not increase significantly in coming years [7]. By implication, it is plausible to assume that no new resources will be allocated to oncology, even if the needs will increase. In Italy, where budget constraints are threatening the sustainability of the healthcare system, a thorough analysis of healthcare expenditures has shown that waste accounts for about 20–30% of global health costs [8]. Wastages derive from inappropriate interventions, i.e. actions that are not recommended by national and international guidelines and do not add significant therapeutic advantages. Avoiding this loss of resources is imperative. In addition, wastages can ultimately damage patients and affect the quality of care. In such a challenging context, policy makers and healthcare providers are striving to create performance measurement systems.

Measuring performance in healthcare is a challenging and debated issue, centered on the value of healthcare, defined as the health outcome achieved at the population level per amount of expenditure [9]. This entails accessing, processing, combining, and analyzing a variety of data from multiple and heterogeneous sources.

In the current paper, we report the preliminary results of a retrospective cohort study in which we evaluated the performance of BC care by connecting information gathered from four data sources in a real-world setting. Our rationale was two-fold: first, to develop a method for identifying areas of wastages with the aim to reallocate these resources into high-value activities; second, to fulfill the gap between health management and clinical practice, i.e. between proper use of the resources and the best clinical results. In detail, our objectives were: *i*) to verify the possibility of data linkage between different sources, each with a different level of validation, completion and timeliness; *ii*) to measure Key Performance Indexes (KPIs), based on international guidelines on BC care and identified in the Economic Appropriateness of an Integrated Care Pathway (Appropriatezza Economica del Percorso Integrato di Cura, E.Pic.A.) study and *iii*) to determine their associated costs in order to identify

areas of low-value use of the resources.

## 2. Methods

### 2.1. Setting

The study was conducted at the Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori IRST of Meldola, Forlì, Italy.

### 2.2. KPIs

Using a new approach for performance evaluation, as proposed in the E.Pic.A. study, a board of professionals identified 7 KPIs in the pattern of BC diagnosis and treatment (local and systemic), on the basis of the current guidelines from the Italian Association of Medical Oncology (Associazione Italiana di Oncologia Medica, AIOM) [10] and the National Comprehensive Cancer Network (NCCN) [11]. These KPIs were defined in consideration of what could be retrieved from administrative databases. In the current paper we show the preliminary results of 4 of the KPIs comprised in the E.Pic.A. study.

KPI 1, pre-surgery, was defined as the proportion of patients with stage I or II disease (defined through the tumor, node, metastasis [TNM] staging of the pathology report obtained at surgery) who underwent one of the following examinations: hepatic ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI) (except for the thorax), positron emission tomography (PET), bone scan, within two distinct timeframes. Since the reasons for performing examinations are generally not indicated in clinical databases, we hypothesized two scenarios: the first was based on the assumption that each test was related to BC, and the second scenario was based on the assumption that patients could have undergone a specific examination for reasons unrelated to cancer, such as the presence of comorbidities and/or the patients' attitude and socio-economic context. In the first scenario, in rigorous adherence to current guidelines, each of the above-mentioned exams was considered as inappropriate if performed within 2 months before breast surgery. In the second scenario, one of the above-mentioned examinations was considered as inappropriate only if it had been performed more than once within 6 months before breast surgery, except for bone scan which was considered as inappropriate in any case. In both scenarios, the number of PET-scans was also measured for stage III patients: these exams were considered as inappropriate in any case. The time windows chosen referred to the date of surgery, because the date of diagnosis is not retrievable from the administrative databases.

KPI 2, post-surgery, was defined as the proportion of patients with stage I or II disease (defined through TNM of the pathology report obtained at surgery) who performed one of the following exams: hepatic US, CT, MRI, bone scan, PET scans (including stage III patients) within 2 months after breast surgery. Each of the above-mentioned exams was considered as inappropriate.

KPI 3, subsequent intervention after mastectomy, was defined as the proportion of patients who received axillary dissection and/or breast reconstruction within 3 months after mastectomy.

KPI 4, chemotherapy (CH) timing, was defined as the proportion of patients who received adjuvant CH within 60 days after surgery.

### 2.3. Data sources

To measure the KPIs, the following information was collected: date of first diagnosis, stage at diagnosis, date and type of surgery, performed examinations and date of first CH. Information retrieval was gained through the use of four data sources: (1) the IRST clinical database Log80; (2) the administrative database Hospital

Discharge Card (HDC) at the regional Department of Health; (3) the outpatient “Specialist Assistance” (SA) database at the regional Department of Health; and (4) the Romagna Cancer Registry (Registro Tumori della Romagna, RTRo).

The IRST clinical database Log80 was used to identify BC patients. Information on the date and type of surgical interventions was retrieved from the HDC database. As fully detailed by Francisci et al. [12], the HDC contains selected coded procedures performed for each patient within a single hospital admission, when he or she is assigned a unique HDC code (in-patient or day hospital setting). The SA database contains all coded procedures received by patients and was used to retrieve radiological examinations. BC patients identified in Log80 were linked with the HDC and SA administrative databases. The time interval between the surgical intervention and the start date of CH was retrieved from Log80, which contains the therapeutic scheme, including the date of first administration. The date of surgery was captured from the HDC database. Data linkage between the latter two was possible only through a personal identification code.

The RTRo, a population-based cancer registry that covers the main catchment area of IRST, was used to extract the date of first diagnosis, as defined according to standard criteria [13], date and type of surgery, tumor laterality (left or right breast), TNM status. At the time this work was done, registration was updated to December 31st, 2012. The linkage between Log80 and the RTRo was performed by matching the following information for each patient: surname, name, date of birth and fiscal code.

The ICD-9 CM and SA codes used to identify all radiological examinations and surgical procedures are reported in the Appendix. The costs for radiological procedures were measured according to the regional Healthcare Range of Fees, in order to estimate the cost actually incurred by the healthcare provider [14].

#### 2.4. Case series

Two thousand seven hundred and ninety-eight patients residing in Emilia Romagna (Italy) referred to IRST from January 1st, 2010 to June 30<sup>th</sup>, 2016 were included in this study. Two thousand eight hundred and seventy-six tumors were associated with these patients, considering only the first diagnosis and the first contra lateral BC, if any. No additional inclusion or exclusion criterion was considered.

### 3. Results

After linkage with the RTRo, that was possible only for 2028 (72.48%) patients, an amount of 1094 records needed to be corrected. The date of diagnosis was corrected for 1047 patients (mean delay 21.77 days, median delay 6 days); the change of date exceeded 60 days only for 67 patients. In 26 patients tumor laterality was incorrect, while staging was changed in 205 patients (46 of which were added *de novo*). By matching the data with the RTRo, excluding the minor variations on the date (<60 days), on a total of 264 patients at least one correction was performed, accounting for about 13% of matched patients. The patients who did not match with the RTRo were manually entered and verified. Table 1 shows the distribution of the 2876 tumors according to staging.

In the first scenario of the “pre-surgery” KPI, or KPI 1, a total of 2192 patients with stage I or II disease was found. Of these, 953 (43.5%) patients received a total of 1486 inappropriate exams in the 2 months before surgery (mean 1.6 exams per patient), accounting for a total cost of € 329,751.40 (mean € 346.00 per patient). For patients with stage III disease, PET scans were performed before surgery in 40 patients out of 237, with a total cost of € 51,235.90 (mean € 1280.90 per patient). Exam distribution is shown in

**Table 1**  
Distribution of tumors according to staging.

Stage	N	%
0	131	4.6
I	1486	51.7
II	853	29.7
III	286	9.9
IV	120	4.2
<b>Total</b>	<b>2876</b>	<b>100.0</b>

**Table 2.** The total cost for inappropriate examinations for stage I-II-III patients amounted to € 380,987.10.

In the second scenario, a wider time window of 6 months before surgery was considered. In this timeframe, 381 patients (17.4%) received a total amount of 423 exams (mean 1.1 exams per patient), for a total cost of € 96,237.90 (mean € 252.60 per patient). PET scans for stage III patients were performed only for 5 patients out of 237, with a total cost of € 6430.00 (mean € 1286.00 per patient). These results are shown in Table 3. The total cost for inappropriate examinations for stage I-II-III patients amounts to € 102,667.90.

In KPI 2, “post-surgery”, we found that out of 2192 patients with stage I or II disease, 685 (31.2%) received a total amount of 976 exams in the 2 months after surgery (mean 1.4 exams per patient), with a total cost of € 174,519.70 (mean € 254.80 per patient). PET scans for stage III patients were performed in 14 patients out of 237, amounting to a total cost of € 18,004.00 (mean € 1286.00 per patient). Exam distribution is shown in Table 4. The total cost for inappropriate examinations for stage I-II-III patients amounts to € 192,523.70.

KPI 3, concerning the local therapeutic phase, measured the amount of subsequent interventions within 3 months after mastectomy. In this case we found that out of 841 patients who received a mastectomy, only 9 (1.07%) received a second axillary dissection and/or breast reconstruction, within the timeframe considered.

In KPI 4 the timing between surgery and CH start date was measured. Out of 808 patients who underwent CH, 445 (55.07%) started treatment within 45 days; extending this time window to 60 days, a total amount of 689 patients (85.27%) was found. These results are reported in Table 5.

### 4. Discussion

Information for this study was obtained from multiple data sources gathered in a real-world setting at the point of care, according to the E.Pic.A. study. The first challenge of this work was to perform data linkage between these sources. We found discrepancies in their completion and missing entries. However, we showed that linking information between electronic health records (EHRs) and RTRo, although time-consuming and laborious, is

**Table 2**  
KPI 1 (first scenario): costs for inappropriate diagnostic examinations.

Type of test for stage I-II patients	N	Cost (€)	%
Hepatic ultrasound	406	23,757.60	7.2
PET	64	82,304.00	25.0
MRI	681	164,679.30	49.9
Bone Scan	196	39,984.00	12.1
CT-scan	139	19,026.30	5.8
<b>Total (stage I-II patients)</b>	<b>1486</b>	<b>329,751.20</b>	<b>100.0</b>
PET (stage III patients)	40	51,235.90	-
<b>Total</b>	<b>1526</b>	<b>380,987.10</b>	<b>-</b>

CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

**Table 3**  
KPI 1 (second scenario): costs for inappropriate diagnostic examinations.

Type of test for stage I-II patients	N	Cost (€)	%
Hepatic ultrasound	18	959.70	1.0
PET	7	9002.00	9.3
MRI	166	39,834.00	41.4
Bone Scan	221	45,021.00	46.8
CT-scan	11	1421.30	1.5
<b>Total (stage I-II patients)</b>	<b>423</b>	<b>96,237.90</b>	<b>100.0</b>
PET (stage III patients)	5	6430.00	-
<b>Total</b>	<b>428</b>	<b>102,667.90</b>	<b>-</b>

CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

**Table 4**  
KPI 2: costs for inappropriate diagnostic examinations.

Type of test for stage I-II patients	N	Cost (€)	%
Hepatic ultrasound	384	21,995.80	12.6
PET	40	51,440.00	29.5
MRI	60	12,985.80	7.4
Bone scan	351	70,687.10	40.5
CT-scan	141	17,411.00	10.0
<b>Total (stage I-II patients)</b>	<b>976</b>	<b>174,519.70</b>	<b>100.0</b>
PET (stage III patients)	14	18,004.00	-
<b>Total</b>	<b>990</b>	<b>192,523.70</b>	<b>-</b>

CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

**Table 5**  
Timing between surgery and start of chemotherapy adjuvant treatment.

Timing (days)	N	%
0–45	445	55.1
46–60	244	30.2
>60	119	14.7
<b>Total</b>	<b>808</b>	<b>100.0</b>

feasible and improves data completeness by 13%. However, it should be pointed out that this estimate is somehow limited due to the amount of patients filed in the cancer registry, since RTRo is updated only to 2012. The availability of more recently updated cancer registries will certainly ensure data completion to a greater extent. Beyond this, we can confirm the findings of previous studies [12,15,16] demonstrating that administrative data are suitable for measuring performance and/or economic expenditures in healthcare.

The results obtained from the diagnostic KPIs demonstrate that a huge number of exams continue to be performed, despite the main BC guidelines (NCCN, AIOM) recommending no additional examination (except for breast imaging and clinical visits) after a diagnosis of early (stage I or II) BC. In the current study, considering the 2 months prior to or after surgery (as indicated in the first scenario of KPI 1 and in KPI 2), we identified up to 2516 exams that, according to the current guidelines, should be considered as inappropriate and which could therefore have been avoided. In addition to the overuse of radiological equipment, these inappropriate exams are associated with an improper use of resources, up to € 573,510.80 within the timeframe considered, that could likely be saved. The total cost of the diagnostic process, which was beyond the scope of the present study, has recently been estimated with great accuracy in a neighboring administrative region [17]. In the public healthcare sector, the wastages reported in Table 1 correspond to approximately 40% of the mean expenditure for

diagnosing breast cancer in northern Italy.

Recognizing these wastages may be the first step of a process of re-allocation of resources to higher-value procedures for patients, such as the neo-adjuvant or adjuvant setting of CH. In addition, reducing the number of unnecessary radiological interventions may help reduce the waiting lists that burden the radiology units, thus increasing accessibility, while limiting exposure to ionizing radiations.

The results of the therapeutic KPI considered, according to which only a small proportion of patients (1.1%) underwent second axillary dissection and/or breast reconstruction after mastectomy, are indicative of a good performance in this setting, in that the risks related to re-interventions are minimized. Similarly, the high proportion of patients that fulfilled the systemic therapeutic KPI considered, i.e. the timeframe between surgery and the start date of CH, suggests that this performance is in line with current guidelines, although with a margin for improvement. It should be pointed out that, to effectively measure performance in these settings and to increase the accuracy of evaluation, identification of a benchmark is essential.

The implementation of cancer care guidelines remains a challenging task. In our opinion, the most rational and updated approach to ensuring that existing breast cancer guidelines are adhered to is to centralize the diagnosis and management of the disease at specialized multidisciplinary breast units [18]. A breast unit should have written clinical protocols, adapted for local use from international or national recommendations, for all stages of the management of breast cancer including diagnosis. A breast unit should also have a comprehensive database for the purpose of monitoring the quality of services, and the team should hold a formal performance review meeting at least annually. Monitoring the provision of breast cancer care at the individual staff level can improve its degree of appropriateness with no need to impose sanctions and other penalties for noncompliance with guidelines.

The current study focused on the performance of breast cancer care because this disease is characterized by high incidence and prevalence, with a similar pattern of distribution in all western countries [1,2]. For this reason, BC care is a highly structured and standardized process [19], facilitating the application of our analysis to other healthcare settings. In addition, BC represents an important economic burden, since most patients are long-survivors and the disease is becoming increasingly chronic, with associated high social costs. This claims, more than for other malignancies, an urgency to accurately evaluate costs and outcome of BC care. Besides, considering the capillarity and homogeneity of administrative data, the analysis reported herein can be extended to other malignancies and be performed at a national level.

Central to the rationale of our study is the fact that the guidelines used as a reference are universally recognized in Italy. They have been developed through a transparent and rigorous process. We firmly believe that it is in the patient's interest that physicians follow these guidelines. In addition, we believe that non-evidence-based clinical approaches may act as a barrier to access to state-of-the-art care for breast cancer survivors.

Some limitations of our study deserve to be mentioned. First, this study was based on a hospital case series and this may imply a selection bias that could compromise the generalizability of findings to the entire population. Second, data were partly obtained from administrative databases, which cannot always capture patients preferences as well as complex or equivocal clinical circumstances that may justify the decision to adopt non-standard diagnostic approaches. For example, our data lack distinction between subgroups of stage II patients, as defined by age, nodal status and histological type, who could require specific diagnostic and therapeutic approaches. Moreover, although guidelines do not

recommend breast MRI for tumor staging, this examination may indeed be appropriate in specific conditions, such as equivocal imaging, suspicion of multifocality, the presence of risk factors, such as genetic risk [10]. Since the date of diagnosis cannot be univocally retrieved from administrative databases, the diagnostic KPIs considered herein focus on the date of surgery, as indicated in the E.Pic.A. study. According to the clinical observation that 60 days is the maximum time interval between BC diagnosis and surgery, all the diagnostic examinations performed during the 60 days preceding surgery (i.e. once diagnosis has already occurred), were considered as inappropriate. However, in the event that a hospital could manage this delay within less than 60 days, a simple data extraction might also incorrectly highlight as inappropriate those examinations performed for diagnosis. In such cases, a further analysis focusing on the integration of administrative data with clinical information may be necessary to clarify this issue.

In conclusion, the current study met its objectives to a satisfactory extent. First, we developed techniques to link and analyze data from multiple routine healthcare data sources; second, we measured a set of KPIs specifically designed for BC care and, third, we identified areas of low-value use of the resources. If systematically applied to other cancer care facilities and other malignancies, this methodology could help to get a complete picture of inappropriateness and waste with the objective to redirect these resources to higher-value interventions for patients.

### Ethical approval

The study was approved by the Independent Ethical Committee of the IRST. Obtainment of the informed consent forms was waived in accordance with the current legislation.

### Conflict of interest

None.

### Role of the funding source

This work was supported by a public-private partnership between Roche and IRST IRCCS. The funding source had a role in the study design, in the writing of the manuscript and in the decision to submit the manuscript for publication.

### Acknowledgements

We thank Ray Hill, an independent medical writer, who provided English-language editing and journal styling prior to submission on behalf of Health Publishing & Services Srl.

### Appendix

The ICD-9 CM codes for the surgical interventions considered are as follows: 40.51, from 85.20 to 85.25, from 85.41 to 85.48, from 85.8 to 85.89 and 85.7 (HDC database). The following are the codes

from regional nomenclature on Specialist Assistance: for US from 88.74.1 to 88.74.5, 88.75.1, 88.75.2, 88.76.1; for CT-scan from 87.03 to 87.03.3, 87.03.7, 87.03.8, 87.41, 87.41.1, 87.42.1, 87.42.2, from 88.01.1 to 88.01.6, from 88.38.1 to 88.38.7, 88.90.3; for MRI from 88.91.1 to 88.91.8, from 88.92.3 to 88.92.9, 88.93, 88.93.1, from 88.94.1 to 88.94.3, from 88.95.1 to 88.95.6, 88.97.C; for bone scan 92.05.6, 92.14.1, 92.14.2, 92.18.2; PET-scan 92.09.1, 92.11.6, 92.11.7, 92.18.6.

### References

- [1] Sullivan R, Peppercorn J, Sikora K, Zalberg J, Meropol NJ, Amir E, et al. Delivering affordable cancer care in high-income countries. *Lancet Oncol* 2011;12:933–80.
- [2] Schnipper LE, Smith TJ, Raghavan D, Blayney DW, Ganz PA, Mulvey TM, et al. American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: the top five list for oncology. *J Clin Oncol* 2012;30:1715–24.
- [3] Cardoso F, Costa A, Senkus E, Aapro M, Andre F, Barrios CH, et al. 3rd ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 3). *Ann Oncol* 2017;28:16–33.
- [4] Centers for Disease Control and Prevention. Cancer among women. 2013. <http://www.cdc.gov/cancer/dcpc/data/women.htm> [Accessed 25 January 2017].
- [5] Perou CM, Sorlie T, Eisen MB, van de Rijn M, Jeffrey SS, Rees CA, et al. Molecular portraits of human breast tumours. *Nature* 2000;406:747–52.
- [6] van Dam PA, Tomatis M, Marotti L, Heil J, Wilson R, Rosselli Del Turco M, et al. The effect of EUSOMA certification on quality of breast cancer care. *Eur J Surg Oncol* 2015;41:1423–9.
- [7] Italian Ministry of Economy and Finance. Italy's draft budgetary plan 2017. 2016. [http://www.rgs.mef.gov.it/\\_Documenti/ENGLISH-VE/Public-Fin1/DBP/2016/DRAFT\\_BUDGETARY\\_PLAN\\_2017.pdf](http://www.rgs.mef.gov.it/_Documenti/ENGLISH-VE/Public-Fin1/DBP/2016/DRAFT_BUDGETARY_PLAN_2017.pdf) [Accessed 25 January 2017].
- [8] Cartabellotta A. Disinvestire e riallocare: la chiave per la sostenibilità del SSN. Un approccio sistematico all riduzione degli sprechi. *Evidence* 2015;7:1–4.
- [9] Gray JA. The shift to personalised and population medicine. *Lancet* 2013;382:200–1.
- [10] Associazione Italiana di Oncologia Medica (AIOM). Linee guida: neoplasie della mammella (breast cancer guidelines). 2016 Edition 2016. updated to October 19th 2016. <http://www.aiom.it/professionisti/documenti-scientifici/linee-guida/1%2C413%2C1%2C> [Accessed 26 January 2017].
- [11] US National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology: breast cancer (version 2.2016). 2016. [https://www.nccn.org/professionals/physician\\_gls/pdf/breast.pdf](https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf) [Accessed 26 January 2017].
- [12] Francisci S, Guzzinati S, Mezzetti M, Crocetti E, Giusti F, Miccinesi G, et al. Cost profiles of colorectal cancer patients in Italy based on individual patterns of care. *BMC Cancer* 2013;13:329.
- [13] Jensen OM, Parkin DM, MacLennan R, Muir CS, Skeet RG, editors. Cancer registration: principles and methods. Lyon, France: International Agency for Research on Cancer; 1991. IARC Scientific Publications, No95. <http://www.iaarc.fr/en/publications/pdfs-online/epi/sp95/> [Accessed 03 February 2017].
- [14] Regione Emilia-Romagna Health. Healthcare range of fees (Nomenclature tariffario regionale). 2016 (Updated November 2016). [http://salute.regione.emilia-romagna.it/documentazione/nomenclature-tariffario-rer/nomenclature\\_tariffario-nov/view](http://salute.regione.emilia-romagna.it/documentazione/nomenclature-tariffario-rer/nomenclature_tariffario-nov/view) [Accessed 03 February 2017].
- [15] Bonastre J, Jan P, Barthe Y, Koscielny S. Metastatic breast cancer: we do need primary cost data. *Breast* 2012;21:384–8.
- [16] Montero AJ, Eapen S, Gorin B, Adler P. The economic burden of metastatic breast cancer: a U.S. managed care perspective. *Breast Cancer Res Treat* 2012;134:815–22.
- [17] Capri S, Russo A. Cost of breast cancer based on real-world data: a cancer registry study in Italy. *BMC Health Serv Res* 2017;17:84.
- [18] Wilson AR, Marotti L, Bianchi S, Biganzoli L, Claassen S, Decker T, et al. The requirements of a specialist breast centre. *Eur J Cancer* 2013;49:3579–87.
- [19] Del Turco MR, Ponti A, Bick U, Biganzoli L, Cserni G, Cutuli B, et al. Quality indicators in breast cancer care. *Eur J Cancer* 2010;46:2344–56.