

# Telehealth in oncofertility and breast cancer patients during COVID-19: preliminary results of insenoallasalute.it project

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**Abstract. – OBJECTIVE:** Breast cancer (BC) is the leading diagnosis in premenopausal patients. Lockdown measures during COVID-19 pandemic reduced facilities for premenopausal patients, impairing oncological and reproductive health. To reduce its effect, a telehealth program called insenoallasalute.it was designed in Italy.

**PATIENTS AND METHODS:** A national-based multicentric observational study was undertaken by insenoallasalute.it study group (Italian Ministry of Health, Modena Hospital and Tor Vergata University Hospital) to raise awareness among women on a) BC and its negative role on reproductive health; b) increase adherence to screening programs and self-examination; c) present oncofertility strategies. A web-based platform with two sections was designed: an informative section and a telehealth application activated with a mobile one-time password. After a self-evaluation test to select premenopausal women with maternal desire and family or personal history for BC or ovarian cancer, and premenopausal women with maternity desires with prior medically assisted procreation, a dedicated agenda for telehealth evaluation was displayed and planned. In case the patients fulfilled the criteria for further evaluation, they were invited to perform an outpatient evaluation in one of the pilot centers.

**RESULTS:** From July 2021 to December 2021, 2,830 single accounts were activated, and 2,450 (86.57%) completed the tests. 53 patients were selected to undergo telehealth consultation and 40 (80.0%) scheduled the telehealth visit. 6 patients underwent surgery in the study centers.

**CONCLUSIONS:** In our experience insenoallasalute.it embodied an innovative solution to spread BC awareness, BC screening

program, and oncofertility opportunities in the oncological population.

*Key Words:*

Breast neoplasms, Telemedicine, Fertility preservation, Oncofertility, Primary prevention, Secondary prevention, Screening programs.

## Introduction

Novel beta-coronavirus disease (COVID-19) was declared a pandemic in March 2020 by the World Health Organization (WHO), and it caused overburdened healthcare systems in most countries due to the high risk of transmission rate and death rate among frail population<sup>1</sup>. Lockdown measures were planned worldwide until the mass vaccination in order to contain cross-infection and reduce hospitalization and mortality<sup>2</sup>. While lockdown measures determined a reduction in human-to-human transmission, the same measures strongly affected hospital admission for non-COVID-19 patients, determining a significant reduction in elective services, such as screening programs or outpatient visits<sup>3</sup>. In addition, a further decrease in admission rate was reported even in patients who required urgent admission such as oncological patients due to the COVID-19-related anxiety, which determined a higher surgical refusal rate with a worsening of long-term outcomes and quality of life<sup>4-6</sup>.

During the pandemic period, physicians designed temporary measures in order to continue surgical

and clinical activities and accelerate innovative technologies and protocols introduction, which were still under investigation with the aim of reducing the negative effects of COVID-19 as much as possible<sup>7-9</sup>. Many physicians faced ethical dilemmas to balance the need for Non-COVID-19 patients against the reduced availability of national resources during the COVID-19 pandemic<sup>3,10,11</sup>. Among different strategies, telehealth applications gained popularity as a strategy to increase the rate of hospital admissions<sup>12,13</sup>. Several experiences<sup>14</sup> demonstrated that patients reported a high level of satisfaction with telemedicine as well as physicians who largely applied these mechanisms in several clinical settings and breast cancer (BC) during the pandemic. However, while several measures were planned for high-risk patients (like patients already in the screening programs), younger patients were and are usually less involved in awareness and health programs<sup>15</sup>.

Despite patients under 40 accounting for up to 7-10% of total BC and BC being the leading oncological diagnosis in patients between 0 and 40 years, most of their needs are unmet<sup>16</sup>. Young BC patients exhibit special characteristics regarding tumor biology, long-term clinical outcome, family planning, and job reintegration, requiring special attention by physicians<sup>17,18</sup>. Specifically, oncofertility is an important issue among young oncological patients; pregnancy and live birth rates are lower in cancer survivors when compared with the general population<sup>19</sup>, with a higher rate of acute ovarian failure and primary ovarian insufficiency<sup>20,21</sup>. Early detection plays a pivotal role in younger patients in order to reduce as much as possible the risk of detrimental effects of therapy on fertility and quality of life, which are strongly linked<sup>22-24</sup>. For instance, whilst risk reduction mastectomy is more common among younger patients, wide local excision seems to reduce the effect of surgery on quality of life<sup>22,25,26</sup>. Moreover, consultation with a reproductive specialist and appropriate information on fertility preservation for these women is an essential aspect of their supportive care, reducing the risk of primary ovarian insufficiency after multidisciplinary treatment<sup>24</sup>.

Tor Vergata and Modena Breast Unit, aiming at the reduction of oncological risk in premenopausal women and thus the reduction of an oncological breast diagnosis on

reproductive health, designed a telehealth program on behalf of the Italian Ministry of Health called [senoallasalute.it](http://senoallasalute.it).

In the present paper, we aim to describe our preliminary results.

## Patients and Methods

A national-based multicentric observational study was undertaken and founded by Italian Ministry of Health (N° CUP E84E19002750006). “In seno alla salute” – a play on word which means “within health” and contains the Italian word for breast (literal meaning “in the health’s breast”) – was chosen for the project and the registered website [insenoallasalute.it](http://insenoallasalute.it).

Declared aims of the project were: a) raise awareness among women on BC and its negative role on reproductive health; b) increase the adherence to self-referred and national health screening programs; c) increase consciousness of breast self-examination; d) present the different oncofertility strategies among oncological patients. Prior to the official launch, a web-based platform divided into two different sections was planned to assist the physician during the pilot study and was developed by Damacon (Rome, Italy) on behalf of the “insenoallasalute Study Group and Italian Ministry of Health” (Figure 1).

The first section published on the website was designed for information purposes. This section was organized into 4 different parts: project presenting, BC epidemiology, BC risk factors, and suggested screening programs. There was also a video blog where physicians answered common questions. All material, designed to provide patient-oriented information, was provided by GV, MM, and MP (Figure 2).

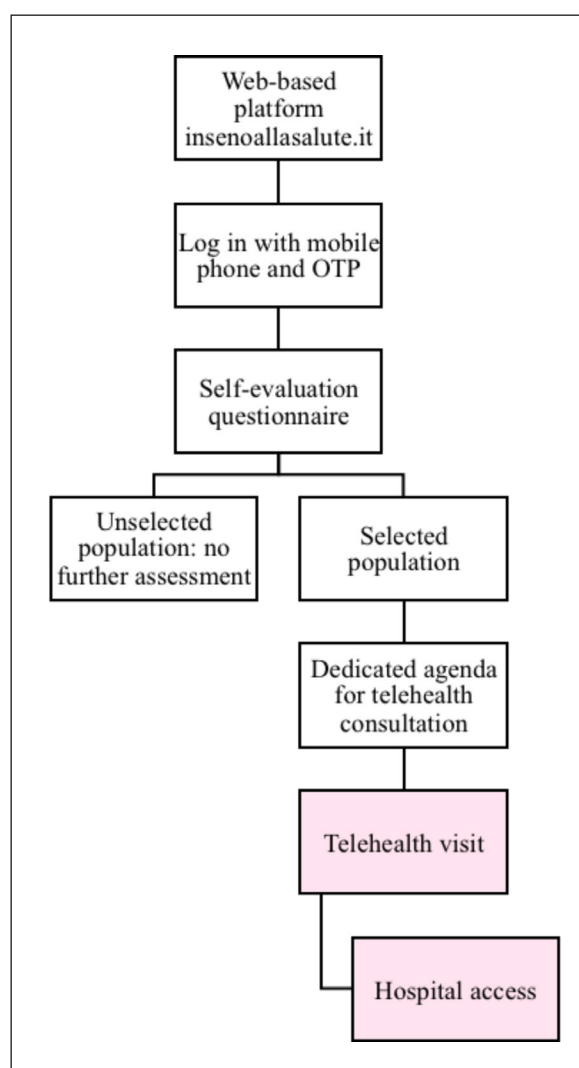
While the first section represented an introduction, the second section consisted of the telehealth application. After informative consent was provided, any web user could anonymously log in to the web platform through their mobile phone number. Privacy policy regarding the web-based platform was available on every web page of the web-based platform ([insenoallasalute.it](http://insenoallasalute.it)). Patients must accept digitally informative consent prior to admission in the self-reported questionnaire of the [insenoallasalute.it](http://insenoallasalute.it) project. Mobile phone numbers were not linked to any demographic data and were used only to obtain a ten-minute one-time-password (OTP). Any time a patient required new access to the telehealth application, a new OTP was

provided. Once admitted to the telehealth application, patients were free to submit a self-evaluation questionnaire to assess their risk.

Self-evaluation questionnaire was designed according to the selection questionnaire for hereditary risk published in 2011 by the Emilia-Romagna region, currently utilized in the region to select patients who should perform genetic assessment<sup>27</sup>. Besides family history assessment, patients had to answer other questions regarding their reproductive history. Table I display the self-evaluation test. The aim of the self-evaluation questionnaire was to select premenopausal women with maternal desire with a positive family history of BC or ovarian cancer, patients with a personal history of BC or ovarian cancer, and patients without a personal history of BC or ovarian cancer with maternity desires who had prior medically assisted procreation. If patients did not meet the criteria for further evaluation, a message suggesting an outpatient clinic evaluation appears (if not performed in the last year). Conversely, a dedicated agenda for telehealth evaluation was displayed in case the patient fulfilled the criteria for further evaluation. Patients were free to change data at any moment and a mobile phone was used to obtain the first contact with the patients. Patients were contacted with a dedicated number and could decide to perform telehealth visits through mobile phones or Microsoft Teams (Microsoft, Redmond, WA, USA) (Figure 3). Once the telehealth assessment finished, in case of further assessment, patients were invited to perform an outpatient evaluation in one of the pilot centers (Modena Hospital or Tor Vergata University Hospital). At the end of any step (self-evaluation test, telehealth consultation booking, telehealth visit) a review questionnaire was planned and reported on a scale ranging from 1 (dislike) to 5 (easy to use). After the organization of the whole project, insenoallasalute.it web platform was launched between July 2021 and December 2021. The web-based platform was advertised on the social media platform of the Italian Ministry of Health, Tor Vergata University Hospital, and Modena University Hospital. Figure 3 summarizes web platform access for a low-risk patient.

### Statistical Analysis

All anonymized data were recorded onto an Excel database (Microsoft, Redmond, WA, USA). Continuous variables were reported as median and interquartile range, Dummy variables were reported as numbers and percentages. SPSS statistical

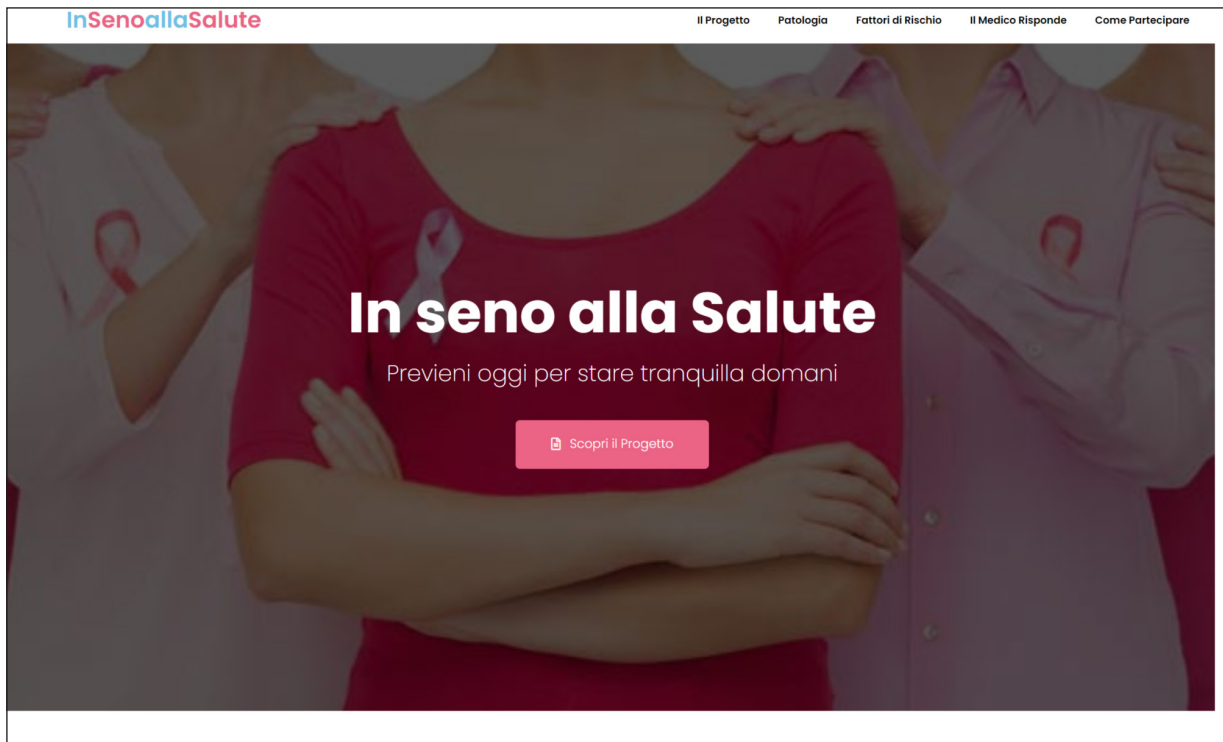


**Figure 1.** Insenoallasalute.it flowchart. Flowchart describing the insenoallasalute.it web-based platform. The web-based platform consisted of two different sections. The first section was planned with information purpose regarding BC epidemiology, BC risk factors, and suggested screening programs, a video-blog. The second section consisted of the telehealth application, starting with a self-evaluation questionnaire to assess BC risk. OTP: One Time Password, BC: Breast Cancer.

package version 23.0 was used (IBM Corp., Armonk, NY, USA). Continuous variables between procedures were compared with Mann-Whitney U test, while for categorical variables Fisher exact test was applied.  $p$ -values  $<0.05$  were considered to be statistically significant.

### Results

From July 2021 to December 2021, a total of 2,830 single accounts were activated, while 2,450



**Figure 2.** Web platform Homepage. The picture represents the homepage (available at <https://insenoallasalute.it>) developed by Damacon (Roma, Italy) on behalf of insenoallasalute study group and Italian Ministry of Health.

(86.57%) single accounts completed the self-evaluation tests. Among this population a total of 53 patients were selected to undergo telehealth consultation and 40 (80.0%) scheduled the telehealth visit. Among all this population, in 8 women outpatient consultation was planned, and subsequently, 6 patients underwent surgery in the study center. The mean value of the review questionnaire was 4.6 (3.7-5.0), 4.4 (3.5-5.0), and 4.3 (3.6-5) after the self-evaluation test, telehealth consultation booking, and telehealth visit, respectively. No statistical difference was reported in the questionnaire between patients undergoing self-evaluation tests and telehealth visits ( $p > 0.05$ ).

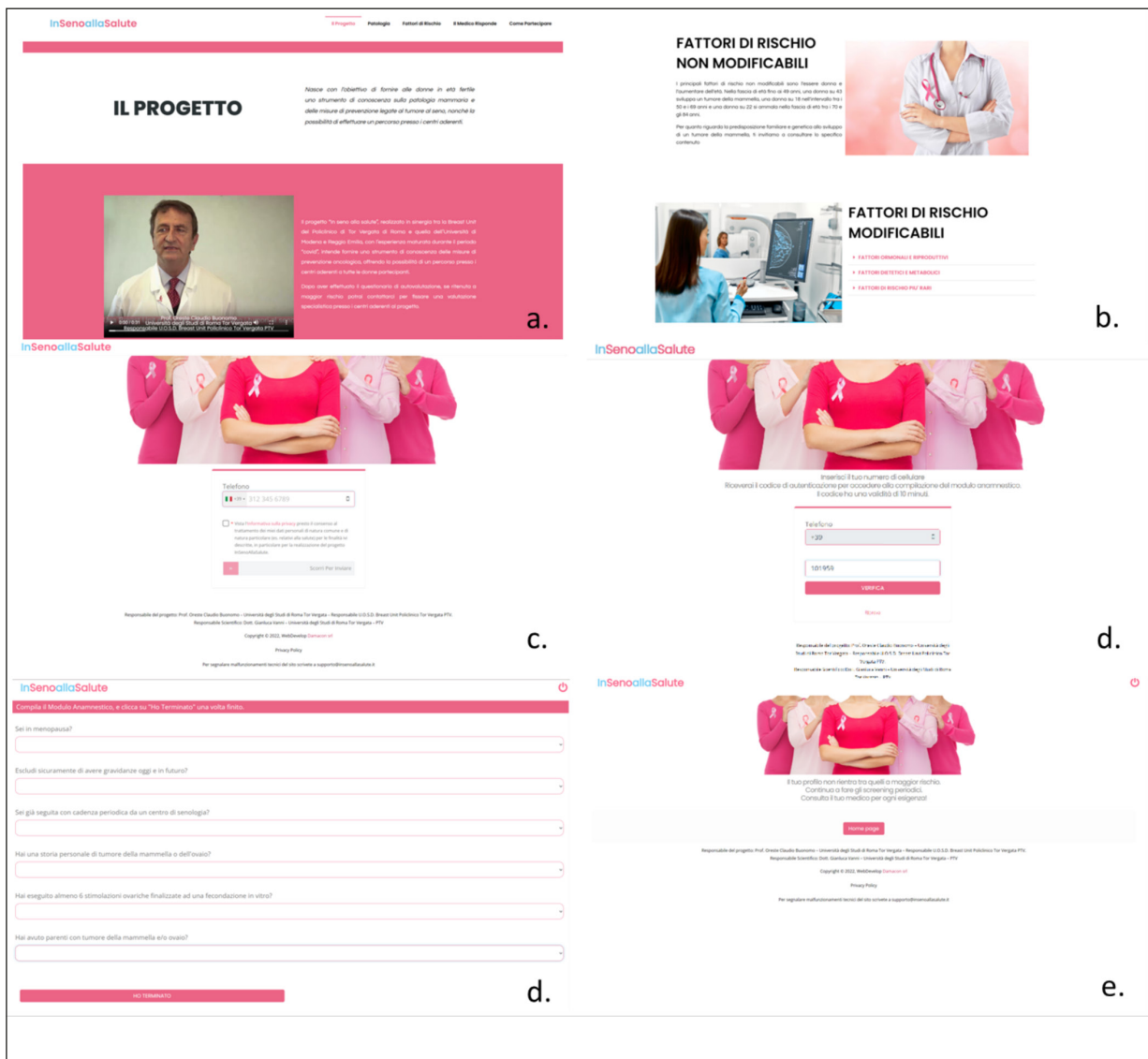
## Discussion

BC is the leading diagnosis in premenopausal women, determining a huge impact on fertility and patients' reproductive history<sup>28</sup>. To reduce the risk of late-stage diagnosis in premenopausal women, insenoallasalute.it project was designed by Tor Vergata and Modena Breast Cancer Center on behalf of the Italian Ministry of Health.

While prior to the pandemic premenopausal patients were enrolled in occasional tailored screening

programs or were referred to oncofertility programs prior to therapy in case of BC diagnosis, COVID-19 led to a forced interruption of elective programs and research protocol on prevention, determining a higher rate of late-stage presentation even in premenopausal woman<sup>29,30</sup>. In the literature, authors estimated that up to 45% of the improvement of BC care in the pre-COVID-19 era was obtained from BC screening programs<sup>31</sup>, with a 30% decrease of T2-T4 stage presentation in less than 8 years from the introduction of the screening programs<sup>32</sup>. As largely known, the beneficial effect of BC screening programs is related to early diagnosis, resulting in better clinical outcomes, treatment de-escalation, and reduced health care costs<sup>33,34</sup>. However, even with the available facilities, patients and healthcare workers strongly suffered from the negative effect of social distancing reducing the admission to the hospital due to the fear of cross-infection<sup>35-38</sup>.

With the aim of supporting BC care and avoiding detrimental effects on survivorship, physicians designed temporary guidelines and enhanced the application of novel treatment or technology in daily clinical practice<sup>7</sup>. In fact, before COVID-19 pandemic, cancer care was shifting from a morphological one-fits-all stage-oriented



**Figure 3.** Web platform screenshot. The picture represents different pages of the web-based platform (available at <https://insenoallasalute.it>) developed by Damacon (Roma, Italy) on behalf of insenoallasalute study group and Italian Ministry of Health. **a-b**, informative section, **(c)** login page, **(d)** self-evaluation test, **(e)** low-risk output.

treatment protocol to a non-invasive tailored assessment, embracing molecular biology technology to promote tailored primary and secondary prevention programs, tailored treatment, and tailored follow-up<sup>39-41</sup>.

For instance, among tailored treatment, enhanced recovery after surgery protocols<sup>42,43</sup>, awake conservative procedure, and day-surgical management were preferred in order to reduce the hospital length<sup>44,55</sup> and postoperative lymphopenia<sup>1,46</sup>. Other tailored strategies include neoadjuvant hormonal bridging therapy in low-risk diseases that was proposed during the maximum COVID-19 spread to reduce the risk of cross-infection and

avoid the detrimental effect of surgical delay<sup>7,9,47</sup>. Other measures involved general suggestions for patients to reduce the spread of the pandemic and telehealth protocols<sup>7,9,48</sup>.

Among different strategies, telehealth protocol represented the major innovation, which provided beneficial effects on several aspects of non-COVID-19 care<sup>12</sup>. Before the COVID-19 pandemic, telehealth implementation was scarce, limited to isolated geographical areas, and physicians were hesitant or doubtful about it<sup>49</sup>. With the COVID-19 outbreak, a forced virtual health implementation substained the continuity of care reducing cross-infection risk, canceling the

**Table I.** “insenoallasalute.it” self-evaluation test.

Are you a menopausal woman?	yes/no
Do you exclude pregnancy in the future?	yes/no
Do you perform regularly follow-up visit in a breast center?	yes/no
Do you have personal history of BC or ovarian cancer?	yes/no
Did you perform one or more medically assisted procreation?	yes/no
Do you have any family history of BC or Ovarian cancer?	If yes, please specify any condition
• Mother with BC	
• Sister with BC	
• A second sister with BC	
• Daughter with BC	
• Another Daughter with BC	
• Paternal grandmother with BC	
• paternal aunt with BC	
• another paternal aunt with BC	
• maternal grandmother with BC	
• maternal aunt with BC	
• another maternal aunt with BC	
• Father with BC	
• Brother with BC	
• Grandchild with BC	
• Cousin with BC	
• Mother with ovarian cancer	
• Sister with ovarian cancer	
• A second sister with ovarian cancer	
• Daughter with ovarian cancer	
• Another daughter with ovarian cancer	
• Paternal grandmother with ovarian cancer	
• Paternal aunt with ovarian cancer	
• Another paternal aunt with ovarian cancer	
• Maternal grandmother with ovarian cancer	
• Maternal aunt with ovarian cancer	
• Another maternal aunt with ovarian cancer	
• Father with ovarian cancer	
• Brother with ovarian cancer	
• Grandchild with ovarian cancer	
• Cousin with ovarian cancer	

Self-evaluation test was designed according to the selection questionnaire for hereditary risk of BC published in 2011 by Emilia-Romagna region plus other questions regarding their reproductive history. The aim of the self-evaluation questionnaire was to select premenopausal women with maternal desire and positive family history of BC or ovarian cancer, patients with a personal history of BC or ovarian cancer, and patients without a personal history of BC or ovarian cancer with maternity desires who had prior repeated medically assisted procreation. When patients do not meet the criteria for further evaluation, a message suggesting an outpatient clinic evaluation appears (if not performed in one year). BC: Breast Cancer.

geographical and physical barrier between physician and patients, and reducing the healthcare carbon footprint in terms of personal protective equipment use and greenhouse gas emission<sup>12,50</sup>. Healthcare digitalization is currently playing a major role in all medical fields and a great effort worldwide to manage this large amount of data is ongoing<sup>51</sup>. Keeping in mind the difficulties in terms of data security, under this perspective telehealth assessment could ease this digital revolution in every medical aspect as oncological follow-ups or in transplant recipients<sup>52,53</sup>. Even the most reluctant physician had to recognize the pivotal role that telehealth and digitalization had in the first wave of the pandemic, in COVID-19 hospitalized

patients and in the post-pandemic recovery adapting to the request of a higher number of patients<sup>12</sup>.

Among the non-COVID-19 patients, oncological patients were one of the first part of the population who were considered for telehealth, and it was implemented to compensate the higher risk of COVID-19 complications due to the immunosuppression induced by cancer and the anti-cancer therapy<sup>54</sup>. In this population, BC patients represented the majority of the patients. Keeping in mind the high number of consultations during multidisciplinary treatment, BC patients were considered one of the best models to whom telehealth could be safely proposed<sup>7,9,55</sup>. Under these conditions, during the pandemic, telehealth

programs spread worldwide in BC centers and many in-person consultations were transferred as teleconsultations with high satisfaction among patients without affecting their anxiety levels<sup>14</sup>. However, while several other experiences<sup>14,56,57</sup> of BC telehealth have been published in literature even before COVID-19 pandemic, in most of them, the population was predominantly aged >50 years and they underwent standard follow-up after BC treatment. Additionally, while personalized screening strategies have been developed in many countries and currently several ongoing clinical trials will provide evidence to promote a tailored BC screening approach, most of them are restricted to post-menopausal women<sup>58</sup>. Little experience has been collected in the literature regarding the younger and premenopausal population<sup>16</sup>.

While postmenopausal women are usually less involved in technology, digitalization, and telehealth<sup>59</sup>, the younger population could benefit more from health digitalization. In fact, the younger population usually refers to doctors only after searching online<sup>60</sup>, mostly in mobile apps without the control of any regulatory authority and without scientific references<sup>61</sup>; thus, gamification may promote and increase awareness, engagement, and self-management of many chronic diseases<sup>62-64</sup>. Therefore, in order to raise the number of women reached, a mobile app of our web-based platform is currently under development.

Keeping in mind these needs, insenoallasalute.it project was designed to provide an easy access to evidenced-based information regarding BC, oncofertility, and primary and secondary prevention to premenopausal women, as reported by the mean age of the participants in the self-reported questionnaire. Through the self-reported questionnaire, insenoallasalute.it platform provided a smart, faster, and easier access to the NHS for patients, reducing the risk of symptoms underestimation among premenopausal women with BC risk. Self-reported questionnaires represented an element of gamification that aimed at BC awareness among patients without any medical purpose to select or triage the population. Patients were aware that the self-reported questionnaire did not substitute telehealth or in-person outpatient evaluation and were advised to perform a breast evaluation at the end of the questionnaire if not selected for telehealth consultation.

### Limitations

We are aware that our research may have two limitations. Firstly, in our study there is not any

control group designed to underline the effect of these measures on patients' reported outcomes. However, a high level of satisfaction was recorded in patients after interaction with the platform, and our research did not focus on patients' reported outcomes. Secondly, we are aware that self-reported questionnaires could give the patients a false sense of security. However, our web-based platform was designed to provide the correct and up-to-date information to the reader. Moreover, several warnings regarding the need for clinical evaluation were included in the first and in the second section before and after the self-reported questionnaire.

### Conclusions

While a small number of patients required surgical intervention in our study, in our experience insenoallasalute.it embodied an innovative solution to spread BC awareness, BC screening program, and oncofertility opportunities in the oncological population. Further studies are needed to evaluate this innovative approach in BC prevention and BC in general.

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### Authors' Contributions

Conceptualization: Gianluca Vanni, Oreste Claudio Buonomo, Giovanni Tazzioli; Methodology: Simona Papi, Francesca Combi; Software: Marco Materazzo; Formal analysis: Data Curation; Marco Pellicciaro; Writing - Original Draft: Marco Materazzo, Simona Papi; Writing - Review & Editing: Simona Papi, Francesca Combi, Gianluca Vanni; Supervision Mariella Mainolfi; Gianluca Vanni, Oreste Claudio Buonomo, Giovanni Tazzioli.

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### Conflict of Interest

The authors declare that they have no conflict of interest to declare.

### Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

### Ethics Approval

The protocol was approved by the Italian Ministry of Health (No. CUP E84E19002750006).

### Informed Consent

Privacy policy regarding the web-based platform was available on every web page of the web-based platform (insenoallasalute.it). Patients had to accept digitally informative consent prior to admission in the self-reported questionnaire for all the insenoallasalute project sections.

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