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Tumour Review

Follow-up of early breast cancer in a public health system: A 2024 AIGOM consensus project

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ABSTRACT

Breast cancer stands as the most frequently diagnosed cancer and the primary cause of cancer-related mortality among women worldwide, including Italy. With the increasing number of survivors, many are enrolled in regular follow-up programs. However, adherence to recommendations from scientific societies (such as ASCO, ESMO, AIOM) for breast cancer follow-up management varies in daily clinical practice across different cancer centers, potentially resulting in unequal management and escalating costs.

To address these concerns, the Italian Association of Multidisciplinary Oncology Groups (AIGOM) orchestrated a Consensus on early Breast Cancer follow-up utilizing the Estimate-Talk-Estimate methodology. Following the identification of 18 Items and 38 statements by a select Board, 46 out of 54 (85.1%) experts comprising a multidisciplinary and multiprofessional panel expressed their degree of consensus (Expert Panel).

The Expert Panel underscores the potential for the multidisciplinary team to tailor follow-up intensity based on the individual risk of recurrence. In selected cases, the general practitioner may be recommended as the clinical lead for breast cancer follow-up, both after completion of adjuvant treatment and at early initiation of endocrine therapy in low-risk patients. Throughout follow-up, and alongside oncologic surveillance, the expert panel advises osteometabolic, cardiologic, and gynecologic surveillance for the early detection and management of early and late treatment toxicities. Moreover, preserving quality of life is emphasized, with provisions for psycho-oncologic support and encouragement to adopt protective lifestyle behaviors.

Introduction

Breast cancer (BC) is the most prevalent cancer globally, representing 24.5 % of the 9.2 million new cases reported in 2020. It remains the leading cause of cancer-related deaths among women, accounting for 15.5 % of the 4.4 million cancer-related deaths [1]. This pattern is consistent across Europe [2] and Italy [3], where BC ranks as the most common neoplasm among women, with 355,457 new cases in Europe and 54,976 in Italy in 2020. It also stands as the primary cause of cancer mortality among females, with 91,826 deaths in Europe and 12,995 in Italy [2,4].

With a improving prognosis, boasting a 5-year survival rate of 81.8 % in Europe [5] and 87 % in Italy [4], the population of BC survivors has grown significantly, with approximately 12.2 million survivors in Europe and 834,154 in Italy in 2020 [3]. Within this cohort, around 30 % were diagnosed within the past 5 years, with an additional 23 % diagnosed between 5 and 10 years ago.

The majority of these patients are enrolled in follow-up programs aimed at early detection of loco-regional recurrence and second breast cancer (homo/contralateral), as well as at monitoring of adjuvant treatment toxicities, lifestyle interventions, optimization of adjuvant endocrine therapy adherence, and facilitation of rehabilitation and reintegration into society and work life.

Despite recommendations from esteemed scientific societies such as AIOM [6], ESMO [7], and ASCO [8,9], adherence to standardized follow-up protocols remains low, both in Europe [10] and Italy [11,12], leading to disparities in BC surveillance across cancer centers.

Recognizing these challenges, the Italian Association of Multidisciplinary Oncology Groups (AIGOM) organized a Consensus Conference on 31 March 2023, engaging experts in the multi-disciplinary and multiprofessional management of BC follow-up to address these issues and foster standardized follow-up practices [13].

Materials and methods

The consensus process started using the Estimate-Talk-Estimate (ETE) methodology (Fig. 1) [14,15].

Achieving a consensus is strongly correlated with motivational (the willingness to engage in decision making) and cognitive (how information is processed) aspects of the individuals involved in the consensus group, as well as the aspects of the social dynamics developing within the consensus group. Meetings that directly bring these individuals to interact are thus influenced by the social-emotional dynamics that govern the functioning of the group [16,17]. The ETE method is a formal means of achieving consensus that was developed precisely in an attempt to overcome some of the negative aspects of group dynamics and to facilitate group decision-making [18,19] by combining activities that limit verbal interactions with face-to-face meetings [20].

A multi-disciplinary Board of nine health professionals involved in BC diagnosis/treatment and follow up was selected and included six medical oncologists, one radiation oncologist, one methodologist, and one general practitioner. Each panelist was requested to blindly suggest the most relevant issues (or items) related to breast cancer follow-up, that deserve attention and discussion.

These issues were then harmonized and grouped by a senior clinical epidemiologist, trained in developing group consensus (the facilitator), into 18 items that were proposed to the board members in a face-to-face meeting. The harmonized items were discussed to reach an agreement between the facilitator's work and the experts' opinions. Thereafter, the Board members individually drew up one or more statements concerning each of the 18 agreed items.

In a second virtual face-to-face meeting, the Board members and the facilitator reviewed and further discussed the harmonized statements, and finally agreed on a total of 38 statements. The statements generated in this way were then presented via an online scoring platform to the 54 members of an extended multidisciplinary panel of experts (Expert Panel) who expressed their degree of consensus by means of a 9-point numerical rating scale ranging from 1 (= totally disagree) to 9 (= totally agree) (Fig. 2). A median score of $\geq$ 7 was considered the threshold of consensus for each statement.

Forty-six out of 54 (85.1 %) members of a multidisciplinary and multiprofessional Expert Panel expressed their degree of consensus for each statement. These 46 experts included 25 medical oncologists, 1 territorial medical oncologist, 8 radiation oncologists, 4 breast surgeons, 2 radiologist, 1 obstetrics and gynecology specialist, 1 case manager, 1 psycho-oncologist, 1 general practitioner and 2 professionals from the IRCCS medical direction.

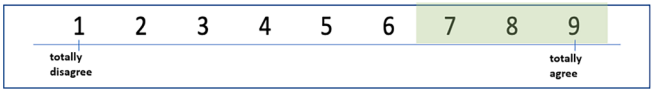

Fig. 2. Numerical rating scale.

The components of the Expert Panel worked in Breast Units with more than 150 new breast cancer cases/year. The 46 experts were located all over Italy, with the following distribution by macroarea: 22 (47.8 %) in the North, 21 (45.6 %) in the Center, and 3 (6.52 %) in the South /Islands.

Finally, scoring results were presented at the AIGOM Consensus Web Conference held on October 30, 2023.

Statements

All statements had a median score $\geq$ 7 (threshold value).

The levels of agreement or disagreement (median score and range) for each statement reported by 46 members of Expert Panel are shown below.

Item 1. Goals of follow up.

Statement 1.1- Early diagnosis of locoregional recurrence and second breast cancer.

Expert Panel recommended this statement with a median score: 9 (range 2–9).

Statement 1.2 – Timely diagnosis of breast cancer distant recurrence.

Expert Panel recommended this statement with a median score: 9 (range 2–9).

Statement 1.3 –Monitoring of acute and chronic toxicities of adjuvant treatments.

Expert Panel recommended this statement with a median score: 9 (range 2–9).

Statement 1.4 – Assessment of patients' adherence to adjuvant therapies.

Expert Panel recommended this statement with a median score: 9 (range 4–9).

Statement 1.5 – Lifestyle interventions.

Expert Panel recommended this statement with a median score: 9 (range 4–9).

Statement 1.6 – Facilitation of rehabilitation pathways and reintegration into social and working life.

Expert Panel recommended this statement with a median score: 8 (range

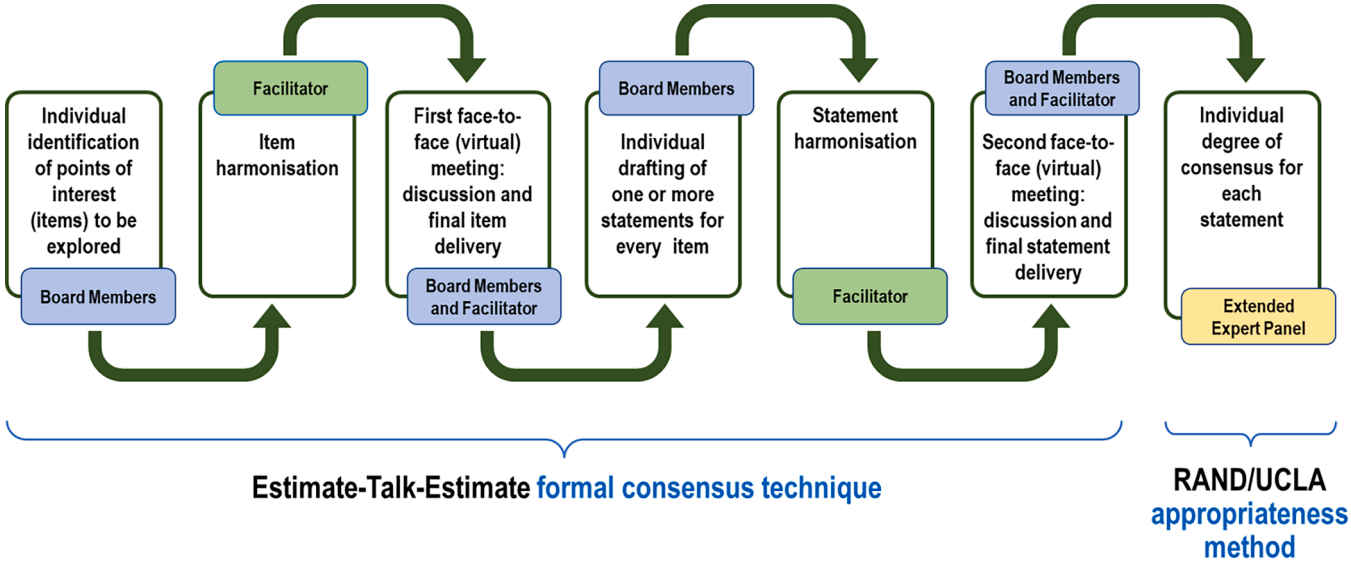

Fig. 1. The workflow of the consensus process.

2–9).

Item 2. Identification of the clinical coordinator and health care actors involved in follow-up.

Statement 2.1 –The multidisciplinary team defines the type and duration of follow-up strategies.

Expert Panel recommended this statement with a median score: 8 (range 1–9).

Statement 2.2 –The clinical coordinator of the surveillance program may be the medical oncologist, radiation oncologist, breast surgeon or general practitioner.

Expert Panel recommended this statement with a median score: 8 (range 2–9).

Statement 2.3- The working group, in addition to oncology and diagnostic specialists, should include the psychologist and the nurse.

Expert Panel recommended this statement with a median score:8.5 (range 2–9).

Item 3. Criteria for patient intake by the general practitioner.

Statement 3.1-The general practitioner can assume the role of clinical referrer after having received from the specialist a personalized oncology history with instructions on how to continue the surveillance program.

Expert Panel recommended this statement with a median score: 8 (range 1–9).

Statement 3.2- It is desirable to build a model of exclusive patient care by the general practitioner according to residual risk of recurrence.

Expert Panel recommended this statement with a median score:7.5 (range 1–9).

Statement 3.3- Referring hospital specialists should always remain available for prompt resumption of patient care in the presence of suspicious signs/symptoms of recurrence.

Expert Panel recommended this statement with a median score: 9 (range 3–9).

Item 4. Patients' expectations with respect to follow-up.

Statement 4.1- Limited experiences report high patient expectations regarding the opportunity for early detection of local or distant recurrence of disease during follow-up.

Expert Panel recommended this statement with a median score: 8 (range 2–9).

Statement 4.2- In general, patients expect to have more instrumental examinations, more frequent blood tests and clinical examinations.

Expert Panel recommended this statement with a median score:8 (range 3–9).

Statement 4.3- Patients tend to feel reassured by a follow-up aimed at early detection of loco-regional or distant recurrence, thinking that, in the presence of disease recurrence, antitumor treatment can be promptly started.

Expert Panel recommended this statement with a median score:8 (range 4–9).

Statement 4.4- In many cases, however, follow-up can create anxiety in the patient especially in the imminence of performing instrumental tests and periodic oncology examination.

Expert Panel recommended this statement with a median score:9 (range 5–9).

Item 5. Follow-up: criteria for inclusion and exclusion

Statement 5.1- All patients who have undergone surgery for breast cancer should be included.

in an oncology surveillance program, with the possible exclusion of patients with very advanced age and/or worsening clinical conditions.

Expert Panel recommended this statement with a median score:9 (range 1–9).

Item 6. Tailoring of procedures.

Statement 6.1- Patients with early-stage breast neoplasia are candidates for more or less intensive and individualized adjuvant treatment based on prognostic risk derived from the association between molecular subtypes and tumor stage and the type of response to neoadjuvant treatment, if performed.

Expert Panel recommended this statement with a median score:9 (range 7–9).

Statement 6.2- Although in the current absence of diriment evidence it is still desirable to adopt the criterion of escalation vs de-escalation in follow-up planning, as already in use for the choice of adjuvant treatment.

Expert Panel recommended this statement with a median score: 9 (range 2–9).

Item 7. Duration and frequency of clinical surveillance.

Statement 7.1- Established practice requires that clinical follow-up be performed every 3–6 months in the first 3 years, every 6 months in the next 2 years, and then annually until excess cancer mortality is defined as negligible ("time to cure"). However, these intervals are arbitrary and worthy of redefinition based on the prognostic risk profile.

Expert Panel recommended this statement with a median score:9 (range 2–9).

Item 8. Imaging for early detection of disease recurrence.

Statement 8.1- To date, mammographic surveillance is the only imaging strategy that is associated.

with a reduction in mortality among women with prior breast cancer, regardless of age.

Expert Panel recommended this statement with a median score: 9 (range 6–9).

Statement 8.2- Mammography monitoring should continue throughout life and is also recommended for elderly patients with reasonable life expectancy and in the absence of major.

comorbidities.

Expert Panel recommended this statement with a median score: 9 (range 5–9).

Statement 8.3- Breast and axillary ultrasound is a useful additional exam in selected cases for early detection of loco-regional recurrences.

Expert Panel recommended this statement with a median score: 8 (range 3–9).

Statement 8.4- Breast Magnetic Resonance Imaging (MRI) of the breast is not recommended in the routine follow-up examinations but can be considered in selected cases.

Expert Panel recommended this statement with a median score: 9 (range 7–9).

Statement 8.5- No further imaging investigations are suggested in the absence of signs/symptoms; however, other instrumental examinations may be considered in selected cases.

Expert Panel recommended this statement with a median score: 9 (range 5–9).

Item 9. Biomarkers for early detection of disease recurrence.

Statement 9.1- The use of tumor markers is not indicated in the surveillance/follow-up pathway.

Expert Panel recommended this statement with a median score: 8 (range 3–9).

Item 10. Osteometabolic surveillance.

Statement 10.1- Osteometabolic surveillance is recommended in order to avoid, or at least reduce,

trabecular bone damage related to adjuvant treatments.

Expert Panel recommended this statement with a median score: 9 (range 7–9).

Item 11. Cardiological surveillance.

Statement 11.1- Cardiological surveillance should be performed in patients during and after

treatment regimens including anthracyclines and/or anti-HER2 antibodies.

Expert Panel recommended this statement with a median score:9 (range 4–9).

Item 12. Gynecologic surveillance.

Statement 12.1- Women taking tamoxifen should be monitored annually with a gynecologic examination and, in selected patients, also with a transvaginal ultrasound.

Expert Panel recommended this statement with a median score: 9 (range

1–9).

Statement 12.2- Iatrogenic problems of the genital sphere should be carefully considered.

Expert Panel recommended this statement with a median score: 9 (range 7–9).

Item 13. Quality of Life Assessment.

Statement 13.1- Psycho-social parameters that can be correlated with illness or ongoing treatment, such as depression, anxiety, worry, stress, difficulties in family and social relationships, difficulties in resuming work, and economic difficulties should be considered during the follow-up visit.

Expert Panel recommended this statement with a median score: 9 (range 4–9).

Item 14. Psycho-oncological support.

Statement 14.1- Patients should be provided with psycho-oncological support even in the phase following active antineoplastic treatments.

Expert Panel recommended this statement with a median score: 9 (range 5–9).

Item 15. Surveillance of late toxicities.

Statement 15.1- Monitoring of late-onset systemic and/or locoregional treatment-induced toxicities (such as, lymphedema, hormonal/hormone deprivation-related disorders, neuropathy,

cognitive impairment, chronic pain, gonadal toxicity, and infertility), which can significantly undermine quality of life, return to work and social life, is strongly recommended.

Expert Panel recommended this statement with a median score: 9 (range 6–9).

Statement 15.2- A multidisciplinary rehabilitation intervention, both physical and psychological, involving hospital/territory/general practitioner/other stakeholders (patient associations/charities) might be quite helpful for the prevention/management of therapy-related toxicities.

Expert Panel recommended this statement with a median score: 9 (range 6–9).

Item 16. Lifestyle recommendations.

Statement 16.1- The adoption of a protective lifestyle, including interventions on alcohol consumption/smoking attitude, control of overweight/obesity, and regular exercise, should be suggested to all patients for cancer risk reduction (recurrence and new cancer) and quality of life improvement.

Expert Panel recommended this statement with a median score: 9 (range 7–9).

Item 17. Role of telemedicine.

Statement 17.1- Telemedicine should improve treatment adherence and provide training, educational, and motivational support to patients' empowerment in their care and surveillance pathway.

Expert Panel recommended this statement with a median score: 8 (range 2–9).

Statement 17.2- Regular teleconsultation meetings between hospital and community health workers could ensure adequate oncology surveillance for patients.

Expert Panel recommended this statement with a median score: 7 (range 4–9).

Item 18. Health sustainability.

Statement 18.1- A model of hospital-territory integration with defined pathways should promote an improvement in the appropriate prescription of examinations and visits and a shared management of patients, capable of ensuring the sustainability of the follow-up program.

Expert Panel recommended this statement with a median score:9 (range 5–9).

Statements and related rationales are reported in Table 1.

Discussion

The comprehensive follow-up of cancer patients is a crucial component of long-term disease management, aimed at optimizing outcomes and enhancing quality of life. In case of localized BC treated with curative intent, the BC surveillance is part of the public health initiatives targeting secondary and tertiary prevention. These public health initiatives diverge from individual diagnostic interventions and are aligned with the goals and principles of health promotion and disease prevention, catering to apparently healthy populations with varying risks of disease recurrence.

Today, there is a compelling argument for re-evaluating the outdated 'one-size-fits-all' approach in BC follow-up strategies. Recent advancements in local and systemic treatments necessitate a discussion on personalized risk prediction models, time-adapted imaging, and clinical assessments for anticipating diagnosis.

This shift in perspective would evolve BC follow-up into an integrated, multidisciplinary medical practice. Such an approach would not only promote adherence to adjuvant therapies, but also facilitate the monitoring of treatment-related toxicities, the implementation of lifestyle interventions, and the provision of support for rehabilitation, as well as social and working-life reintegration

In this evolving scenario, the consensus explored 3 major areas of interest in the BC follow-up:

- the first area focuses on the general objectives and tailored management of the BC follow-up (items 1–9);
- the second area delves into the role of clinical surveillance in different disciplinary contexts (items 10–12);
- the final area addresses psychosocial intervention, quality of life, working-life reintegration, and lifestyle modifications (items 13–16).

The experts panel agrees that a comprehensive BC follow-up is essential for optimizing long-term outcomes and patients' quality of life (Statement1.1). This entails early diagnosis of loco-regional recurrence, adherence to adjuvant therapies, monitoring of treatment-related toxicities, lifestyle interventions, and support for rehabilitation and working-life re-integration (Statements 1.3–1.6).

While timely identification of BC loco-regional recurrence and second BC is considered critical in the BC follow-up for improving outcomes, the role of early distant recurrence detection remains debated among the panelists (Statement 1.2). Few studies are evaluating new strategies to increase the rate of detection of BC early distant recurrence [131,132] and further trials are necessary, especially for patients at mid to high risk of recurrence. One notable ongoing effort is the prospective SURVIVE trial (NCT05658172), which uses circulating tumor cells (CTC) and circulating tumor DNA (ctDNA) biomarkers to guide standard versus intensive early BC surveillance.

The experts recognized the crucial role of effective management of treatment-related toxicities in ensuring adherence to adjuvant therapies and increasing the patients' quality of life. In particular, since adherence to adjuvant therapies plays a crucial role in reducing the risk of recurrences, the panels underscore the relevance of providing patient support to enhance treatment compliance.

The panel concurs that in specific instances (including advanced age, co-morbidities, low risk), enhancing the involvement of general practitioners (GPs) should be advocated, having them assume full responsibility for the patient's follow-up, in close coordination with the referring hospital, and ensuring prompt resumption of breast cancer (BC) specialist evaluation when necessary (Statements 3.2–3.3). Moreover, recognizing the disparity between patients' expectations and healthcare professionals' perceptions regarding follow-up, the panelists suggest educational initiatives and effective communication to enhance patients' understanding of follow-up objectives and management (Statements 4).

There was widespread consensus on the crucial role of the multidisciplinary team (MDT) in designing and orchestrating a personalized follow-up plan for breast cancer (BC), taking into account the unique characteristics of each patient and their disease (Statement 2.1)..

Table 1
Statements and related rationales.

ITEM 1. Goal of follow up

Statement 1.1 –Early diagnosis of locoregional recurrence and second breast cancer.
Overall survival, detection of breast cancer (BC) recurrence, and quality of life (QoL) are critical parameters for assessing the effectiveness of surveillance programs. Both national and international guidelines emphasize the importance of timely and early diagnosis of locoregional recurrence and second BC as key principles of BC follow-up. Evidence suggests that patients who experience local recurrence have a lower survival rate compared to those who do not [21,22]. Additionally, early detection of metachronous contralateral BC has been shown to improve survival outcomes [23].

Statement 1.2- Timely diagnosis of breast cancer distant recurrence. In asymptomatic patients, current guidelines recommend conducting a thorough history, physical examination, and counseling to detect any signs or symptoms of distant breast cancer recurrence. There is no evidence supporting the use of additional laboratory tests or imaging during a surveillance program to improve overall survival [24–26]. However, caution is advised when interpreting data from randomized clinical trials, as these studies were conducted nearly two decades ago, when our understanding of breast cancer biology was limited, advanced imaging technologies were not as readily available, and the range of effective treatments, both local and systemic, was not as comprehensive as it is today [27].

Statement 1.3- Monitoring of acute and chronic toxicities of adjuvant treatments. A careful assessment and management of early and late side-effects of different BC treatments (including surgery, radiotherapy and systemic therapy) should represent one of the main aims of the surveillance program [6–8]. Thus, the clinicians should provide the patient with a cancer treatment summary to identify all possible side effects, with particular attention to body image concerns, lymphedema, cardiotoxicity, cognitive impairment, distress, depression and anxiety, fatigue, bone health, pain and neuropathy, sexual dysfunction, infertility and premature menopause [8].

Statement 1.4- Assessment of patients' adherence to adjuvant therapies. In early hormone receptor-positive breast cancer (BC) patients, increased survival and reduced recurrence or second primary BC are strongly correlated with the use of adjuvant endocrine therapy. However, this therapy can cause adverse events that limit treatment adherence and affect patients' quality of life (QoL) [28]. Research indicates that treatment adherence decreases by an average of 25.5 % from the first to the fifth year [29]. These findings underscore the importance of not only developing effective treatments but also managing side effects to improve long-term adherence and ultimately overall patient outcomes [7,8].

Statement 1.5- Lifestyle interventions.
Adopting protective lifestyle behaviors is generally recommended for preventing cancer, reducing the risk of BC recurrence, and mitigating treatment adverse effects, thereby enhancing QoL [30,31]. While data on the improvement of BC patients' clinical outcomes through lifestyle interventions are limited and primarily derived from observational studies [32], lifestyle modifications (as changes in diet, body-weight control, physical activity, and smoking cessation) can have broader implications in reducing BC recurrence and beyond. Indeed, these modifications may impact other medical conditions, ultimately influencing survival outcomes. Therefore, clinicians should advise BC patients to adopt or maintain a healthy lifestyle [6–8].

Statement 1.6 – Facilitation of rehabilitation pathways and reintegration into social and working life
The physical and psychological adverse effects of therapies can substantially influence breast cancer (BC) patients' reintegration into social and working life [33]. The surveillance program should provide support and information, facilitating access to specialized rehabilitation services to ensure a return to normal life after BC [7,34,35].

Item 2. Identification of the clinical coordinator and health care actors involved in follow-up.

Statement 2.1 –The multidisciplinary team (MDT) defines the type and duration of follow-up strategies.
The MDT comprises various specialists, including medical oncologists, surgeons, radiation oncologists, radiologists, pathologists, breast care nurses and others health care professionals involved in the comprehensive treatment of BC patients, with the goal of identifying the most suitable diagnostic and therapeutic approach for each individual patient [36]. This interdisciplinary approach ensures that patients receive personalized care tailored to their unique medical history, tumor characteristics, and personal preferences, leading to optimized treatment outcomes and improved overall quality of care. BC patients evaluated by MDTs derived a greater BC survival than those who did not (HR = 0.80; 95 % CI 0.73–0.88) [37]. Indeed, the MDT plays a crucial role in not only determining the initial treatment plan, but also in defining the type and duration of the patient follow-up [38,39]. In selected cases, this follow-up may be tailored at individual level according to the specific characteristics of patients and disease, for a comprehensive surveillance strategy.

Statement 2.2 –The clinical coordinator of the surveillance program may be the medical oncologist, radiation oncologist, breast surgeon or general practitioner. In a scoping review conducted to identify and classify the definitions and characteristics of multidisciplinary BC care [36], the composition of the MDT was described in 62 % of the 191 studies evaluated, but there was no indication of which professional figure was best suited to perform as clinical coordinator during the follow up. As of now, the appointment of this person is typically governed by local policies and healthcare professionals who usually assume this role include medical oncologists, radiation oncologists, breast surgeons, or general practitioners. The choice of clinical coordinator is often determined by the expertise of the individual practitioner, the specific needs of the patient, and the resources available within the healthcare setting. This flexible approach allows for adaptation to the unique circumstances of each patient and facilitates comprehensive and patient-centered follow-up care.

Statement 2.3- The working group, in addition to oncology and diagnostic specialists, should include the psychologist and the nurse.
The composition of the MDT includes a breast nurse [36]. Reconstructive surgeon, psychologist, physical therapist, pharmacist, and clinical trial coordinator may be called if their presence is necessary in the MDT for the discussion of individual clinical cases. However, the role of the psychologist in the MDT should be defined both in the initial discussion and during the follow up, in order to improve the quality of care [40].

Item 3. Criteria for patient intake by the general practitioner

Statement 3.1-The general practitioner can assume the role of clinical referrer after having received from the specialist a personalized oncology history with instructions on how to continue the surveillance program
Typically, early BC patients are followed up by the medical oncologist for up to 5 years after diagnosis or until the end of adjuvant hormone therapy.After the conclusion of the specialist oncology follow-up period, a sequential follow-up model may be implemented, wherein the patient transitions back to the care of their general practitioner (GP) . The specialist provides the general practitioner with a personalized oncology history, along with instructions on how to continue the surveillance regimen. At this juncture, the general practitioner may undertake the role of clinical referrer, assuming full responsibility for the patient's ongoing surveillance program. Given that the risk of recurrence persists for up to 15 years following primary treatment and beyond, particularly in ER-positive breast cancer patients [41], it is imperative that continuity of care is maintained by a general practitioner with expertise in the surveillance of cancer patients and proficiency in breast examination [42]. This ensures that patients receive consistent monitoring and support throughout their survivorship journey, thereby optimizing long-term outcomes and QoL.

Statement 3.2- It is desirable to build a model of exclusive patient care by the general practitioner according to residual risk of recurrence. In 3 randomized studies that evaluated follow-up conducted by a specialist at a multidisciplinary breast clinic compared to that delivered by a general practitioner [43–45], no difference was reported in the rate of recurrence-related serious clinical event [45], time between first presentation of symptoms and recurrence confirmation [43] and time to detection of recurrence [44]. The Cochrane systematic review reported no differences in terms of overall survival and disease-free survival between centralized and de-centralized follow-up [27,43,45], supporting the participation of the general practitioner in the delivery of follow-up care, within an organization that ensures easy access to hospital care when needed.
A model of exclusive patient care by the general practitioner may be envisaged in low risk patients.

Statement 3.3- Referring hospital specialists should always remain available for prompt resumption of patient care in the presence of suspicious signs/symptoms of recurrence.
All the guidelines [6–8] emphasize that, in the presence of suspicious signs/symptoms of recurrence, the specialist should be available for prompt resumption of patient care [27]. Indeed, in the presence of local or regional recurrence, a strong collaboration among all the specialists of the MDT is crucial to define and start the optimal diagnostic and therapeutic approach in the shortest time [46].

Item 4. Patients' expectations with respect to follow-up.

Statement 4.1- Limited experiences report high patient expectations regarding the opportunity for early detection of local or distant recurrence of disease during follow-up.
Few studies have evaluated patients' perspectives regarding follow-up strategies and the most important emerging theme was the patients' desire for reassurance regarding the non-recurrence of their cancer. A study conducted in 288 patients revealed that the primary expectation regarding follow-up was surveillance aimed at early detection of recurrence (reported by 93 % of the participants), followed by the need for addressing anxiety related to side effects from adjuvant treatments [47].

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Table 1 (*continued*)

ITEM 1. Goal of follow up

Statement 1.1 –Early diagnosis of locoregional recurrence and second breast cancer.

Overall survival, detection of breast cancer (BC) recurrence, and quality of life (QoL) are critical parameters for assessing the effectiveness of surveillance programs. Both national and international guidelines emphasize the importance of timely and early diagnosis of locoregional recurrence and second BC as key principles of BC follow-up. Evidence suggests that patients who experience local recurrence have a lower survival rate compared to those who do not [21,22]. Additionally, early detection of metachronous contralateral BC has been shown to improve survival outcomes [23].

Statement 4.2- In general, patients expect to have more instrumental examinations, more frequent blood tests and clinical examinations.

A significant portion of women expressed a preference for incorporating additional diagnostic investigations, such as X-ray and blood tests, into their routine follow-up visits, and more than half of the patients indicated a preference for a life-long follow-up [48]. Patient preferences appear to diverge from the existing evidence that does not report an advantage in OS in detecting asymptomatic metastases by intensive follow up [24,25]. Despite the disappointing evidence, the patient's preference for intensive follow-up still persists [49].

Statement 4.3- Patients tend to feel reassured by a follow-up aimed at early detection of loco-regional or distant recurrence, thinking that, in the presence of disease recurrence, antitumor treatment can be promptly started.

The patients' expectation that increased testing for the early detection of metastases could increase their chances of survival may indicate a gap in the understanding of the primary objectives of follow-up care. Current data from a *meta*-analysis of 2263 BCE survivors from 13 studies shows a survival benefit from early detection of asymptomatic loco-regional or contra-lateral breast cancer recurrences [50] but, at this time, surveillance for distant recurrence is not considered amenable to curative treatment or associated with a survival benefit [24,25].

Statement 4.4- In many cases, however, follow-up can create anxiety in the patient, especially in the imminence of performing instrumental tests and periodic oncology examination. In a cross-sectional survey, patients with high scores on the HADS-anxiety and depression scale showed a greater preference for performing further investigations [49]. However, nonessential interventions worsen patients' anxiety and depression, increase unnecessary testing, and increase treatment costs and resource utilization [51]. Distress can be intensified by long waiting times, lack of information, poor communication with staff, and lack of psychosocial support. Efforts should be made to improve patients' understanding of follow-up goals and to provide more psychological support even after treatment ends [40,52,53].

Item 5. Follow-up: criteria for inclusion and exclusion.

Statement 5.1- All patients who have undergone surgery for breast cancer should be included in an oncology surveillance program, with the possible exclusion of patients with very advanced age and/or worsening clinical conditions. After the diagnosis of BC, a surveillance program, including mammographic evaluation, is recommended for all BC patients (1,2) with sufficient life expectancy, as such a program has been shown to reduce mortality from BC even in elderly patients (see Statement 8.1) [54,55].

However, elderly patients with BC often have additional chronic conditions, competing health risks, and represent a complex and heterogeneous population, so evidence-based guidelines about optimal follow-up are not available today [56]. Physicians should carefully assess all concomitant chronic conditions and integrate them into an appropriate individual follow-up program, including the option of excluding patients from oncology follow-up in selected cases, transferring their care to the primary care physician [57].

Item 6. Tailoring of procedures.

Statement 6.1- Patients with early-stage breast neoplasia are candidates for more or less intensive and individualized adjuvant treatment based on prognostic risk derived from the association between molecular subtypes and tumor stage and the type of response to neoadjuvant treatment, if performed. BC patients receive tailored adjuvant treatments based on the estimated risk of BC recurrence and on relevant prognostic factors, including molecular subtypes, disease stage and individual features (age and comorbidities). Accordingly, more aggressive therapies (local and systemic) are recommended in BC patients with high risk of recurrence, while less intensive treatments are indicated in case of low-risk [39,58]. Recently, the introduction of genomic and genetic BC assessment has led to a further refinement of tailored care [59]. Furthermore, the adoption of a neoadjuvant approach facilitates the personalized adjustment of subsequent adjuvant therapies, considering individual responsiveness to prior treatments, as showed by the Katherine, CREATEX, KEYNOTE 522, MonarchE, and Olympia trials.

Statement 6.2- Although in the current absence of diriment evidence, it is still desirable to adopt the criterion of escalation vs de-escalation in follow-up planning, as already in use for the choice of adjuvant treatment.

Literature findings confirmed varying timings and patterns of metastatic spread associated with molecular subtypes and disease stage [60–62]. This evidence underscores the need for a risk-adapted surveillance strategy to enable early detection of recurrent breast cancer in high-risk patients, while considering de-intensification of follow-up in low-risk patients. Despite previous randomized data [24–26] not advocating for "intensive" surveillance, recent advancements in imaging, biology, and therapies necessitate a fundamental reassessment of current follow-up practices [38,63]. Indeed, the possibility of an early diagnosis of a distant recurrence could be of greater value in case of oligometastatic disease, where the use of effective systemic therapies and local ablative treatments may impact on long-term outcomes [64–66]. In the era of personalized medicine, a multidisciplinary effort is needed to assess a risk-based surveillance program and further research in this field is urgently awaited.

Item 7. Duration and frequency of clinical surveillance.

Statement 7.1- Established practice requires that clinical follow-up be performed every 3–6 months in the first 3 years, every 6 months in the next 2 years, and then annually until excess cancer mortality is defined as negligible ("time to cure"). However, these intervals are arbitrary and worthy of redefinition based on the prognostic risk profile. The available evidence suggests that clinical examinations, combined with adequate history taking, are a decisive tool in detecting locoregional recurrence and/or second breast neoplasia (15 %- 46 %) [8,9,49,67,68]. To ensure timely detection of treatable BC recurrences, ASCO [8,9], ESMO [7], and AIOM [6] guidelines recommend regular follow-up visits for up to 10 years post-treatment or beyond [69]. In the initial 3 years post-treatment, when a peak in distant relapses is observed, intensified follow-up with clinical examinations every 3–6 months is advised. After the first 3 years, follow-up visits every 4–6 months for an additional 2 years, followed by annual visits for 5 years or more, are recommended, but these intervals are arbitrary. However, the primary focus of follow-up is the identification of potentially treatable locoregional disease relapses rather than distant recurrences, as the risk of locoregional relapse persists for at least 10 years at a consistent rate [70,71]. Uncertainties remain regarding the long-term impact and optimal timing of clinical examinations compared to self-detection or mammography, given the relatively low detection rate of overall relapses after breast-conservation surgery [71,72]. Due to the heterogeneity of BC subtypes in terms of prognosis and treatments received, there is a growing call for more tailored recommendations that consider individual patient characteristics [38].

Item 8. Imaging for early detection of disease recurrence.

Statement 8.1- To date, mammographic surveillance is the only imaging strategy that is associated with a reduction in mortality among women with prior breast cancer, regardless of age. Surveillance mammography aims to detect ipsilateral BC recurrence (IBTR), ipsilateral second primary cancer in the residual breast after conservative surgery, and metachronous contralateral BC (MCBC) [73]. Evidence evaluating the impact of early detection on survival comes from observational studies. A *meta*-analysis [50] and 4 observational studies reported positive impacts on overall survival, mortality from all causes, and breast cancer-specific mortality [54,55,74,75] with mammography, also in older patients [55,75].

However, other imaging strategies like MRI, breast ultrasound, bone scan, chest x-ray, and liver ultrasound did not show a reduction in mortality in women with prior breast cancer [24,25].

Statement 8.2- Mammography monitoring should continue throughout life and is also recommended for elderly patients with reasonable life expectancy and in the absence of major comorbidities.

There is no age threshold for which it is possible to suggest discontinuance of surveillance mammography. Mammography should be performed in all patients with a reasonable life expectancy in the absence of serious comorbidities. Data from an observational study in 1846 patients aged 65 years or older with stage I-II BC diagnosed from 1990 to 1994 suggest that mammography reduces the risk of death even among elderly patients [55]. Significant reduction of BC mortality was associated with annual mammograms (odds ratio = 0.69; 95 % CI, 0.52–0.92) [Lash JCO 2007] and the protective effect of surveillance mammography was stronger in women 80 years or older at diagnosis.

Statement 8.3- Breast and axillary ultrasound is a useful additional exam in selected cases for early detection of locoregional recurrences.

Breast ultrasound plays a crucial role in the diagnosis and evaluation of BC. However, it is generally not considered a standalone screening method for women at average risk. Mammography has shown higher sensitivity in detecting early breast cancers, particularly those that are not palpable or visible on ultrasound. Nonetheless, breast ultrasound is frequently employed as an adjunctive or supplementary screening method in specific situations, including: evaluation of dense breasts (where mammography may be less sensitive; combining findings from six single-center trials [76–81] and three multi-center trials [82–84], showed that supplementary breast ultrasound screening significantly boosts the

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Table 1 (*continued*)

ITEM 1. Goal of follow up

Statement 1.1* –*Early diagnosis of locoregional recurrence and second breast cancer.

Overall survival, detection of breast cancer (BC) recurrence, and quality of life (QoL) are critical parameters for assessing the effectiveness of surveillance programs. Both national and international guidelines emphasize the importance of timely and early diagnosis of locoregional recurrence and second BC as key principles of BC follow-up. Evidence suggests that patients who experience local recurrence have a lower survival rate compared to those who do not [21,22]. Additionally, early detection of metachronous contralateral BC has been shown to improve survival outcomes [23].

detection of node-negative invasive BC in women with mammographically dense breast tissue); characterization of abnormal findings (in cases where a suspicious mass or lesion is detected on mammography); screening in high-risk women (for those with a higher risk due to family history or genetic factors, in addition to mammography and/or MRI [85]). Additionally, continuing annual ultrasound screening (incidence screening) reveals an extra detection of 3.7 cancers per 1000 women screened each year, exceeding the efficacy of mammography alone, especially for node-negative BC and specific subtypes (invasive lobular carcinoma and low-grade ductal invasive carcinoma). However, despite a potential decrease of the risk of false positives with annual screening ultrasound compared to mammography alone, it may still be responsible for a considerable rate of futile biopsies (5.0 % of woman perform a biopsy prompted solely by incidence screening ultrasound, 92 % of them without cancer) [85].

Statement 8.4- Breast Magnetic Resonance Imaging (MRI) of the breast is not recommended in the routine follow-up examinations but can be considered in selected cases. In line with established guidelines, MRI is typically not included in routine follow-up examinations, with preference given to alternative imaging modalities such as mammography [86]. Nevertheless, it may be considered in specific cases, for a personalized and targeted breast cancer surveillance [86], including: high risk patients (due to genetic factors (e.g., BRCA1/2) or family history, particularly those with a lifetime risk exceeding 20–25 %); uncertain findings (when other imaging modalities, as mammography or ultrasound, yield inconclusive results or when further characterization is needed); post-surgical outcomes evaluations.

Statement 8.5- No further imaging investigations are suggested in the absence of signs/symptoms; however, other instrumental examinations may be considered in selected cases. Data from randomized trials failed to demonstrate any benefit from screening for metastatic recurrences and more intensive follow-up did not translate in a survival advantage [24–26]. Consequently, the follow-up for early BC is based on a "minimalist" policy aimed at detecting locoregional recurrences and managing treatment-related adverse effects. This approach does not account for differences in breast cancer subtypes, individual prognosis, and treatment options. Moreover, it is crucial to note that those studies were often underpowered, with some limitation in the sensitivity and accuracy of the diagnostic tests employed. Additionally, there were limited treatment options available for recurrent cases, including the oligometastatic setting. In light of these limitations, the management of follow-up varies widely from center to center, irrespective of guideline recommendations. Hence in selected cases, based on an individual's breast cancer risk of recurrence, there is the possibility of considering more intensive assessment surveillance and time-adapted imaging.

Item 9. Biomarkers for early detection of disease recurrence.

Statement 9.1- The use of tumor markers is not indicated in the surveillance/follow-up pathway.

Observational studies, most retrospective, evaluating the use of CA 15- and CEA as markers for recurrence after primary and/or adjuvant therapy. A CA 15–3 [87,88] or CEA [87,88] elevation was observed in about 50–70 % of patients with cancer recurrence, while normal values appeared in 88–96 % of patients without recurrence. Marker elevation can predict recurrence 5 to 6 months, on average, before other symptoms or tests. A prospective observational clinical trial [89] found elevated CA 27.29 levels in 57.7 % of patients with breast cancer recurrence. There are no prospective randomized clinical trials to demonstrate whether detection and treatment of occult or asymptomatic metastases using tumor markers will impact on the most significant outcomes (disease-free survival, overall survival, quality of life, toxicity, or cost-effectiveness) and because a solid evidence supporting their use is lacking in the literature, the ASCO [8,87], ESMO [7] and AIOM [6] guidelines do not recommend routine measurement of CEA, CA 15–3 and CA 27.29 in the follow-up of asymptomatic patients with early BC.

Item 10. Osteometabolic surveillance

Statement 10.1- Osteometabolic surveillance is recommended in order to avoid, or at least reduce, trabecular bone damage related to adjuvant treatments. The estrogen deprivation caused by adjuvant endocrine therapies or chemotherapy can lead to increased production of RANKL (Receptor activator of nuclear factor kappa-B ligand) , resulting in enhanced osteoclast activity and bone resorption and subsequent skeletal complications. While tamoxifen has a protective effect on bone density in postmenopausal women, it induces bone loss in premenopausal women. Aromatase inhibitors, particularly when associated with LHRH analogs, also lead to bone loss, especially in premenopausal patients.Apart from cancer treatment-induced bone loss, other risk factors such as smoking, alcohol consumption, sedentary lifestyle, diet, advanced age, steroid use, and family history also need consideration. Dual-energy X-ray absorptiometry (DXA) is commonly used to assess bone mineral density (BMD) , but it may not detect early trabecular damage due to high bone turnover seen in cancer treatment-induced bone loss [90] and bone biomarkers of both resorption (e.g., HYP, CTX-1, CTSK) and formation (e.g., ALP, BALP, P1NP) can aid in monitoring bone turnover during therapy with aromatase inhibitors [91], potentially predicting fracture risk in women treated for BC. Currently, there is no consensus on the BMD threshold to initiate anti-osteoporotic therapy. The AIOM guidelines 2023 [6] strongly recommend evaluating bone metabolism and considering bisphosphonate or denosumab during adjuvant endocrine therapy for early BC, regardless of T-score values, to reduce fracture risk [92–97]. In these patients, measurements of bone resorption markers before the treatment and then at 3 and 6 months may be helpful and bone densitometry should be performed at the beginning and end of adjuvant endocrine treatment [6].

However, every treatment decision and monitoring strategies should involve collaboration between oncologists, rheumatologists, endocrinologists, and general practitioners [98].

Item 11. Cardiological surveillance

Statement 11.1- Cardiological surveillance should be performed in patients during and after treatment regimens including anthracyclines and/or anti-HER2 agents. For asymptomatic patients, left ventricular ejection fraction (LVEF) measurement every 3 months is recommended during (neo)-adjuvant treatment with trastuzumab ± pertuzumab or trastuzumab emtansine [99,100] and only at the end of therapy (after baseline evaluation) in patients during anthracycline-based therapy, as the current dosages used in the (neo)-adjuvant setting are below 250 mg/m2 for doxorubicin and 600 mg/m2 for epirubicin [101,102]. After (neo)-adjuvant therapy, indications for monitoring vary according to different subgroups of patients. Patients who experienced cardiac dysfunction during treatment with anthracyclines and/or anti-HER2 agents should undergo regular cardiology monitoring indefinitely, although randomized studies are lacking. In patients at increased risk for cardiac dysfunction, an echocardiogram may be considered between 6 and 12 months after treatment completion [103]. Patients developing asymptomatic LVEF reduction or clinical signs/symptoms of cardiac dysfunction during (neo)-adjuvant therapy or follow-up should be referred to a cardiologist for assessment and management [103]. Management of cardiovascular risk is recommended before, during, and after cancer therapy, with regular evaluation and management of modifiable risk factors (including smoking, hypertension, diabetes, dyslipidemia, and obesity) [103,104]. While the routine use of cardiac biomarkers during potentially cardiotoxic anticancer therapy is not well-established, interdisciplinary cardio-oncology cooperation is crucial for improving management and long-term outcomes, as cardiovascular diseases are a leading cause of morbidity and mortality among cancer survivors.

Item 12. Gynecologic surveillance.

Statement 12.1- Women taking tamoxifen should be monitored annually with a gynecologic examination and, in selected patients, also with a transvaginal ultrasound. Tamoxifen, a selective estrogen receptor modulator (SERM) used in BC treatment, is associated with an increased risk of endometrial cancer, particularly in postmenopausal women. The risk is marginal in premenopausal women, but regular gynecologic screening is crucial for monitoring endometrial health in all women taking tamoxifen [105,106]. The ASCO [8,9], ESMO [7], and AIOM [6] guidelines recommend individualized approaches to gynecologic screening in tamoxifen users, considering factors such as abnormal gynecologic symptoms (e.g., unusual vaginal bleeding or pelvic pain), endometrial thickness monitoring, duration of tamoxifen use (long-term use of tamoxifen is associated with a higher risk of endometrial abnormalities and cancer), and individual risk factors (e.g., age, obesity, personal or family history of cancer or gynecologic issues). Transvaginal ultrasound may be recommended based on these considerations. More frequent monitoring, including transvaginal ultrasound, may be indicated for patients on extended tamoxifen treatment (especially five years or longer) or with higher risk profiles for gynecologic morbidity. Regular communication between patients and healthcare providers is essential to promptly address any concerns or symptoms.

Statement 12.2- Iatrogenic problems of the genital sphere should be carefully considered.

Tamoxifen has estrogen-like effects on various tissues, leading to specific alterations in post-menopausal women's genital sphere [106], such as endometrial changes (especially in post-menopausal women, risk of endometrial hyperplasia, polyps, and, in some cases, endometrial cancer, and regular monitoring through gynecologic examinations and imaging studies is crucial for early detection), vaginal dryness and discharge, decreased libido, ovarian cysts (generally benign and asymptomatic) and, in premenopausal women, menstrual changes (irregular periods or amenorrhea). Close monitoring, regular gynecologic examinations, and ongoing communication with patients are vital for managing these changes and

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ITEM 1. Goal of follow up

Statement 1.1 –Early diagnosis of locoregional recurrence and second breast cancer.

Overall survival, detection of breast cancer (BC) recurrence, and quality of life (QoL) are critical parameters for assessing the effectiveness of surveillance programs. Both national and international guidelines emphasize the importance of timely and early diagnosis of locoregional recurrence and second BC as key principles of BC follow-up. Evidence suggests that patients who experience local recurrence have a lower survival rate compared to those who do not [21,22]. Additionally, early detection of metachronous contralateral BC has been shown to improve survival outcomes [23].

ensuring an overall high quality of life [105]. Vagina dryness and decreased libido are reported by patients postmenopausal from chemotherapy or endocrine therapy associated to LHRH-analogs. These iatrogenic problems should be considered, referring the patient to the gynecologist, sexologist, or other specialists.

Item 13. Quality of Life Assessment.

Statement 13.1- Psycho-social parameters that can be correlated with illness or ongoing treatment, such as depression, anxiety, worry, stress, difficulties in family and social relationships, difficulties in resuming work, and economic difficulties should be considered during the follow-up visit.

Survivorship care increasingly represents an important aspect of quality cancer care. Therefore, BC patients should receive an accurate and appropriate multidimensional assessment during the follow up and, if possible, every effort should be made to activate a personalized rehabilitation program [107,108].

Item 14. Psycho-oncological support.

Statement 14.1- Patients should be provided with psycho-oncological support even in the phase following active antineoplastic treatments.

The post-treatment phase can be emotionally and psychologically challenging as patients face changes in their health, body image and lifestyle. During follow-up, health care providers should assess the patients' psychosocial well-being and refer them to psycho-oncology support services, if necessary [109,110], to help patients manage anxiety, depression, and post-traumatic stress symptoms and improve their overall quality of life [111,112].

Item 15. Surveillance of late toxicities.

Statement 15.1- Monitoring of late-onset systemic and/or locoregional treatment-induced toxicities (such as lymphedema, hormonal/hormone deprivation-related disorders, neuropathy, cognitive impairment, chronic pain, gonadal toxicity, and infertility), which can significantly undermine quality of life, return to work and social life, is strongly recommended.Surveillance of late toxicities in BC follow-up has to involve regular monitoring and assessments of potential long-term effects of cancer treatment in order to impact the quality of life of patients. The healthcare providers have to assess the side effects and support them through a multidisciplinary approach. At the same time, patients should be encouraged to report any new or persistent symptoms (such as fatigue, pain, cognitive changes, neuropathy, pain, sexual and gonadal toxicity) in order to promptly evaluate and manage the problems [109,113–115].

Statement 15.2- A multidisciplinary rehabilitation intervention, both physical and psychological, involving hospital/territory/general practitioner/other stakeholders (patient associations/charities) might be quite helpful for the prevention/management of therapy-related toxicities.

A multidisciplinary approach involving hospitals, community health services, and patient associations plays a vital role in preventing and managing the side effects of BC treatments. Through close collaboration, these entities ensure that BC patients receive comprehensive care addressing medical, emotional, and social needs, ultimately enhancing outcomes and quality of life [116–120].

Item 16. Lifestyle recommendations.

Statement 16.1-The adoption of a protective lifestyle, including interventions on alcohol consumption/smoking attitude, control of overweight/obesity, and regular exercise, should be suggested to all patients for cancer risk reduction (recurrence and new cancer) and quality of life improvement.Women should be encouraged to maintain their overall health and well-being through the promotion of healthy lifestyles (no alcohol, no smoking, control of overweight/obesity and regular exercise) that can reduce the risk of BC recurrence or new cancers (breast and non-breast)

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[121–126].

The adoption of a protective lifestyle is achievable when the patient is not a passive recipient of care and surveillance, rather she is an active performer of her own health promoting empowerment and/or engagement [124,127,128].

Item 17. Role of telemedicine

Statement 17.1- Telemedicine should improve treatment adherence and provide training, educational, and motivational support to patients' empowerment in their care and surveillance pathway.

Telehealth is defined as the delivery and facilitation of healthcare and related services (including medical care, provider and patient education, health information services, and self-care) through telecommunications and digital communication technologies, via video conferencing, mobile health apps, electronic "store and forward" transmission, and remote patient monitoring [129]. Telemedicine represents an innovative resource to develop new models of care, including breast cancer surveillance, but many questions have yet to be answered, in terms of feasibility (users' training, costs and workflow) and efficacy of the intervention.

Statement 17.2- Regular teleconsultation meetings between hospital and community health workers could ensure adequate oncology surveillance for patients.

Communication between oncologists and general practitioners represents an important element of quality of care [130] also during a surveillance program, particularly for treatment toxicity management, rehabilitation, prompt treatment of any cancer recurrence [6].

or the patient. Teleconsultation allows to remove geographical and functional distance among different health care providers. The meeting should be scheduled, have a predefined duration, with a detailed form to record the patient's history, the open questions, a summary of the discussion and the shared decisions. The use of systems that guarantee security in the processing of health data would be strongly advocated.

Item 18. Health sustainability.

Statement 18.1- A model of hospital-territory integration with defined pathways should promote an improvement in the appropriate prescription of examinations and visits and a shared management of patients, capable of ensuring the sustainability of the follow-up program.

Highest variability in costs was observed, especially for the follow up costs, due to the variability of the follow-up regimens and the use of intensive follow ups. If follow ups were carried out according to the guidelines, the estimated cost would be more than ten times lower than the actual cost.

(Statement 6.1). A early triple-negative breast cancers are often associated with a high risk of early recurrence, which significantly diminishes after the first three years post-diagnosis. This characteristic may support intensive monitoring during the initial years following treatment. In contrast, patients with estrogen receptor-positive tumors face a substantial ongoing risk of late recurrences (up to 10 years and beyond), suggesting the need for long-term surveillance. These different time-dependent risks of recurrence suggest tailored follow-up strategies to manage the diverse potential for early and late recurrences, although no evidence-based recommendations currently exist. (Statement 6.2).

While routine follow-up visits are typically advised for up to 10 years post-treatment, there remains uncertainty regarding the optimal surveillance frequency, which should be personalized based on individual prognostic risk profiles (Statement 7). Mammography remains pivotal in imaging surveillance, significantly reducing breast cancer mortality. Supplementary imaging modalities such as breast and axillary ultrasound may complement mammography in specific cases, with breast MRI being considered for high-risk patients (e.g., those patients harboring BRCA pathogenetic variants) (Statements 8). In the majority of patients, further clinical investigations and imaging are discouraged in the absence of signs or symptoms of recurrence. However, in selected cases where the high-risk status and diagnostic anticipation are predicted to positively impact survival, additional investigations may be warranted (Statement 8.5).

The consensus explored the role of medical surveillance in various disciplinary contexts related to BC and the consequences of adjuvant treatments. Osteometabolic surveillance is considered crucial to mitigate treatment-induced bone-loss. Adjuvant therapies such as endocrine therapy and chemotherapy can elevate bone resorption, necessitating monitoring of bone turnover markers and consideration of anti-

osteoporotic therapy (Statements 10). Similarly, cardiological surveillance is essential during and after patients' exposure to regimens involving anthracyclines and/or anti-HER2 agents. Regular monitoring of left ventricular ejection fraction is advised, alongside the management of modifiable cardiovascular risk factors (Statements 11). The panelists agree that gynecologic surveillance is relevant for women treated with tamoxifen, due to heightened endometrial cancer risk. Regular gynecologic examinations and, when indicated, transvaginal ultrasound (but not regular endometrial biopsies) are recommended for endometrial health monitoring and detection of iatrogenic genital sphere issues associated with tamoxifen therapy (Statements 12). Additionally, gynecologic surveillance must address issues of sexual discomfort and dyspareunia caused by the long-term use of estrogen-depleting drugs, such as aromatase inhibitors. These side effects significantly interfere with treatment adherence, especially in young patients. Therefore, effective management strategies to mitigate these side effects are of paramount importance.

Finally, a group of dedicated statements questioned the role of psychosocial support and rehabilitation programs as part of the BC follow-up. According to the panel's agreement, depression, anxiety, stress, social and economic challenges, should be assessed and addressed for a comprehensive survivorship care (Statements 14). In particular, multidisciplinary rehabilitation interventions, encompassing physical and psychological aspects, are pivotal in late toxicity prevention and management (Statements 15). For instance, the panelists recognized the disabling nature of taxane-induced peripheral neuropathy and emphasized the importance of managing this side effect to ensure a better quality of life. Encouraging a protective lifestyle, involving interventions targeting alcohol consumption, smoking cessation, weight management, and regular exercise, is considered crucial for reducing cancer recurrence risk and enhancing quality of life. Patients should be empowered to promote their health through lifestyle modifications. Adopting healthy lifestyle behaviors can positively influence outcomes, although further research is needed to elucidate optimal interventions and their long-term impact (Statements 13). Support for rehabilitation and reintegration addresses physical and psychological challenges, improving overall quality of life (Statements 15), including with the implementation of remote/digital support.

The panelists concur that telemedicine holds promise in providing ongoing patient education and support, even during long-term surveillance (Statement 17.1). Furthermore, they acknowledge that regular teleconsultation meetings between hospital and community health workers can enhance collaboration and improve patient outcomes, reducing unnecessary hospital access (Statement 17.2). In this context, integrating hospital and community care services with clearly defined care pathways presents an opportunity to ensure the sustainability of follow-up programs and optimize resource allocation (Statement 18.1). Innovative approaches, adherence to guidelines, and streamlined follow-up regimens can help mitigate variability in surveillance costs and enhance the quality of care for breast cancer patient.

Conclusions

This document represents the first Italian consensus on follow-up management of patients with early BC. Notwithstanding the comprehensive multidisciplinary effort, we recognized the limited inclusion of certain specialties such as radiology, reconstructive surgery, cardiology, endocrinology, and patient advocates in our consensus panel. This is an important aspect that could enhance the strength of our recommendations and calls for more inclusive collaboration in subsequent consensus updates. Nevertheless, this AIGOM consensus wholeheartedly sheds light on the importance of the multidisciplinary approach in tailoring the BC follow-up intensity and the crucial role of the general practitioner as clinical lead for breast cancer follow-up, in selected cases. The consensus emphasizes the relevance of a comprehensive monitoring that includes cancer surveillance and assessment for osteometabolic, cardiologic, and gynecologic health along with the promotion of protective lifestyle behaviors.

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Declaration of competing interest

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