



Research Article

# Challenges for Follow-Up of Sides Effects and Sequelae After Ovarian and Endometrial Cancers Treatments

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## Abstract

**Purpose :** Multimodal treatments for ovarian cancer (OC) and endometrial cancer (EC) are susceptible to induce long-term disorders and to alter the quality of life of patients. This review aims to underline the necessity to move forward to better identify and manage the sides effects and sequelae in order to enhance quality of life of gynecological cancer survivors. **Methods :** narrative review. **Results :** OC and EC patients experience a wide range of symptoms that may persist over time: fatigue, pain, nausea, abdominal discomfort, peripheral neuropathy, anxiety, depression, sleep disorders, menopausal symptoms and sexual disorders. Management of these disorders need to be included in follow-up care plans that help to summarize cancer history, long-term side effects and to give information on health promotion and prevention. Long term patient-reported outcome measures may contribute to cover the full range of these toxicities such as fatigue, lymphedema, and cognitive impairment. The coordination between the supportive care and the health-care provider is crucial needed to offer a personalized management for OC and EC survivors and to ensure adapted supportive care along survivorship. **Conclusion:** Gynecological cancer survivors have specific needs that should be addressed systematically by caregivers. The implementation of a survivorship care plan after cancer treatment is recommended and can be useful to monitor patient's needs. Coordination and development of networks of supportive care providers for long-term survivors after gynecological cancer is needed to reduce long-term toxicities and improve the quality of life of these patients.

**Keywords:** Ovarian Cancer; Endometrial Cancer; Survivorship; Long-Term Survival; Supportive Care; Survivorship Care Plan;

**Methods:** This manuscript is a narrative review of the litterature aiming to describe the sides effects and sequelae after ovarian and endometrial cancers treatments and their management (detailed methodology available in supplementary material).

**Clinical Outcome in Ovarian and Endometrial Cancers**

Thanks to progresses in surgical expertise and medical advances, ovarian cancer (OC) prognosis have improved, with

survival rates around 44% at 5 years [1]. In addition, endometrial cancer (EC) long term survivors are also increasing, with a 5years overall survival rate of 90.1% in France [2].

Treatment complications and long-term toxicities in OC and EC survivors are sum-marized in table 1. This review targets endometrial and ovarian cancers as they offer some similarities in survivorship: patients have approximatively the same age, experience heavy pelvic/abdominal surgery, and are exposed to the same drugs of chemotherapy. Thus, the needs observed during survivorship have some similarities.

Long-term potential toxicities and their prevalence for ovarian and endometrial cancers survivors.	References
Fatigue (40-60%)	(3,8)
Pain (50%)	(26,28)
Depression and psychological concerns (55%)	(3,4,12)
Sleep disorders (60%)	(3,4,10)
Urinary/stool incontinence (50%)	(15,16)
Menopausal symptoms (65%)	-20
Sexuality concerns (from 6% to 50% depending on patient's age)	(22,23)
Gastrointestinal concerns (30%)	(17,19)
Chemotherapy induced polyneuropathy (CIPN) (75%)	(28,29)
Cognitive impairment (up to 60% after completion of primary treatment)	-38
Risks for cardiovascular disorders: 60% overweight, 55% hypertension Lymphedema (30%)	-42
Secondary and new primary cancers	(31,32)
Reproductive issues (if indicated)	
Social issues	

**Table 1:** Long-term potential toxicities for ovarian and endometrial cancers survivors.

Here comes the necessity to move forward to better identify and manage the sides ef-fects and sequelae in order to enhance quality of life (QoL) in these populations who often present some other comorbidities. Propositions for management of potential long-term potential toxicities experienced by ovarian and endometrial cancers survivors are reported in table 2.

Symptoms	Options for symptom management
<b>Fatigue</b>	Systematic screening of cancer related fatigue
	Risk factors prevention: fight against altered sleep and comorbidities, warning young patients
	Promote physical activity and good general health conditions (nutritionnal counseling, smoking sevrage, ...)
<b>Psychological issues and sleep disturbance</b>	Identification of anxiety, distress, depression from the outset of primary care
	Vigilance on risk factors: elderly patients with comorbidities or functional limitations
	Psychological support, adaptation of lifestyle conditions, limitation of pharmaceutical intervention
	Specialized intervention if necessary: psychological care, support group, behavioral interventions

<b>Chronic pain / Chemotherapy induced neuropathy (CIPN) (50-75%)</b>	Identification of chronic pain and CIPN by systematic evaluation throughout the time
	Management of CIPN demands a combination of local therapies (Transcutaneous Electrical Nerve Stimulation, Capsaicine, Acupuncture) and pharmacological treatments (anti-epileptic and/or antidepressant drugs)
	If standard pain management fails, specialized intervention in pain clinics may be necessary
<b>Urinary and bowel disorders (50% and 30% respectively)</b>	Early detection and evaluation of the gravity of urinary and/or bowel impairment
	Prevention on patients at risk: older age, advanced disease, high BMI
	Dietetic counseling, perineal readaptation or specialized intervention may help to manage
<b>Sexual Disorders</b>	Open the discussion on sexual dysfunction, especially with young patients, to evaluate its impact on quality of life,
	Treatment for vaginal dryness or dyspareunia (for example vaginal laser therapy in case of estrogen therapy contraindication)
	Specialized support can be offered by specialized sexo-oncologists
<b>Menopausal Symptoms -50%</b>	Hormonal replacement therapy is oftenly possible in case of early menopause
	Bone health prevention and osteoporosis detection
	and treatment particularly for young patients
<b>Lymphedema -40%</b>	Prevention using minimally invasive node surgery and/or reduce pelvic radiation fields
	Patient education in order to prevent risk-factors for lymphedema relying on physical activity and weight loss
	Regular assessment and management of lymphedema with specialized physical pressure therapists
<b>Social Issues</b>	Identification of social issues induced by cancer treatments and counseling with patient's supports groups and/or social workers
<b>General Health Conditions</b>	Promotion for healthy living and physical activity
	Fight against obesity
	Particular focus on cardiovascular disorders
	Ensure other cancers detection

**Table 2:** Management of potential long-term potential toxicities experienced by ovarian and en-dometrial cancers survivors.

In OVQUEST trial [3], including 1360 cancer survivors, of which 421 (31%) OC survivors, 78% had chemotherapy induced peripheral neuropathy (CIPN), 60% suffered from persistent fatigue, 48% psychological issues and 59% sleep disorders. VIVROVAIRE I [4] demonstrated that, compared with healthy women, OC survivors had similar QoL but re-reported long-term fatigue, CIPN, distress and depression, and insomnia. Long-term fatigue was associated with depression, neuropathy, and sleep disorders. For EC patients, POR-TEC-3 [5] was a phase III trial in high risk EC comparing adjuvant chemoradiation followed by chemotherapy versus radiotherapy only. Long-term toxicity PORTEC-3 analysis demonstrated that chemoradiation was associated with more toxicity, such as CIPN, and deteriorated QoL [6]. The negative impact for the patients treated with chemoradiation was observed until 3 years with a physical and role functioning impairments.

The negative impact on QoL of the multimodal treatments in OC and EC is long lasting. Zanderberg [7] reported the evolution of QoL among gynecological cancer survivors two years after the end of initial management: patients with comorbidities, with an advanced disease or treated with chemotherapy, had more physical functioning impairment during treatment and persistent cognitive and social functioning impairment after 12 months. Treatments sides effects appeared early with 50% of complications beginning during the first year after treatment. Nonetheless, 10% of treatments sequelae appeared after 60 months of follow-up, altering quality of life in emotional and physical domains of EC survivors.

Beyond these general side effects, OC and EC cancer survivors suffer from specific symptoms and sequelae directly related with gynecological cancer and treatments.

### **Fatigue, Sleep Disturbance and Psychological Disorders**

Long-term fatigue is the most common issue among cancer survivors. Patients treated for gynecological cancer experienced fatigue for 50% of them after surgery, 44% at 6 months and 39% at 12 months [8]. Long-term fatigue at 12 months, was associated with depression, or multiple comorbidities. In a cohort of 134 EC survivors, Xu et al [9], also described that altered sleep, comorbidities and younger age were risk factors for long-term fatigue.

Sleep disorders, such as insomnia, are frequent among OC and EC survivors during, and after their treatment. Sleep difficulties have a negative impact on QoL in this population of cancer survivors. In a study describing insomnia and sleep disorders in ovarian cancer [10], insomnia was associated with psychological issues (ie distress, depression) and altered QoL. Taking these difficulties into account, an interventional trial (NCT05044975) is ongoing to optimize a behavioral sleep intervention in order to dimin-

ish sleep disturbance among gynecologic cancer survivors [11].

The proportion of patients suffering from distress after OC and EC treatment is high [12]. In a cohort of 92 survivors who were at a median time of 7.6 months from primary treatment, 57% reported distress such as fatigue and worry. Distress was mainly observed for patients who had a high number of problems, or had unmet needs for rehabilitation services.

Anxiety and depression are the most prevalent psychological disorders, and are more frequent among cancer survivors than in the general population. Women treated for EC or OC are at higher risk for depression compared with healthy women [13]. The risk for depression symptoms is increased during primary care and remains increased for years after diagnosis, despite oncologic care. Pharmacological solutions, such as antidepressant use, are preferentially observed for patients with comorbidities, advanced disease, or short education. Management of depression symptoms can rely on physical activity which had the ability to lower depressive symptoms in cancer survivors, but studies specifically concerning gynecological cancer survivors are lacking. Depression is particularly an issue among elderly women treated for OC or EC, and is more frequently reported for patients with comorbidities or functional limitations [14].

### **Genito-Urinary and Bowel Disorders**

EC survivors are at higher risk for many genitourinary outcomes compared to women from the general population: a cohort of 2648 EC survivors showed that, between 1 and 5 years after cancer diagnosis, those with higher stage, higher grade, older age and treated with radiation or chemotherapy were at higher risk for urinary disorders [15]. In another retrospective cohort of 149 EC survivors [16], 51% of women reported urine leakage. Significant risk factors for urinary incontinence were age (OR 1.06 95% CI 1.02, 1.10) and body mass index (BMI) (OR 1.07 95% CI 1.02, 1.11).

Bowel symptoms are also frequent. In a study including 623 gynecological cancer survivors (including EC and OC) and 344 population-based controls, Steineck et al. [17] found 30% urgency, 26% leakage syndrome, 15% excessive gas discharge, 16% excessive mucus discharge and 10% blood discharge after pelvic radiation. External beam pelvic radiation is responsible for long-term disorders as demonstrated in PORTEC-2 long term analysis. PORTEC-2 [18] is a phase III trial in EC comparing adjuvant vaginal brachytherapy to standard pelvic radiation. In PORTEC-2 long-term analysis, more than 7 years after treatment, patients treated by radiotherapy reported more bowel symptoms with impact on daily activities, and a trend for more urinary symptoms compared with those treated with vaginal brachytherapy [19].

### **Menopausal Symptoms and Sexual Disorders**

Vasomotor symptoms and sexual disorders are frequently reported by OC survivors, particularly among patients with surgical menopause. In a cohort of 166 OC patients with relapse-free =3 years after the end of treatment, Gernier et al. [20] reported that half of patients had vasomotor symptoms, 2/3 had a decrease in libido, 14% had osteoporosis and 50% osteopenia. Women treated for gynecological malignancies with surgery and adjuvant chemotherapy have significantly lower bone mineral density than age-matched women who have undergone oophorectomy for noncancer indications [21].

In a cohort of 126 young (mean age of 42.4 years) gynecologic cancer survivors (including OC, EC and cervical carcinomas), 43.7% of sexual dysfunction associated with distress was reported. The main sexual disorders were: loss of sexual interest and arousal disorder [22]. Among 2946 EC and 1165 OC survivors treated between 1997 and 2012, 6.6% had complaint on sexual dysfunction 1-5 years after the end of cancer primary treatment. Compared with healthy women, OC and EC survivors had higher risks of overall sexual dysfunction (HR: 2.51, 95% CI: 2.16, 2.93), vaginal dryness (HR: 2.63, 95% CI: 2.21, 3.12), and dyspareunia (HR: 3.27, 95% CI: 2.63, 4.06) [23]. Despite increasing knowledge of sexual impairment after gynecological cancer treatment, this topic remains an unmet medical need. Indeed, in a recent Australian study [24], only 22% of OC survivors had the opportunity to discuss the impact of OC on their sexuality with their healthcare team, while 52% had wished to have a discussion on sexual disorders during primary care and 43% still felt the need to discuss 5 years after OC diagnosis. If clinicians wish to address cancer survivors' sexual health concerns, in order to improve their QoL, they may need help for understanding the strengths and limitations of sexual health screening tools which are complex and multiple [25]. Educational sessions on sexual health concerns among gynecological cancer survivors are needed to help clinicians feeling more comfortable with these issues.

### **Chronic Pain, Peripheral Neuropathy**

Chronic pain is also a major issue in cancer survivorship and can concern around one third of cancer survivors, with an negative impact on their QoL [26]. Cancer treatment related pain is made up of multiple components such as post-surgery pain, CIPN, genito-urinary or bowel pain, arthralgia or musculoskeletal pain. A dedicated management is therefore needed and patients may be referred to a pain clinic for multidisciplinary approaches [27].

Chemotherapy-induced peripheral neuropathy (CIPN) is frequent, particularly in OC and EC patients who received chemotherapy. Long-term negative impact of CIPN on QoL has been observed among OC survivors, even a long time after diagnosis. In a cohort of 129 OC patients treated with chemotherapy,

51% suffered from neuropathy up to 12 years after diagnosis, with a frank impairment of their health-related QoL [28]. Among 165 gynecologic cancer survivors, 21.8% patients had CIPN of Common Toxicity Criteria for Ad-verse Events grade 1 or higher [29]. In order to address the impact of CIPN symptoms in OC and EC survivor's QoL, early detection and adapted management of CIPN are crucial. Multimodal strategies are needed in order to reduce CIPN symptoms. For example, physical activity can help to improve psychosocial outcomes among gynecologic cancer survivors suffering from severe CIPN [30].

### **Lymphedema**

Lymphedema is a frequent, with a potential prevalence as high as 40% in OC survivors [31], but poorly understood side effect of gynecologic cancer treatment. In an EC population, a Korean study including 19,027 patients, found that 2493 (13.1%) developed lymphedema [32]. Risk factor for lymphedema were most commonly age and multimodal therapy such as pelvic lymphadenectomy incremented by pelvic radiotherapy [33,34].

Lymphedema is associated with decreased physical functioning and activities of daily living limitations, inducing financial difficulties [34]. Among 900 elderly women diagnosed with EC, OC or colorectal cancer, with a mean age of 78.5 years and a mean time since cancer diagnosis of 8.75 years, Zhang et al. [35], reported that nearly one-third of elderly female survivors experienced lymphedema and that it was associated with decreased physical functioning. These findings suggest that clinicians may need to regularly assess lymphedema among older survivors of cancer and provide effective interventions to reduce lymphedema symptoms.

### **Geriatric Concerns and Cognition Impairment**

With a median age at diagnosis of 65-70 years and an improved prognosis due to medical advances, the number of elderly EC and OC survivors is constantly growing. Management of these patients needs to rely on comprehensive data concerning their long-term health-related QoL and their specific needs. Long-term sexuality and QoL of elderly OC and EC patients has been reported by Mamguem Kamga A et al [36] : EC survivors had more deterioration on their physical QoL compared with OC survivors. For OC survivors, only physical functioning was impacted ( $p = 0.012$ ), while EC survivors QoL was altered in multiple areas: physical functioning ( $p < 0.0001$ ), role emotional ( $p = 0.018$ ), role physical ( $p = 0.001$ ), and chronic pain ( $p = 0.001$ ). Concerning neurotoxicity, it has been demonstrated that CIPN is associated with advanced age. Therefore, elderly OC and EC survivors may require specific attention on this point. Raising awareness and education of patients and professional caregivers for management of long-term CIPN impacts is crucial for survivors QoL [37].

Changes in cognitive function also have been described in OC and EC. In a large pro-spective study, the NRG oncology/gynecologic oncology group identified a subset of pa-tients had evidence of cognitive decline from baseline during chemotherapy treatment [38]. Cognitive impairment did not seem to be dependent on depression state after treat-ment or to a menopausal condition in a cohort of 73 gynecological cancer survivors, in-cluding 40 EC and 16 OC [39]. Various behavioral interventions have been demonstrated to show improvements in patient's quality of life and in their perceived cognitive abilities and memory [40]. Management of OC and EC survivors should include prevention strate-gies to avert chemotherapy-related cognitive dysfunction's effects.

### **General Long-Term Concerns and Comorbidities**

EC patients are particularly affected by comorbidities, mainly cardiovascular morbid-ity which is one of the most frequent cause of death among EC survivors. In comparison with the general population, EC survivors have higher risk for long-term cardiovascular disease, even many years after EC diagnosis [41]. Long time (4-14 years) after cancer diag-nosis, this cohort of 1582 multiple cancer survivors (including 402 gynecologic cancers), reported that cancer survivors were at higher risk of cardiovascular disorders than women from the general population [42]: overweight was observed in 62% of cancer survivors, hypertension for 55.0 %, diabetes in 20.7 % of cases and 18.1 % were inactive. In addition, central adiposity and metabolic syndrome in EC survivors are associated with poor prog-nosis [43]. Nock et al. [44] also compared severe obese EC survivors with BMI = 40 kg/m<sup>2</sup>, to class I obesity EC survivors and demonstrated that severe obesity was associated with global lower QoL, more sleep disorders and higher depression. In comparison with obese EC patients, EC patients with a normal BMI experienced an improved QoL [45]. Obese EC survivors deterioration of QoL is manifested by decreased vitality, physical function im-pairment, increased lymphedema, and elevated fatigue [46].

Global health promotion during survivorship is essential, particularly for patient with risk factors for cardiovascular disease, but this discussion had been addressed by their caregiver for only for one third of cancer survivors [47]: Physical activity and promo-tion of healthy living is perceived as important for OC and EC patients. Their involvement in physical activity programs can provide improvement in physical functioning and psy-chological well-being [48].

### **Specificities of Rare Ovarian Tumors**

In the aim to assess the specific needs in survivorship for women treated for germ cell and sex cord stromal tumors the GINECO-VIVROVAIRE-Rare tumor study is a two-step

investigation to assess i) chronic fatigue and quality of life and ii) long-term side-effects of chemotherapy with a focus on cardiovascular and pulmonary disorders. First results were recently reported at ESMO and ESGO congress 2022 [49]: 6 years after cisplatin-based chemotherapy, similar scores of fatigue and global quality of life were observed between patients and controls. However, patients had more cognitive complaints and more neu-ropathy, higher risk of premature menopause and reported negative impact on their sexu-al health. Health conditions interfered more in patient's daily lives than controls. Long-term neurotoxicity and Raynaud's phenomenon in patients treated with cisplatin-based chemotherapy for malignant ovarian germ cell tumor has been described by Solheim et al [50]: among 83 patients, 28 (57%) women treated with cisplatin-based chemotherapy re-ported overall neuropathy, compared with 20 (45%) in the non-chemotherapy group (P = .06).

### **Follow-Up Care in Ovarian and Endometrial Cancers**

It is now well known that gynecological cancers long-term survivors still have ongo-ing health concerns and long-term side effects following cancer treatment. The aim of fol-low-up care programs is to address these difficulties more effectively, in coordination with general health providers.

Late side-effects of gynecologic cancer treatment have become an increased aware-ness over the past few years. Description of these late side-effects on patient's quality of life have been broadly reported but effective ways to reduce these effects are lacking [51]. Iden-tifying the risk factors for gynecological cancer survivors to have unmet needs many years after primary care is a fundamental issue. Repeated assessments of survivor's needs dur-ing and after their treatment may contribute to reveal the different issues that should re-ceive further attention by caregivers [52]. These regular assessments could rely on survi-vorship questionnaires such as EORTC QLQ-SURV100 or, in France, the use of INCa sur-vivorship questionnaire [53]. These tools are complete and browse every potential symp-tom experimented by the patient, which is quite interesting for systematic screening as part of clinical trials but, because of the numerous items, their use seem heavy in routine practice. Moreover, these questionnaires are general for all tumors types and they lack of site-specific modules for gynecologic cancers. The integration of technology, including digital companions to facilitate remote monitoring, and patient's reported outcome can contribute to accelerate implementation of some programs for survivorship care [54].

A useful tool to identify the needs of cancer survivors is the survivorship planning. For gynecologic cancer patients this planning aims to screen for disease relapse, manage the long-term side effects induced by cancer treatment and coordinate the survivorship care between the different healthcare providers

[55]. Scientific societies are now aware of the specific needs of cancer survivors and were able to edit recommendations in order to encourage cancer survivors to receive a survivorship care plan [56]. The survivorship care plan briefly describes cancer diagnosis and treatment, furnishes further detailed information about long-term side effects and their management, and reminds global health concerns. Survivorship care plans contribute to facilitate the communication between specialized hospital practitioners and primary care providers, and provide key information to the patients on long-term follow-up. The NCCN guidelines [56] provide recommendations for the identification and the management of side effects of cancer and its treatment; to promote healthy lifestyle and preventive care in survivors; and to build a framework for care coordination. The MASCC guidelines of cancer supportive care and survivorship [57] describe cancer symptoms, treatment side effects and disparities in supportive care, they provide detailed recommendations for supportive care management during and after cancer treatments. Recently, ESMO expert consensus statements on cancer survivorship reminded the different components of survivorship care [58]: physical and psychological side effects of cancer, social impact of cancer, surveillance for cancer relapse and global health promotion. These different guidelines are the cornerstone for survivorship care and provide help for physicians in charge of these patients, but they are not specific for gynecological cancers.

The recommendations for long-term follow-up for survivors from gynecologic cancer have been defined in the GCIG-Consensus guideline which proposes a gynecologic long term survivorship plan [59]. This plan describes the long-term side effects, sequelae after gynecologic cancer and proposes and health maintenance.

Providing comprehensive and coordinated management for gynecological cancer survivors is a pending issue. Known survivorship care models need a high level of communication and coordination between oncologists, primary care providers and all the other caregivers involved in survivor's management and care. In models of survivorship relying on the primary care physician, the primary care health professionals collaborate with the cancer hospital specialists to achieve optimal care of cancer survivors. The limitations of a such model are the means available for primary care physicians to get fully involved in survivorship care. Another option, broadly used in many countries, are the survivorship clinics. These clinics aim to provide comprehensive survivorship care in one location where all the health caregivers collaborate to deliver specialized and high-quality care. These clinics are a very interesting model of survivorship care, but their establishment may seem difficult to organize in some regions where health care provider's scarcity is a current issue.

Another existing model relies on specialized nurses who will, under the cancer specialists and primary care physician's

responsibility, assume the global survivorship care. These models of survivorship care are complementary and their optimization is needed to have a better coordination between the different caregivers. For example, in a nurse-led gynecology oncology clinic, an audit found that EC patients treated with radiation had to come to many several appointments in order to access the different care offers [60]. This audit generated a working group of clinic health care professionals in order to optimize survivorship care pathways where patients could consult different professionals at one appointment, and evaluate if it could help the move forward in life after treatment. Halfway between survivorship clinics and primary care physician's models, there is a room for another model which may be the daycare hospitalization. Based on our previous experience in OC survivorship [4,20,49], we aim to design a clinical trial for survivorship care in OC and EC, which could be ultimately extended to cervical carcinomas. This study (NCT05731661) will be a randomized multicentric trial comparing two pathways of survivorship care: patients with OC or EC, at the end of initial treatments, will be evaluated on their specific needs induced by treatments complications with dedicated screening tools developed by an InCa working group [53]. Then, patients will be randomized between (a) an experimental arm where patients will be evaluated by a supportive care team during a daycare hospitalization, and their personalized follow-up care plan will be coordinated by a specialized nurse to ensure its application by all caregivers and primary care physicians; (b) a standard arm where patients will receive a personalized survivorship plan only. At 6 and 12 months after inclusion, patients will be re-evaluated on their different needs in supportive care to investigate their adherence to the survivorship program.

A priority in survivorship care is to achieve coordinated pathways, which can be facilitated by scientific guidelines, personalized health survivorship coordinated passports and education of patients and caregivers.

As previously underlined, a better identification and management of the sides effects and sequelae can contribute to enhance quality of life of gynecological cancer survivors. Another way to limit long-term toxicities and sequelae is to prevent them using de-escalation methods during the primary treatment. Minimally invasive surgery based on laparoscopy for surgical staging of OC, or sentinel node biopsy for surgical mapping in EC are options to reduce surgical morbidity [61,62]. Recent advances on molecular and genomic profiling in EC contributed to identify several prognostic subtypes [63]. Of note, the POLE mutated subtype has very favorable prognosis and may be eligible for de-escalation of adjuvant therapies. Tailoring adjuvant strategies for early stage EC, based on genomic and molecular profiling, is a challenge to take up in order to refine the selection of patients eligible for multimodal treatments [64,65].

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To conclude, OC and EC survivors experience long-term disorders that have a great impact on their QoL and general well-being. To treat and ameliorate the late side-effects such as fatigue, genito-urinary and bowel disorders, sexual dysfunction, CIPN, lymphedema, chronic pain, cognition impairment or psychological disorders must be a priority of survivorship care. Survivorship care needs to be delivered by structured care models integrating primary care and oncology services, with the help of tools to facilitate implementation of coordinated care. Survivorship educational programs for health care teams and patients are needed to improve the quality of survivorship care.

#### **Author Contributions:**

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