TNBC in Younger Women: Unique Challenges and Considerations

Mishaal Elbasheer Babiker[1], Mohammed N E Mohammed[2]

[1]Pathology department, Faculty of Medicine, Widad University College, Kuantan, Pahang, Malaysia.

[2]Universiti Malaya, 50603 Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur, Malaysia.

Corresponding Author: emishaal@gmail.com

Abstract

Triple-negative breast cancer (TNBC) in young women presents unique biological, clinical, and psychosocial challenges. This review examines issues faced by women under 40 with TNBC, focusing on epidemiology, biology, diagnosis, treatment, fertility preservation, psychosocial impacts, and survivorship. TNBC is disproportionately prevalent in young women, especially African Americans, with aggressive characteristics leading to delayed diagnoses. Treatment strategies balance aggressive therapy with quality of life concerns, including fertility preservation. While chemotherapy remains standard, emerging targeted therapies and immunotherapies offer new hope but raise concerns about long-term effects. The psychosocial burden of TNBC affects body image, relationships, and careers. Long-term survivorship challenges include cardiovascular complications and secondary malignancies. This review emphasizes the need for personalized, multidisciplinary care addressing the unique needs of young TNBC patients to improve outcomes and quality of life.

Introduction

Triple-negative breast cancer (TNBC) is a particularly aggressive form of breast cancer that lacks the expression of estrogen receptors (ER), progesterone receptors (PR), and human epidermal growth factor receptor 2 (HER2) (Foulkes & Reis-Filho, 2010). Although TNBC accounts for only 15-20% of breast cancers, it is disproportionately more prevalent among women under 40, particularly African American women (Sineshaw et al., 2014). The unique biological features of TNBC in younger women lead to more aggressive disease progression, fewer treatment options, and significant concerns regarding fertility and long-term quality of life (Dietze et al., 2015; Partridge et al., 2004).

Young women with TNBC face multifaceted challenges, spanning from the biological aggressiveness of the disease to complex psychosocial impacts, such as disruptions to their career and family planning (Champion et al., 2014). These patients often have heightened concerns regarding fertility preservation, given the gonadotoxic nature of many TNBC treatments. Furthermore, the psychosocial burden of TNBC, including issues of body image and sexuality, is profound, with significant impacts on mental health and relationships (Rosenberg & Partridge, 2015).

Despite the increasing awareness of these issues, there remains a gap in comprehensive care tailored specifically to young women with TNBC. Current clinical guidelines often fail to fully address their unique biological and psychosocial needs(Partridge et al., 2004). A multidisciplinary approach that addresses not only immediate medical concerns, but also long-term survivorship and psychosocial support is critical.

This review seeks to explore the challenges faced by younger women diagnosed with TNBC, focusing on biological characteristics, diagnostic difficulties, treatment considerations, fertility preservation, and psychosocial impacts. By synthesizing current research, we aim to provide a holistic perspective on the care needs of this vulnerable population.

Materials & Methods

This narrative review explores the challenges faced by young women diagnosed with triple-negative breast cancer (TNBC), with a focus on fertility preservation, treatment considerations, and psychosocial impacts. The review concentrates on women under the age of 40, a demographic that experiences more aggressive disease and unique psychosocial challenges compared to older patients (Partridge et al., 2004).

Study Design

A narrative review approach was chosen to allow for a broad exploration of the complexities surrounding TNBC in younger women, encompassing biological, clinical, and psychosocial factors. This methodology enables the integration of diverse types of research, providing a synthesized understanding of the key issues.

Literature Search Strategy

A comprehensive literature search was conducted using databases such as PubMed, MEDLINE, and Web of Science, focusing on articles published between January 2000 and June 2024. Priority was given to recent studies to ensure up-to-date information. Key search terms included:

- "Triple-negative breast cancer" OR "TNBC"
- "Young women" OR "Premenopausal women"
- "Fertility preservation"
- "Psychosocial impact" OR "Quality of life"
- "Survivorship" OR "Long-term outcomes"

In addition, relevant reference lists were manually reviewed, and key clinical guidelines were consulted to ensure comprehensive coverage of the topic.

Selection Criteria

Articles were selected based on their relevance to the unique challenges young women face with TNBC, including treatment, fertility preservation, and psychosocial impacts. Priority was given to peer-reviewed research, clinical trials, and guidelines. Studies that focused on young women, TNBC biology, or psychosocial aspects were included. Studies with small sample sizes, low methodological rigor, or lack of focus on younger women were excluded.

Data Synthesis

The collected data were synthesized into thematic sections addressing the key challenges of TNBC in younger women. These include epidemiology, biological characteristics, diagnostic challenges, treatment strategies, fertility preservation options, and psychosocial and survivorship issues. Emphasis was placed on highlighting the unique needs of younger patients, while identifying gaps in current research and clinical practice.

Limitations

This review, being narrative in nature, does not involve formal statistical analysis or a systematic quality assessment of included studies. As a result, the conclusions drawn may be influenced by the selection of studies. Additionally, while every effort was made to include the most relevant and high-quality research, some studies may have limitations related to sample size or design.

Results and Discussion

Epidemiology of TNBC in Younger Women

TNBC is disproportionately prevalent in younger women, accounting for approximately 15-20% of all breast cancers, but up to 40% in women under 40 (Ademuyiwa et al., 2017). This aggressive subtype is also more common among African American women, who experience a higher incidence compared to Caucasian or Hispanic women (Dietze et al., 2015). In a large-scale analysis of SEER registries, the prevalence of TNBC was found to be 24.2% in women under 40, compared to 14.7% in those over 50 (Sineshaw et al., 2014).

The bimodal age distribution of TNBC peaks between 30-34 and 35-39 years, indicating possible differences in risk factors within the under-40 age group (Agarwal et al., 2016). Triple-negative breast cancer (TNBC) is strongly associated with BRCA1 mutations, particularly in younger women. Studies have shown that 48% of BRCA1 mutation carriers had TNBC compared to only 12% of non-carriers. This association is especially pronounced in Ashkenazi Jewish women, who were about five times more likely to have TNBC among BRCA1 mutation carriers (Lee et al., 2011).

Young women with TNBC often present with more advanced disease due to delayed diagnosis, which is attributed to the aggressive nature of TNBC and the lack of routine breast cancer screening for women under 40 (Rosenberg & Partridge, 2015).

Biological Characteristics of TNBC in Younger Patients

The aggressive nature of TNBC in younger women is partly due to unique biological features. TNBC is not a homogenous disease; it includes several molecular subtypes. The basal-like subtypes (BL1 and BL2), which are more prevalent in younger women, are associated with high cell proliferation rates and aggressive tumor behavior. These subtypes also show increased expression of genes related to DNA damage repair and cell cycle regulation (Lehmann et al., 2011).

Genetic mutations such as BRCA1 are common in young TNBC patients. BRCA1 mutations are present in about 17% of women under 40 with TNBC, compared to only 5% in those over 50 (Tung et al., 2020). Other alterations, such as TP53 mutations and PTEN loss, are also more frequent, further contributing to the aggressive nature of the disease (Beg et al., 2015).

The tumor microenvironment plays a critical role in TNBC progression. Young women with TNBC tend to have higher levels of tumor-infiltrating lymphocytes (TILs), which are associated with better responses to immunotherapy but may also signal increased immune system engagement with more aggressive tumors (Rosa et al., 2024). Additionally, higher rates of angiogenesis and stromal interactions are observed in younger TNBC patients, indicating a more dynamic tumor environment (Nederlof et al., 2021).

Diagnosis and Screening Challenges

Diagnosing TNBC in young women poses several challenges due to biological factors and current screening limitations. Standard breast cancer screening guidelines recommend starting mammography at age 40 or 50, leaving younger women outside routine screening protocols (Oeffinger et al., 2015). Even when mammography is used, it has lower sensitivity in younger women due to their denser breast tissue, leading to potential delays in diagnosis (Hooley et al., 2017).

Young women with TNBC are more likely to present with symptomatic disease, such as palpable masses, rather than through screening detection(Mathis et al., 2010). The aggressive nature of TNBC often leads to rapid tumor growth, which can emerge between regular screenings, further complicating early detection(Griffiths & Olin, 2012).

Pregnancy-associated breast cancer adds another layer of complexity. The physiological changes in breast tissue during pregnancy can mask symptoms of TNBC, leading to delayed diagnosis in pregnant women (Loibl et al., 2018). Additionally, the imaging challenges in dense breast tissue further complicate early diagnosis, with ultrasound and MRI often used but not without limitations (Abu Abeelh & AbuAbeileh, 2024).

Emerging diagnostic technologies, such as liquid biopsies and advanced imaging techniques, offer hope for improving the accuracy and timeliness of TNBC diagnosis in young women (Dass et al., 2021). However, these are still in developmental stages and not widely available.

Treatment Considerations

The treatment of TNBC in younger women presents unique challenges due to the aggressive nature of the disease and the need to balance effective cancer control with long-term quality of life. Standard treatment includes surgery, chemotherapy, radiation, and emerging targeted therapies, all of which carry distinct implications for young patients.

Surgery

Surgical options for TNBC in younger women often involve a choice between breast-conserving surgery (BCS) and mastectomy. While studies indicate equivalent survival rates between BCS with radiation and mastectomy, many young women opt for mastectomy due to fears of recurrence (Frasier et al., 2016). Furthermore, the trend toward contralateral prophylactic mastectomy (CPM) has increased, though the survival benefit remains controversial for non-BRCA carriers (Kurian et al., 2014).

Young women often prioritize cosmetic outcomes post-surgery, making immediate breast reconstruction a common choice. However, this option can complicate future radiation therapy if needed, necessitating careful coordination between surgical and radiation oncologists (Kronowitz & Robb, 2004).

Systemic Therapy

Chemotherapy remains the backbone of TNBC treatment. Neoadjuvant chemotherapy (NAC) is frequently used, allowing for tumor downstaging and an assessment of pathological complete response (pCR), a key prognostic factor in TNBC (Spring et al., 2017). Younger patients often have higher pCR rates, which are associated with better long-term outcomes.

Dose-dense anthracycline and taxane regimens are typically employed, showing enhanced efficacy in younger women. The addition of platinum-based agents, particularly in BRCA-mutated tumors, has demonstrated improved outcomes, with higher pCR rates (Loibl et al., 2018). For younger patients, recent advances in immunotherapy, such as pembrolizumab combined with chemotherapy, have shown promising results in improving disease-free survival (Schmid et al., 2020).

PARP inhibitors like olaparib have also shown benefit in BRCA-mutated TNBC, a common mutation in younger patients (Tutt et al., 2021). Additionally, sacituzumab govitecan, an antibody-drug conjugate, has demonstrated efficacy in metastatic TNBC, providing an option for young patients with advanced disease (Bardia et al., 2021).

Radiation Therapy

Radiation therapy plays a critical role in TNBC management, particularly following breast-conserving surgery. Boosts to the tumor bed are often recommended for younger women to improve local control rates (Bartelink et al., 2015). Hypofractionated radiation schedules, which reduce the overall number of treatment sessions, are gaining traction; however, their long-term effects in younger patients need further study (Ritter, 2008).

Long-Term Toxicity and Survivorship

Younger TNBC patients face long-term toxicities from treatment, including cardiotoxicity from anthracycline use and the risk of secondary malignancies, particularly with radiation exposure (Armenian et al., 2016). Moreover, chemotherapy-induced menopause and its associated effects on bone health and cardiovascular risk are of particular concern for long-term survivorship in young women (Shapiro et al., 2001).

Fertility Preservation

Fertility preservation is a critical consideration for younger women diagnosed with TNBC, as many cancer treatments can significantly impact ovarian function. Timely discussions about fertility preservation options are essential for allowing patients to make informed decisions before starting treatment.

Impact of Treatment on Fertility

Chemotherapy, particularly with alkylating agents like cyclophosphamide, poses a high risk of gonadotoxicity, leading to premature ovarian failure (Lambertini et al., 2016). Radiation, though less commonly used in breast cancer, can also damage ovarian function if applied near reproductive organs (Sklar, 2005).

Fertility Preservation Options

Several fertility preservation methods are available for young women with TNBC:

- Embryo Cryopreservation: This is the most established method with the highest success rates, requiring hormonal stimulation and egg retrieval followed by in vitro fertilization (Practice Committee of the American Society for Reproductive Medicine, 2013). However, it necessitates a male partner or sperm donor, and the process typically takes 2-3 weeks, potentially delaying cancer treatment.
- Oocyte Cryopreservation: A viable option for single women, this technique involves the freezing of unfertilized eggs. Success rates are improving, and it offers more flexibility compared to embryo preservation (Cobo et al., 2013).
- Ovarian Tissue Cryopreservation: Still considered experimental, this method involves surgically removing and freezing ovarian tissue before chemotherapy. It is suitable for patients who cannot afford delays in starting treatment, although future transplantation is required to restore fertility (Şükür et al., 2010).
- Ovarian Suppression: The use of gonadotropin-releasing hormone (GnRH) agonists during chemotherapy has been shown to preserve ovarian function in some cases, although the extent of protection is debated (Moore et al., 2015).

Challenges and Considerations

Time is a critical factor in TNBC treatment, often leaving little opportunity for fertility preservation procedures, which require hormonal stimulation and egg retrieval (Sonmezer & Oktay, 2006). Another unique challenge is the high prevalence of BRCA mutations in young TNBC patients. These women may be concerned about passing the mutation to their children, making genetic counseling an important component of fertility discussions there are concerns that the estrogen surge from fertility treatments could potentially fuel TNBC growth, although evidence suggests that short-term exposure may be safe (Lee et al., 2011).

Long-Term Considerations

For young women who preserve fertility before TNBC treatment, pregnancy after cancer is increasingly considered safe, with studies showing no increase in recurrence risk for most patients (Lambertini et al., 2016). However, the optimal timing of pregnancy is still debated, with most experts recommending waiting at least two years post-treatment before attempting conception (Vuković, 2019).

Psychosocial Impacts

A diagnosis of TNBC in young women has profound psychosocial effects that intersect with their life stage, impacting relationships, career, and family planning. The aggressive nature of TNBC, coupled with the uncertainty of prognosis, amplifies psychological distress, body image issues, and challenges in social integration.

Psychological Distress

Young women with TNBC experience heightened levels of psychological distress, including anxiety, depression, and fear of recurrence. Up to 50% of younger breast cancer patients report significant anxiety and depression (Champion et al., 2014). The aggressive nature of TNBC exacerbates these issues, contributing to a persistent fear of recurrence, even after treatment completion. Younger age has been associated with higher levels of fear of recurrence compared to older patients (Thewes et al., 2017).

Post-traumatic stress disorder (PTSD) is also prevalent among young survivors of breast cancer, with some studies indicating that nearly one-quarter of patients meet the criteria for PTSD (Vin-Raviv et al., 2013). This psychological burden often extends into survivorship, affecting overall mental health and quality of life.

Body Image and Sexuality

The physical changes resulting from TNBC treatment can have a lasting impact on body image and sexual health. Mastectomy, commonly chosen by younger TNBC patients, can lead to feelings of altered femininity and loss of self-esteem (Rosenberg & Partridge, 2015). Chemotherapy-induced hair loss, weight changes, and early menopause further contribute to negative body image and can strain intimate relationships.

Sexual dysfunction is another significant issue, with many young breast cancer survivors reporting decreased libido, vaginal dryness, and painful intercourse (Rosenberg & Partridge, 2015). The psychosocial impact of fertility loss can also deeply affect women's perceptions of their femininity and future family plans (Gorman et al., 2012).

Relationships and Social Support

TNBC impacts not only the patient but also their relationships with partners, family, and peers. For young women in relationships, the stress of cancer treatment can strain partnerships. Single women, meanwhile, may find it difficult to date or form new relationships due to concerns about body image, fertility, and the possibility of recurrence (Ahmad et al., 2015).

Social isolation is common among young TNBC patients, who often feel that their peers cannot relate to their experiences (Bollinger, 2018). While social support is crucial, younger patients may struggle with the burden of managing others' reactions to their diagnosis and treatment.

Career and Financial Impact

Young women diagnosed with breast cancer, particularly triple-negative breast cancer (TNBC), face significant career disruptions and financial challenges. Many patients need extended time off work or quit their jobs to manage treatment, impacting career progression and income (Mudaranthakam et al., 2023). Financial toxicity is a major concern, with nearly half of young breast cancer survivors experiencing financial decline due to treatment costs. Factors associated with financial vulnerability include late-stage diagnosis, multiple comorbidities, and self-funded insurance (Tangka et al., 2020). Despite these challenges, patient-provider discussions about treatment costs and financial burden are often lacking. Employment decisions are heavily influenced by the need to maintain health insurance coverage (Tangka et al., 2020). The financial burden of breast cancer treatment can lead to treatment non-adherence and negatively impact quality of life. Patients with breast cancer worldwide, especially in low- and middle-income countries, face high rates of financial toxicity from the costs of care (Ehsan et al., 2023).

Fertility and Family Planning

The impact of TNBC treatment on fertility can cause significant distress for young women, particularly those who wish to have children. The potential loss of fertility due to chemotherapy is a major source of grief and anxiety, affecting both mental health and life planning (Gorman et al., 2012). For women who become pregnant post-treatment, concerns about the impact on recurrence risk are common, though evidence suggests pregnancy does not increase this risk (Lambertini et al., 2016).

Long-Term Survivorship Issues

As treatment for TNBC improves, more young women are living as long-term survivors, facing unique health and psychosocial challenges that extend beyond active treatment. Survivorship for this population requires ongoing attention to physical, emotional, and financial well-being.

Physical Health Concerns

Long-term survivors of TNBC face significant physical health risks, including cardiotoxicity and secondary malignancies. Anthracycline-based chemotherapy, commonly used in TNBC treatment, is associated with an increased risk of heart failure and other cardiovascular complications. (Armenian et al., 2016) reported that young breast cancer survivors have a nearly two-fold higher risk of heart failure compared to the general population.

Additionally, radiation therapy increases the risk of secondary cancers, such as lung cancer or leukemia, particularly in younger patients with a long life expectancy (Grantzau & Overgaard, 2015). Chemotherapy-induced menopause also accelerates bone density loss, raising the risk of osteoporosis and fractures later in life (Pistilli et al., 2016).

Cognitive impairment, commonly referred to as "chemo brain," is another long-term issue for TNBC survivors. It can affect daily functioning, work performance, and overall quality of life, persisting years after treatment has ended (Shapiro et al., 2001).

Psychosocial and Emotional Well-being

Psychosocial challenges extend into long-term survivorship for young TNBC patients. Chronic anxiety about recurrence is common, given TNBC's higher recurrence rates compared to other breast cancer subtypes (Thewes et al., 2017). This persistent fear can significantly affect emotional well-being, even years after initial treatment.

Survivors may also struggle with their identity, feeling caught between the roles of a cancer patient and a healthy young adult(Tindle et al., 2009). Relationship difficulties are also more common, with higher rates of divorce or separation reported among breast cancer survivors (Kirchhoff et al., 2012).

Reproductive Health and Family Planning

Fertility remains a central concern for young TNBC survivors. Many women experience infertility because of chemotherapy. While pregnancy post-treatment does not appear to increase recurrence risk, concerns about timing and the ability to conceive often linger (Lambertini et al., 2018). Surgical and radiation treatments can also complicate breastfeeding for young mothers.

Lifestyle and Health Behaviors

Adopting healthy lifestyle behaviors is crucial for long-term survivorship. Regular physical activity has been shown to reduce the risk of recurrence and improve overall well-being in breast cancer survivors (Vijayvergia & Denlinger, 2015). Maintaining a healthy weight and avoiding alcohol and tobacco use are also important for reducing the risk of recurrence and managing overall health. Research indicates that maintaining a healthy lifestyle is crucial for cancer survivors to reduce the risk of recurrence and improve overall health. Studies show that many survivors make positive changes after diagnosis, with 81% quitting smoking (Evangelista et al., 2003). However, a significant proportion continue risky behaviors, including smoking, alcohol consumption, and being overweight (Bellizzi et al., 2005; Evangelista et al., 2003). These behaviors are associated with poorer perceived health status (Evangelista et al., 2003). Younger survivors (18-40 years) are at higher risk for continued smoking. Physical activity, healthy diet, and cancer screening are important for survivors' well-being, with survivors more likely to meet physical activity and cancer screening recommendations compared to non-cancer controls (Bellizzi et al., 2005). Interventions

targeting multiple risk factors are needed to improve overall health outcomes for cancer survivors (Evangelista et al., 2003)

Financial Toxicity

Adolescents and young adults (AYA) cancer survivors face long-term financial hardship that impacts their healthcare and personal finances(Thom et al., 2023).The financial burden of TNBC does not end with treatment. Many young survivors face ongoing medical costs related to surveillance, management of side effects, and necessary follow-up care. Many experience financial decline, with 25% attributing this to breast cancer (Jagsi et al., 2014). These expenses, combined with potential career disruptions, can lead to long-term financial hardship. Financial consequences include decreased credit scores, debt collection, and spending over 10% of income on medical expenses. Survivors often resort to coping behaviors like using savings, taking on credit card debt, and borrowing money (Thom et al., 2023)

Survivorship Care and Follow-Up

Comprehensive survivorship care plans are essential for young TNBC survivors, detailing follow-up recommendations, monitoring for late effects, and addressing ongoing psychosocial needs. However, many young survivors report gaps in care, particularly when transitioning from oncology to primary care providers. This highlights the need for better coordination in long-term survivorship care (Blanch-Hartigan et al., 2014).

Conclusion

This review highlights the complex challenges faced by young women with triple-negative breast cancer (TNBC), emphasizing the need for tailored approaches in diagnosis, treatment, and care. The unique biological characteristics of TNBC in this population, including higher rates of BRCA mutations and aggressive subtypes, underscore the importance of age-specific research and early detection strategies.

While chemotherapy remains the primary treatment, emerging therapies offer new hope. However, balancing aggressive treatment with long-term quality of life is crucial, particularly regarding fertility preservation and managing potential long-term health impacts. The profound psychosocial burden on young TNBC patients necessitates comprehensive support addressing body image, relationships, and career concerns.

Long-term survivorship presents additional challenges, including managing treatment-related complications and addressing financial toxicity. Future efforts should focus on developing personalized screening strategies, conducting age-specific research, and integrating fertility preservation and psychosocial care into standard treatment protocols. Addressing racial disparities in TNBC prevalence and outcomes is also critical for improving care for all young patients.

References

Abu Abeelh, E., & AbuAbeileh, Z. (2024). Comparative Effectiveness of Mammography, Ultrasound, and MRI in the Detection of Breast Carcinoma in Dense Breast Tissue: A Systematic Review. *Cureus*. https://doi.org/10.7759/cureus.59054

Ademuyiwa, F. O., Tao, Y., Luo, J., Weilbaecher, K., & Ma, C. X. (2017). Differences in the mutational landscape of triple-negative breast cancer in African Americans and Caucasians. *Breast Cancer Research and Treatment*, *161*(3), 491–499. https://doi.org/10.1007/s10549-016-4062-y

Ahmad, S., Fergus, K., & McCarthy, M. (2015). Psychosocial issues experienced by young women with breast cancer: The minority group with the majority of need. *Current Opinion in Supportive & Palliative Care*, *9*(3), 271–278. https://doi.org/10.1097/SPC.0000000000000162

Armenian, S. H., Xu, L., Ky, B., Sun, C., Farol, L. T., Pal, S. K., Douglas, P. S., Bhatia, S., & Chao, C. (2016). Cardiovascular Disease Among Survivors of Adult-Onset Cancer: A Community-Based Retrospective Cohort Study. *Journal of Clinical Oncology*, *34*(10), 1122–1130. https://doi.org/10.1200/JCO.2015.64.0409

Bardia, A., Hurvitz, S. A., Tolaney, S. M., Loirat, D., Punie, K., Oliveira, M., Brufsky, A., Sardesai, S. D., Kalinsky, K., Zelnak, A. B., Weaver, R., Traina, T., Dalenc, F., Aftimos, P., Lynce, F., Diab, S., Cortés, J., O'Shaughnessy, J., Diéras, V., … Rugo, H. S. (2021). Sacituzumab Govitecan in Metastatic Triple-Negative Breast Cancer. *New England Journal of Medicine*, *384*(16), 1529–1541. https://doi.org/10.1056/NEJMoa2028485

Bartelink, H., Maingon, P., Poortmans, P., Weltens, C., Fourquet, A., Jager, J., Schinagl, D., Oei, B., Rodenhuis, C., Horiot, J.-C., Struikmans, H., Van Limbergen, E., Kirova, Y., Elkhuizen, P., Bongartz, R., Miralbell, R., Morgan, D., Dubois, J.-B., Remouchamps, V., … Collette, L. (2015). Whole-breast irradiation with or without a boost for patients treated with breast-conserving surgery for early breast cancer: 20-year follow-up of a randomised phase 3 trial. *The Lancet Oncology*, *16*(1), 47–56. https://doi.org/10.1016/S1470-2045(14)71156-8

Beg, S., Siraj, A. K., Prabhakaran, S., Jehan, Z., Ajarim, D., Al-Dayel, F., Tulbah, A., & Al-Kuraya, K. S. (2015). Loss of PTEN expression is associated with aggressive behavior and poor prognosis in Middle Eastern triple-negative breast cancer. *Breast Cancer Research and Treatment*, *151*(3), 541–553. https://doi.org/10.1007/s10549-015-3430-3

Bellizzi, K. M., Rowland, J. H., Jeffery, D. D., & McNeel, T. (2005). Health Behaviors of Cancer Survivors: Examining Opportunities for Cancer Control Intervention. *Journal of Clinical Oncology*, *23*(34), 8884–8893. https://doi.org/10.1200/JCO.2005.02.2343

Blanch-Hartigan, D., Forsythe, L. P., Alfano, C. M., Smith, T., Nekhlyudov, L., Ganz, P. A., & Rowland, J. H. (2014). Provision and Discussion of Survivorship Care Plans Among Cancer Survivors: Results of a Nationally Representative Survey of Oncologists and Primary Care Physicians. *Journal of Clinical Oncology*, *32*(15), 1578–1585. https://doi.org/10.1200/JCO.2013.51.7540

Bollinger, S. (2018). Biopsychosocial Challenges and Needs of Young African American Women with Triple-Negative Breast Cancer. *Health & Social Work*, *43*(2), 84–92. https://doi.org/10.1093/hsw/hly006

Champion, V. L., Wagner, L. I., Monahan, P. O., Daggy, J., Smith, L., Cohee, A., Ziner, K. W., Haase, J. E., Miller, K. D., Pradhan, K., Unverzagt, F. W., Cella, D., Ansari, B., & Sledge, G. W. (2014). Comparison of younger and older breast cancer survivors and age-matched controls on specific and overall quality of life domains. *Cancer*, *120*(15), 2237–2246. https://doi.org/10.1002/cncr.28737

Cobo, A., Garcia-Velasco, J. A., Domingo, J., Remohí, J., & Pellicer, A. (2013). Is vitrification of oocytes useful for fertility preservation for age-related fertility decline and in cancer patients? *Fertility and Sterility*, *99*(6), 1485–1495. https://doi.org/10.1016/j.fertnstert.2013.02.050

Dass, S. A., Tan, K. L., Selva Rajan, R., Mokhtar, N. F., Mohd Adzmi, E. R., Wan Abdul Rahman, W. F., Tengku Din, T. A. D. A.-A., & Balakrishnan, V. (2021). Triple Negative Breast Cancer: A Review of Present and Future Diagnostic Modalities. *Medicina*, *57*(1), 62. https://doi.org/10.3390/medicina57010062

Dietze, E. C., Sistrunk, C., Miranda-Carboni, G., O'Regan, R., & Seewaldt, V. L. (2015). Triple-negative breast cancer in African-American women: Disparities versus biology. *Nature Reviews Cancer*, *15*(4), 248–254. https://doi.org/10.1038/nrc3896

Ehsan, A. N., Wu, C. A., Minasian, A., Singh, T., Bass, M., Pace, L., Ibbotson, G. C., Bempong-Ahun, N., Pusic, A., Scott, J. W., Mekary, R. A., & Ranganathan, K. (2023). Financial Toxicity Among Patients With Breast Cancer Worldwide: A Systematic Review and Meta-analysis. *JAMA Network Open*, *6*(2), e2255388. https://doi.org/10.1001/jamanetworkopen.2022.55388

Evangelista, L. S., Sarna, L., Brecht, M. L., Padilla, G., & Chen, J. (2003). Health perceptions and risk behaviors of lung cancer survivors. *Heart & Lung*, *32*(2), 131–139. https://doi.org/10.1067/mhl.2003.12

Foulkes, W. D., & Reis-Filho, J. S. (2010). Triple-Negative Breast Cancer. *The New England Journal of Medicine*.

Frasier, L. L., Holden, S., Holden, T., Schumacher, J. R., Leverson, G., Anderson, B., Greenberg, C. C., & Neuman, H. B. (2016). Temporal Trends in Postmastectomy Radiation Therapy and Breast Reconstruction Associated With Changes in National Comprehensive Cancer Network Guidelines. *JAMA Oncology*, *2*(1), 95. https://doi.org/10.1001/jamaoncol.2015.3717

Gorman, J. R., Bailey, S., Pierce, J. P., & Su, H. I. (2012). How do you feel about fertility and parenthood? The voices of young female cancer survivors. *Journal of Cancer Survivorship*, *6*(2), 200–209. https://doi.org/10.1007/s11764-011-0211-9

Grantzau, T., & Overgaard, J. (2015). Risk of second non-breast cancer after radiotherapy for breast cancer: A systematic review and meta-analysis of 762,468 patients. *Radiotherapy and Oncology*, *114*(1), 56–65. https://doi.org/10.1016/j.radonc.2014.10.004

Griffiths, C. L., & Olin, J. L. (2012). Triple Negative Breast Cancer: A Brief Review of its Characteristics and Treatment Options. *Journal of Pharmacy Practice*, *25*(3), 319–323. https://doi.org/10.1177/0897190012442062

Hooley, R. J., Durand, M. A., & Philpotts, L. E. (2017). Advances in Digital Breast Tomosynthesis. *American Journal of Roentgenology*, *208*(2), 256–266. https://doi.org/10.2214/AJR.16.17127

Jagsi, R., Pottow, J. A. E., Griffith, K. A., Bradley, C., Hamilton, A. S., Graff, J., Katz, S. J., & Hawley, S. T. (2014). Long-Term Financial Burden of Breast Cancer: Experiences of a Diverse Cohort of Survivors Identified Through Population-Based Registries. *Journal of Clinical Oncology*, *32*(12), 1269–1276. https://doi.org/10.1200/JCO.2013.53.0956

Kirchhoff, A. C., Yi, J., Wright, J., Warner, E. L., & Smith, K. R. (2012). Marriage and divorce among young adult cancer survivors. *Journal of Cancer Survivorship*, *6*(4), 441–450. https://doi.org/10.1007/s11764-012-0238-6

Kronowitz, S. J., & Robb, G. L. (2004). Breast Reconstruction with Postmastectomy Radiation Therapy: Current Issues: *Plastic and Reconstructive Surgery*, *114*(4), 950–960. https://doi.org/10.1097/01.PRS.0000133200.99826.7F

Kurian, A. W., Lichtensztajn, D. Y., Keegan, T. H. M., Nelson, D. O., Clarke, C. A., & Gomez, S. L. (2014). Use of and Mortality After Bilateral Mastectomy Compared With Other Surgical Treatments for Breast Cancer in California, 1998-2011. *JAMA*, *312*(9), 902. https://doi.org/10.1001/jama.2014.10707

Lambertini, M., Del Mastro, L., Pescio, M. C., Andersen, C. Y., Azim, H. A., Peccatori, F. A., Costa, M., Revelli, A., Salvagno, F., Gennari, A., Ubaldi, F. M., La Sala, G. B., De Stefano, C., Wallace, W. H., Partridge, A. H., & Anserini, P. (2016). Cancer and fertility preservation: International recommendations from an expert meeting. *BMC Medicine*, *14*(1), 1. https://doi.org/10.1186/s12916-015-0545-7

Lambertini, M., Kroman, N., Ameye, L., Cordoba, O., Pinto, A., Benedetti, G., Jensen, M.-B., Gelber, S., Del Grande, M., Ignatiadis, M., De Azambuja, E., Paesmans, M., Peccatori, F. A., & Azim, H. A. (2018). Long-term Safety of Pregnancy Following Breast Cancer According to Estrogen Receptor Status. *JNCI: Journal of the National Cancer Institute*, *110*(4), 426–429. https://doi.org/10.1093/jnci/djx206

Lee, E., McKean-Cowdin, R., Ma, H., Spicer, D. V., Van Den Berg, D., Bernstein, L., & Ursin, G. (2011). Characteristics of Triple-Negative Breast Cancer in Patients With a *BRCA1* Mutation: Results From a Population-Based Study of Young Women. *Journal of Clinical Oncology*, *29*(33), 4373–4380. https://doi.org/10.1200/JCO.2010.33.6446

Lehmann, B. D., Bauer, J. A., Chen, X., Sanders, M. E., Chakravarthy, A. B., Shyr, Y., & Pietenpol, J. A. (2011). Identification of human triple-negative breast cancer subtypes and preclinical models for selection of targeted therapies. *Journal of Clinical Investigation*, *121*(7), 2750–2767. https://doi.org/10.1172/JCI45014

Loibl, S., O'Shaughnessy, J., Untch, M., Sikov, W. M., Rugo, H. S., McKee, M. D., Huober, J., Golshan, M., Von Minckwitz, G., Maag, D., Sullivan, D., Wolmark, N., McIntyre, K., Ponce Lorenzo, J. J., Metzger Filho, O., Rastogi, P., Symmans, W. F., Liu, X., & Geyer, C. E. (2018). Addition of the PARP inhibitor veliparib plus carboplatin or carboplatin alone to standard neoadjuvant chemotherapy in triple-negative breast cancer (BrighTNess): A randomised, phase 3 trial. *The Lancet Oncology*, *19*(4), 497–509. https://doi.org/10.1016/S1470-2045(18)30111-6

Mathis, K. L., Hoskin, T. L., Boughey, J. C., Crownhart, B. S., Brandt, K. R., Vachon, C. M., Grant, C. S., & Degnim, A. C. (2010). Palpable Presentation of Breast Cancer Persists in the Era of Screening Mammography. *Journal of the American College of Surgeons*, *210*(3), 314–318. https://doi.org/10.1016/j.jamcollsurg.2009.12.003

Moore, H. C. F., Unger, J. M., Phillips, K.-A., Boyle, F., Hitre, E., Porter, D., Francis, P. A., Goldstein, L. J., Gomez, H. L., Vallejos, C. S., Partridge, A. H., Dakhil, S. R., Garcia, A. A., Gralow, J., Lombard, J. M., Forbes, J. F., Martino, S., Barlow, W. E., Fabian, C. J., … Albain, K. S. (2015). Goserelin for Ovarian Protection during Breast-Cancer Adjuvant Chemotherapy. *New England Journal of Medicine*, *372*(10), 923–932. https://doi.org/10.1056/NEJMoa1413204

Mudaranthakam, D. P., Hughes, D., Johnson, P., Mason, T., Nollen, N., Wick, J., Welch, D. R., & Calhoun, E. (2023). Career disruption and limitation of financial earnings due to cancer. *JNCI Cancer Spectrum*, *7*(4), pkad044. https://doi.org/10.1093/jncics/pkad044

Nederlof, I., Horlings, H. M., Curtis, C., & Kok, M. (2021). A High-Dimensional Window into the Micro-Environment of Triple Negative Breast Cancer. *Cancers*, *13*(2), 316. https://doi.org/10.3390/cancers13020316

Oeffinger, K. C., Fontham, E. T. H., Etzioni, R., Herzig, A., Michaelson, J. S., Shih, Y.-C. T., Walter, L. C., Church, T. R., Flowers, C. R., LaMonte, S. J., Wolf, A. M. D., DeSantis, C., Lortet-Tieulent, J., Andrews, K., Manassaram-Baptiste, D., Saslow, D., Smith, R. A., Brawley, O. W., & Wender, R. (2015). Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. *JAMA*, *314*(15), 1599. https://doi.org/10.1001/jama.2015.12783

Partridge, A. H., Gelber, S., Peppercorn, J., Sampson, E., Knudsen, K., Laufer, M., Rosenberg, R., Przypyszny, M., Rein, A., & Winer, E. P. (2004). Web-Based Survey of Fertility Issues in Young Women With Breast Cancer. *Journal of Clinical Oncology*, *22*(20), 4174–4183. https://doi.org/10.1200/JCO.2004.01.159

Ritter, M. (2008). Rationale, Conduct, and Outcome Using Hypofractionated Radiotherapy in Prostate Cancer. *Seminars in Radiation Oncology*, *18*(4), 249–256. https://doi.org/10.1016/j.semradonc.2008.04.007

Rosa, M. L., Reinert, T., Pauletto, M. M., Sartori, G., Graudenz, M., & Barrios, C. H. (2024). Implications of tumor-infiltrating lymphocytes in early-stage triple-negative breast cancer: Clinical oncologist perspectives. *Translational Breast Cancer Research*, *5*, 4–4. https://doi.org/10.21037/tbcr-23-43

Rosenberg, S. M., & Partridge, A. H. (2015). Management of breast cancer in very young women. *The Breast*, *24*, S154–S158. https://doi.org/10.1016/j.breast.2015.07.036

Schmid, P., Cortes, J., Pusztai, L., McArthur, H., Kümmel, S., Bergh, J., Denkert, C., Park, Y. H., Hui, R., Harbeck, N., Takahashi, M., Foukakis, T., Fasching, P. A., Cardoso, F., Untch, M., Jia, L., Karantza, V., Zhao, J., Aktan, G., … O'Shaughnessy, J. (2020). Pembrolizumab for Early Triple-Negative Breast Cancer. *New England Journal of Medicine*, *382*(9), 810–821. https://doi.org/10.1056/NEJMoa1910549

Shapiro, C. L., Manola, J., & Leboff, M. (2001). Ovarian Failure After Adjuvant Chemotherapy Is Associated With Rapid Bone Loss in Women With Early-Stage Breast Cancer. *Journal of Clinical Oncology*, *19*(14), 3306–3311. https://doi.org/10.1200/JCO.2001.19.14.3306

Sineshaw, H. M., Gaudet, M., Ward, E. M., Flanders, W. D., Desantis, C., Lin, C. C., & Jemal, A. (2014). Association of race/ethnicity, socioeconomic status, and breast cancer subtypes in the National Cancer Data Base (2010–2011). *Breast Cancer Research and Treatment*, *145*(3), 753–763. https://doi.org/10.1007/s10549-014-2976-9

Sklar, C. (2005). Maintenance of Ovarian Function and Risk of Premature Menopause Related to Cancer Treatment. *Journal of the National Cancer Institute Monographs*, *2005*(34), 25–27. https://doi.org/10.1093/jncimonographs/lgi018

Sonmezer, M., & Oktay, K. (2006). Fertility Preservation in Young Women Undergoing Breast Cancer Therapy. *The Oncologist*, *11*(5), 422–434. https://doi.org/10.1634/theoncologist.11-5-422

Spring, L., Greenup, R., Niemierko, A., Schapira, L., Haddad, S., Jimenez, R., Coopey, S., Taghian, A., Hughes, K. S., Isakoff, S. J., Ellisen, L. W., Smith, B. L., Specht, M., Moy, B., & Bardia, A. (2017). Pathologic Complete Response After Neoadjuvant Chemotherapy and Long-Term Outcomes Among Young Women With Breast Cancer. *Journal of the National Comprehensive Cancer Network*, *15*(10), 1216–1223. https://doi.org/10.6004/jnccn.2017.0158

Şükür, Y. E., Özmen, B., & Sönmezer, M. (2010). Cancer and ovarian tissue cryopreservation. *Turkish Journal of Medical Sciences*. https://doi.org/10.3906/sag-0905-4

Tangka, F. K. L., Subramanian, S., Jones, M., Edwards, P., Flanigan, T., Kaganova, Y., Smith, K. W., Thomas, C. C., Hawkins, N. A., Rodriguez, J., Fairley, T., & Guy, G. P. (2020). Insurance Coverage, Employment Status, and Financial Well-Being of Young Women Diagnosed with Breast Cancer. *Cancer Epidemiology, Biomarkers & Prevention*, *29*(3), 616–624. https://doi.org/10.1158/1055-9965.EPI-19-0352

Thewes, B., Kaal, S. E. J., Custers, J. A. E., Manten-Horst, E., Jansen, R., Servaes, P., Van Der Graaf, W. T. A., Prins, J. B., & Husson, O. (2017). Prevalence and correlates of high fear of cancer recurrence in late adolescents and young adults consulting a specialist adolescent and young adult (AYA) cancer service. *Supportive Care in Cancer*. https://doi.org/10.1007/s00520-017-3975-2

Thom, B., Friedman, D. N., Aviki, E. M., Benedict, C., Watson, S. E., Zeitler, M. S., & Chino, F. (2023). The long-term financial experiences of adolescent and young adult cancer survivors. *Journal of Cancer Survivorship*, *17*(6), 1813–1823. https://doi.org/10.1007/s11764-022-01280-2

Tindle, D., Denver, K., & Lilley, F. (2009). Identity, Image, and Sexuality in Young Adults With Cancer. *Seminars in Oncology*, *36*(3), 281–288. https://doi.org/10.1053/j.seminoncol.2009.03.008

Tung, N. M., Boughey, J. C., Pierce, L. J., Robson, M. E., Bedrosian, I., Dietz, J. R., Dragun, A., Gelpi, J. B., Hofstatter, E. W., Isaacs, C. J., Jatoi, I., Kennedy, E., Litton, J. K., Mayr, N. A., Qamar, R. D., Trombetta, M. G., Harvey, B. E., Somerfield, M. R., & Zakalik, D. (2020). Management of Hereditary Breast Cancer: American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Guideline. *Journal of Clinical Oncology*, *38*(18), 2080–2106. https://doi.org/10.1200/JCO.20.00299

Tutt, A. N. J., Garber, J. E., Kaufman, B., Viale, G., Fumagalli, D., Rastogi, P., Gelber, R. D., De Azambuja, E., Fielding, A., Balmaña, J., Domchek, S. M., Gelmon, K. A., Hollingsworth, S. J., Korde, L. A., Linderholm, B., Bandos, H., Senkus, E., Suga, J. M., Shao, Z., … Geyer, C. E. (2021). Adjuvant Olaparib for Patients with *BRCA1*—Or *BRCA2* -Mutated Breast Cancer. *New England Journal of Medicine*, *384*(25), 2394–2405. https://doi.org/10.1056/NEJMoa2105215

Vijayvergia, N., & Denlinger, C. (2015). Lifestyle Factors in Cancer Survivorship: Where We Are and Where We Are Headed. *Journal of Personalized Medicine*, *5*(3), 243–263. https://doi.org/10.3390/jpm5030243

Vin-Raviv, N., Hillyer, G. C., Hershman, D. L., Galea, S., Leoce, N., Bovbjerg, D. H., Kushi, L. H., Kroenke, C., Lamerato, L., Ambrosone, C. B., Valdimorsdottir, H., Jandorf, L., Mandelblatt, J. S., Tsai, W.-Y., & Neugut, A. I. (2013). Racial Disparities in Posttraumatic Stress After Diagnosis of Localized Breast Cancer: The BQUAL Study. *JNCI Journal of the National Cancer Institute*, *105*(8), 563–572. https://doi.org/10.1093/jnci/djt024

Vuković, P. (2019). Fertility Preservation in Young Women with Early-Stage Breast Cancer. *Acta Clinica Croatica*. https://doi.org/10.20471/acc.2019.58.01.19