Gynecologic Oncology 209 (2026) 99–106

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Longitudinal dynamics of post-diagnosis frailty among older women with ovarian cancer

Minh Tung Phung [a,b,c,d,*], Lisa M. Barroilhet [b,e], Neil Binkley [f], Ronald E. Gangnon [a,g], Amy Trentham-Dietz [a,b]

[a] Department of Population Health Sciences, University of Wisconsin-Madison, Madison, WI, United States of America
[b] University of Wisconsin-Madison Carbone Cancer Center, Madison, WI, United States of America
[c] Center for Demography of Health and Aging, University of Wisconsin-Madison, Madison, WI, United States of America
[d] Department of Epidemiology, University of Michigan School of Public Health, Ann Arbor, MI, United States of America
[e] Department of Obstetrics and Gynecology, University of Wisconsin-Madison, Madison, WI, United States of America
[f] Department of Medicine, University of Wisconsin-Madison, Madison, WI, United States of America
[g] Department of Biostatistics and Medical Informatics, University of Wisconsin-Madison, Madison, WI, United States of America

HIGHLIGHTS

- Post-diagnosis frailty among older women with ovarian cancer is dynamic.
- No frailty at diagnosis-survival association after adjusting for current frailty.
- Current frailty is strongly associated with survival.
- Patient and cancer factors associated with frailty worsening were identified.

ARTICLE INFO

Article history:
Received 30 January 2026
Received in revised form 27 April 2026
Accepted 28 April 2026
Available online xxxx

Keywords:
Ovarian cancer
Older adults
Frailty
Frailty dynamics
Survival

ABSTRACT

Objective. Leading oncology societies recommend assessing pre-treatment frailty to guide care for older adults with cancer. However, frailty may change post-diagnosis. This study characterized post-diagnosis frailty and its association with overall survival among older women with ovarian cancer.

Methods. We included 24,725 women aged 65+ diagnosed with ovarian cancer between 2000 and 2019 from Surveillance, Epidemiology, and End Results (SEER)-Medicare. Frailty was quantified at diagnosis and 1–3 years post-diagnosis using a validated claims-based index. We compared patients' frailty at the beginning and end of each year. At 1, 2, and 3 years post-diagnosis, we fit a Cox proportional hazards model including frailty at diagnosis and current frailty to assess associations with survival.

Results. Frailty distribution at diagnosis was: 7.1% non-frail, 71% pre-frail, 18% mildly frail, 3.4% moderately frail, and 0.9% severely frail. During year 1, 38% of women maintained frailty status, 4% improved, 26% worsened, and 32% died. In years 2–3, some women remained stable while others improved or worsened. There were 21,309 deaths during a median follow-up of 25 months (interquartile range 7–58). Frailty at diagnosis was not associated with survival after adjusting for current frailty (hazard ratios [HRs] for severely frail versus non-frail =0.98, 1.00, 0.76 at 1, 2, 3 years, respectively, all *p*-values>0.20). Current frailty was strongly associated with survival, and the association increased over time (HRs =2.26, 2.77, 3.70, respectively; all p-values<0.001).

Conclusions. Post-diagnosis frailty is dynamic. Current frailty has a stronger association with overall survival compared to frailty at diagnosis. Repeated frailty assessments should be incorporated into clinical practice.

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1. Introduction

Ovarian cancer is one of the deadliest gynecologic malignancies, with about 21,000 new cases and 13,000 deaths from the disease in the United States (U.S.) annually [1]. The overall 5-year survival rate remains alarmingly low at just 52% [2]. Ovarian cancer disproportionately

* Corresponding author at: Department of Population Health Sciences, University of Wisconsin-Madison, 610 Walnut St, Madison, WI 53726, United States of America.
E-mail address: phungmt@umich.edu (M.T. Phung).

https://doi.org/10.1016/j.ygyno.2026.04.019
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affects older women (aged 65+), who account for nearly half of diagnoses but about 70% of deaths from the disease [2]. Thus, there is a critical need to improve care for older women with ovarian cancer to improve their outcomes. This need will only worsen given that this population is projected to increase by 50% over the next 25 years as the U.S. population is aging [3].

Frailty, defined as a clinical state with reduced physiological reserves and increased vulnerability to stressors [4], is gaining recognition as an important measure to guide care for older adults with cancer. This is particularly relevant due to the high prevalence of frailty among older adults with cancer and its strong association with cancer outcomes. For ovarian cancer specifically, up to 25% of older women are considered frail at diagnosis, and this figure rises to 60% one year after diagnosis [5,6]. Independent of age, frailty is associated with higher rates of postoperative complications, chemotherapy-related toxicity, lower health-related quality of life, and poorer survival among women with ovarian cancer [6–13]. Several oncological societies, including the International Society of Geriatric Oncology (SIOG) and the American Society of Clinical Oncology (ASCO), recommend assessing frailty once before cancer therapy initiation and using this information to guide care decisions [14–16]. However, it is increasingly recognized that frailty is not a static construct that just needs to be measured at a single time point [16–21]. Indeed, post-diagnosis frailty can vary over time among older adults with various cancer types [20,21]. However, to our knowledge, no published data exist describing the dynamics of post-diagnosis frailty among women with ovarian cancer. Furthermore, it is largely unknown whether frailty measured after ovarian cancer diagnosis is a better predictor for overall survival compared to frailty measured at diagnosis. This study aimed to characterize the dynamics of post-diagnosis frailty among older women with ovarian cancer and to assess the association of frailty measured at different timepoints and overall survival.

2. Methods

2.1. Data source

This study used data from the linkages between the Surveillance, Epidemiology, and End Results (SEER) cancer registries and Medicare claims. SEER includes population-based cancer registries that collect information on newly diagnosed cancer cases for about 46% of the U.S. population [22]. Medicare is the primary health insurer for approximately 94% of U.S. adults aged 65+ [22]. SEER and Medicare data are linked together by the National Cancer Institute and the Centers for Medicare & Medicaid Services, with about 96% of SEER cancer patients aged 65+ successfully matched to Medicare claims [22]. The linked dataset includes detailed information on patient demographics, medical history, tumor characteristics and survival. This study was determined as non-human subjects research by the University of Wisconsin-Madison Minimal Risk Research Institutional Review Board (submission number 2024–1710, date of determination January 22, 2025).

2.2. Study population

We included women with pathologically confirmed primary invasive epithelial ovarian cancer (International Classification of Diseases for Oncology 3rd edition [ICD-O-3] code C56.9) diagnosed at age 65+ between 2000 and 2019. We selected an age cutoff of 65 years to specifically focus on the older adult demographic, a group that is rapidly growing and historically experiences disproportionately poor outcomes in ovarian cancer. This age cutoff is consistent with clinical guidelines for geriatric oncology, which commonly use age 65 as the threshold for recommending frailty assessment [14–16]. Because SEER provides the month and year but not the day of cancer diagnosis, the diagnosis date was set as the first day of the diagnosis month. To ensure completeness of claims data to calculate frailty (described below), we restricted the cohort to women with continuous enrollment in Medicare fee-for-service Parts A and B, and no enrollment in Part C, for at least 12 months before cancer diagnosis and 36 months after diagnosis (or until death, whichever occurs first). This is because, unlike Medicare fee-for-service claims that provide detailed information on diagnosis/procedure/treatment codes and dates of service for beneficiaries, patient-level claims for services provided to Part C beneficiaries are not fully captured in Medicare claims files [22]. As we required at least 12 months of pre-diagnosis enrollment, the minimum age at diagnosis in our cohort was 66 years. We excluded patients who had an unknown month of cancer diagnosis, an unknown age at diagnosis, were diagnosed by autopsy or death certificate only, had missing vital status or follow-up duration, had a follow-up duration of 0 months, or had mismatched dates of death between SEER and Medicare files (Fig. 1).

2.3. Frailty

Frailty was measured using the Claims-based Frailty Index (CFI), developed by Kim et al. [23]. The CFI calculates frailty using 93 variables defined by diagnosis and procedure codes in Medicare claims data [23]. The CFI has been validated against clinical assessments of frailty, including the Frailty Phenotype and the Deficit Accumulation Frailty Index [23]. It has also been validated against physical performance measures, functional impairments, and key adverse outcomes including mortality, hospitalizations, skilled nursing facility stays, and institutionalization [24]. The CFI has been applied across diverse older adult populations, including individuals with cancer [25,26]. Frailty was calculated at landmark time points: at cancer diagnosis and 1, 2, and 3 years post-diagnosis. Frailty at each time point was calculated using the diagnosis and procedure codes that occurred in a 12-month window prior to that time point. This 12-month "look-back" is a standardized requirement by the algorithm developers to ensure sufficient capture of conditions and healthcare utilization patterns that define a patient's frailty at a given time point [27]. CFI scores ranged from 0 to 1, with higher scores indicating a greater frailty. Consistent with prior literature [25], frailty status was categorized as: non-frail (CFI <0.10), pre-frail (0.10–0.19), mildly frail (0.20–0.29), moderately frail (0.30–0.39), and severely frail (CFI ≥0.40).

2.4. Statistical analysis

2.4.1. Patient characteristics at cancer diagnosis

Descriptive statistics were used to summarize participant characteristics. An ordinal logistic regression model was fit to identify factors associated with frailty at diagnosis, regressing on age at diagnosis (continuous), Charlson Comorbidity Index (continuous), tumor stage (local, regional, distant, unknown), histotype (serous versus non-serous), race/ethnicity (Asian/Pacific Islander, Hispanic, non-Hispanic Black, non-Hispanic White, other), and Medicaid enrollment (yes/no) as a proxy for social economic status. The model was adjusted for year of diagnosis and SEER registry.

2.4.2. Frailty dynamic

A Sankey diagram was constructed to visualize transitions in frailty status across the landmark timepoints. For each of the first three years following diagnosis, we evaluated changes in frailty status by comparing each patient's classification at the beginning and end of the year. Patients were categorized as: no change (remaining in the same frailty category), improved (transitioning to a less severe category), worsened (transitioning to a more severe category), or deceased. Multivariate logistic regression models were fitted to identify factors associated with worsening frailty status compared to no change/improved in the overall population and stratified by tumor stage. Patients who were deceased or severely frail at the beginning of the year were excluded from this analysis because they could not transition to a more severe frailty category. The models regressed on age at diagnosis, Charlson Comorbidity Index, tumor stage, histotype, frailty category at the beginning of the

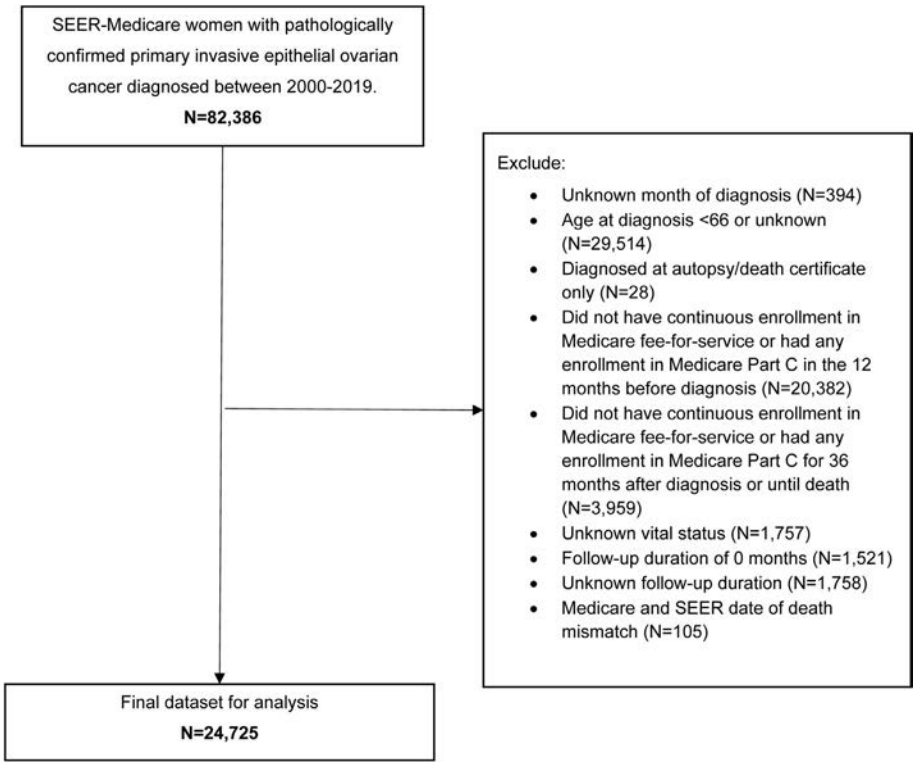

Fig. 1. Participant flowchart.

year, types of treatment received (surgery only, chemotherapy only, both, neither), race/ethnicity, Medicaid enrollment, and were adjusted for year of diagnosis and SEER registry.

2.4.3. Association between frailty measured at different timepoints and overall survival

We fit Cox proportional hazards models to assess the association between frailty and overall survival at each landmark timepoint (i.e., diagnosis and 1, 2, 3 years post-diagnosis). Overall survival was defined as the time from the landmark timepoint to death from any cause or the last follow-up date (December 31, 2020). For each post-diagnosis timepoint, we fit one model that included both frailty measured at diagnosis and current frailty measured at the corresponding timepoint. The models were adjusted for the covariates described above. Hazard ratios (HRs) and 95% confidence intervals (CIs) are reported. Statistical significance was defined as $p \leq 0.05$ using two-sided tests. Data were analyzed using R version 4.0.3.

3. Results

A total of 24,725 older women with ovarian cancer were included in the analysis. Median age at diagnosis was 75 years (interquartile range [IQR] 70–81 years). The majority of participants were non-Hispanic White (85%), diagnosed at a distant stage (71%), and had serous histotype (56%) (Table 1**)**. The median CFI score at diagnosis was 0.15 (IQR 0.12–0.19). Frailty categories at diagnosis were distributed as follows: 7.1% non-frail, 71% pre-frail, 18% mildly frail, 3.4% moderately frail, and 0.9% severely frail. Women with more severe frailty at diagnosis tended to be older and have greater comorbidity, non-serous histotype, Hispanic ethnicity (compared to non-Hispanic White), and be enrolled in Medicaid. In contrast, Asian/Pacific Islander women were less likely to be in a more severe frailty category at diagnosis (odds ratio OR = 0.80, 95% CI 0.66–0.97), whereas non-Hispanic Black women had a similar distribution of frailty as non-Hispanic White women (OR = 1.08, 95% CI 0.95–1.22; Supplementary Table S1).

The cumulative proportion of deaths at 1, 2, and 3 years after diagnosis was 32%, 49%, and 60%, respectively (Fig. 2). At each landmark time point, most living patients were pre-frail, followed by mildly frail. When comparing frailty status at the beginning and end of the first year after diagnosis, 38% of patients remained in the same frailty category, 4.3% improved (i.e., moving to a less severe frailty category), 26% worsened (i.e., moving to a more severe frailty category), and 32% were deceased. During the second year, among those who were alive at one year after diagnosis (N = 16,838), 47% remained in the same frailty category, 18% improved, 10% worsened, and 25% were deceased. During the third year, among those alive at two years after diagnosis (N = 12,716), 52% remained in the same category, 10% improved, 15% worsened, and 22% were deceased.

Older age at diagnosis, higher Charlson Comorbidity Index, later tumor stage, and Medicaid enrollment were associated with greater odds of worsening frailty status in each year after diagnosis (Table 2, Supplementary Tables S2 and S3). In contrast, women who began a year in a more severe frailty category were less likely to worsen during that year. These patterns remained consistent in analyses stratified by tumor stage (Supplementary Tables S4-S6). Non-Hispanic Black and Hispanic women had greater odds of worsening frailty status compared to non-Hispanic White women; however, this association was not consistently observed across tumor stages.

Of 24,725 participants included in the analysis, there were 21,309 deaths during a median follow-up of 25 months (IQR 7–65 months). More severe frailty at diagnosis was associated with poorer overall survival calculated from diagnosis (HR for severely frail versus non-frail = 1.51, 95% CI 1.29–1.76; Table 3). However, at each post-diagnosis landmark timepoint, frailty at diagnosis was not associated with survival after adjusting for current frailty (HRs for severely frail versus non-frail = 0.98, 1.00, and 0.76 at 1, 2, and 3 years post-diagnosis, respectively; all p-values >0.20). In contrast, current frailty was strongly associated with overall survival at each landmark timepoint, with the strength of association increasing over time (HRs for severely frail

Table 1
Participant characteristics.

Characteristic	Total study population, N (%) $N = 24,725$
Age at diagnosis (years)	
Median (Interquartile range)	75 (70–81)
Year of diagnosis	
2000–2004	9052 (37%)
2005–2009	6786 (27%)
2010–2014	5854 (24%)
2015–2019	3033 (12%)
Tumor stage	
Localized	1879 (7.6%)
Regional	3710 (15%)
Distant	17,550 (71%)
Unknown	1586 (6.4%)
Histotype	
Serous	13,777 (56%)
Non-serous	10,948 (44%)
Charlson Comorbidity Index	
Median (Interquartile range)	0 (0–1)
Frailty at diagnosis	
Non-frail	1753 (7.1%)
Pre-frail	17,505 (71%)
Mildly frail	4407 (18%)
Moderately frail	840 (3.4%)
Severely frail	220 (0.9%)
Race/ethnicity	
Asian/Pacific Islander	674 (2.7%)
Hispanic	1667 (6.7%)
Non-Hispanic Black	1404 (5.7%)
Non-Hispanic White	20,893 (85%)
Other	87 (0.4%)
Medicaid enrollment	
No	23,462 (95%)
Yes	1263 (5.1%)
SEER registry	
Connecticut	976 (3.9%)
Greater California (excluding San Francisco, Los Angeles & San Jose)	2835 (11%)
San Francisco-Oakland	499 (2.0%)
Los Angeles	1119 (4.5%)
San Jose-Monterey	321 (1.3%)
Greater Georgia (excluding Atlanta and Rural Georgia)	1443 (5.8%)
Metropolitan Atlanta	513 (2.1%)
Rural Georgia	47 (0.2%)
Hawaii	124 (0.5%)
Idaho	310 (1.3%)
Iowa	1078 (4.4%)
Kentucky	1001 (4.0%)
Louisiana	890 (3.6%)
Metropolitan Detroit	1007 (4.1%)
New Jersey	2466 (10.0%)
New Mexico	360 (1.5%)
New York	4107 (17%)
Seattle (Puget Sound)	987 (4.0%)
Texas	4261 (17%)
Utah	381 (1.5%)

versus non-frail = 2.26, 2.77, and 3.70 at 1, 2, and 3 years post-diagnosis, respectively; all p-values <0.001; Table 3).

4. Discussion

Our study is the first to demonstrate the dynamic nature of quantified frailty status after diagnosis among older women with ovarian cancer. We found that frailty status can remain stable, improve or worsen over time after diagnosis. To our knowledge, no previous studies have characterized the longitudinal dynamics of quantified post-diagnosis frailty among women with ovarian cancer. Only one previous study examined changes in frailty measured at two time points before cancer diagnosis [6] and another one characterized changes from pre-diagnosis versus post-diagnosis frailty [5]. While analyses of changes in post-diagnosis frailty status have not been conducted in ovarian cancer, our findings are consistent with the literature in other cancer types, which found varying trajectories of post-diagnosis frailty [19,21].

We identified several factors that predict worsening of post-diagnosis frailty among older women with ovarian cancer. Older age at diagnosis, higher comorbidity, later stage, and Medicaid enrollment were associated with a higher likelihood of worsening frailty. Our findings are consistent with a study on multiple myeloma [19]. Older age and higher comorbidity likely reflect diminished physiological reserve and resilience to treatment-related stress. Later-stage disease may further compound this vulnerability due to the effects of cancer itself and intensive treatments. Although Medicaid beneficiaries often present with a higher burden of pre-existing conditions and disabilities at the time of cancer diagnosis, our models were adjusted for both baseline comorbidity and frailty status; thus, the observed association between Medicaid enrollment and frailty worsening is independent of baseline health status. Although residual confounding by baseline health status may exist, it is unlikely to fully account for the observed strong association. The association between Medicaid enrollment and worsening in frailty status may be partially explained by greater barriers to supportive resources that affect post-diagnosis frailty, such as occupational and physical therapy [28]. Our findings highlight the importance of patient navigation and oncology social work support for patients of low socioeconomic status backgrounds. Patient navigation and social work support may play an important role by facilitating care coordination and enabling timely referral to rehabilitation and other supportive services. We also found that patients with a more severe frailty category at the beginning of a year were less likely to worsen in frailty status during that year, consistent with findings from a study among patients with multiple myeloma [19]. This could possibly be explained by a ceiling effect, i.e., there is less biological room for patients in more severe categories to further deteriorate. Collectively, our findings underscore that both biological factors and social determinants shape frailty trajectories following an ovarian cancer diagnosis.

Our study is the first to examine the association between frailty measured at different timepoints post-diagnosis and overall survival among older women with ovarian cancer. We found that current frailty is associated with overall survival and the strength of the association increases over time. In contrast, frailty at diagnosis is not associated with overall survival after adjusting for current frailty, indicating that baseline frailty influences mortality primarily through its impact on subsequent frailty. Our findings suggest that current frailty is more clinically and prognostically relevant than baseline frailty. Our results are consistent with another study in patients with multiple myeloma [19] and highlight the importance of repeated frailty assessments in management for older women with ovarian cancer. Repeated measures of frailty in clinical practice are feasible given the existence of validated frailty models that use data from electronic health records (EHRs) to automatically measure frailty. While comprehensive geriatric assessment remains the gold standard for evaluating frailty, its implementation in oncological settings is often limited by requirements for specialized expertise and the considerable time needed to complete the assessment [29]. By leveraging continuously and routinely collected EHR data, frailty assessment could be automated without additional burden on patients or providers. Several EHR-based frailty indices have been developed and validated against clinical frailty assessment and demonstrated feasibility in clinical practice, even when data are incomplete [30,31]. Further research evaluating the effect of frailty models on clinical care and outcomes is appropriate.

A strength of our study is the use of the SEER-Medicare data, which includes a large sample size of older women with ovarian cancer. Additionally, the longitudinal nature of the data enables us to assess the frailty dynamics. Furthermore, an important contribution of this work is the demonstration that frailty can be quantitatively measured and that more severe frailty is associated with poorer survival. This quantification enables more precise risk stratification, facilitates comparisons across studies and populations, and supports the integration of frailty

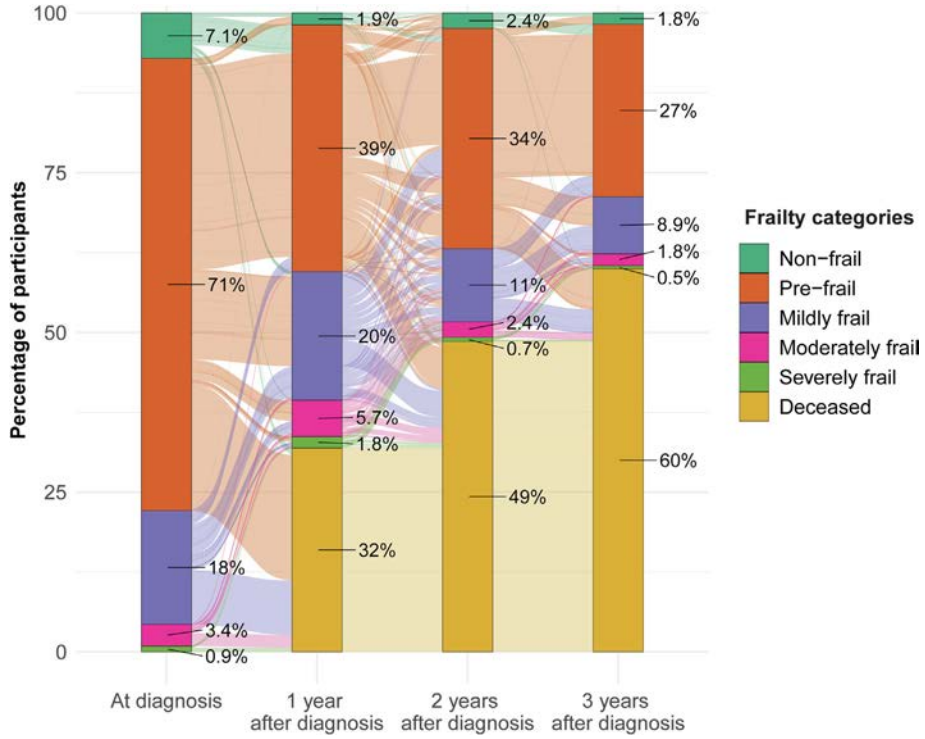

Fig. 2. Dynamics of post-diagnosis frailty among older women with ovarian cancer.

Table 2
Association between participant characteristics and worsening in frailty status during the first year after cancer diagnosis.

Characteristic	No worsening $N = 10{,}330$	Worsening $N = 6445$	OR (95% CI)[a]	*p* value
Age at diagnosis[b]	74 (6)	75 (6)	1.05 (1.04–1.06)	<0.001
Charlson Comorbidity Index[b]	0.67 (1.10)	0.76 (1.10)	1.47 (1.42–1.52)	<0.001
Frailty at diagnosis				
Non-frail	148	1327	1	
Pre-frail	8184	4463	0.04 (0.03–0.05)	<0.001
Mildly frail	1724	588	0.012 (0.009–0.015)	<0.001
Moderately frail	274	67	0.005 (0.003–0.007)	<0.001
Tumor stage				
Localized	1276	466	1	
Regional	1952	1013	1.54 (1.32–1.79)	<0.001
Distant	6475	4653	2.35 (2.04–2.72)	<0.001
Unknown	627	313	1.61 (1.30–1.98)	<0.001
Histotype				
Serous	6244	4095	1	
Non-serous	4086	2350	0.98 (0.90–1.05)	0.53
Race/ethnicity				
Asian/Pacific Islander	284	184	1.08 (0.86–1.35)	0.52
Hispanic	635	441	1.18 (1.03–1.37)	0.02
Non-Hispanic Black	466	326	1.22 (1.04–1.43)	0.02
Non-Hispanic White	8911	5473	1	
Other	34	21	1.04 (0.55–1.92)	0.90
Medicaid enrollment				
No	9937	6137	1	
Yes	393	308	1.43 (1.20–1.71)	<0.001
Treatment				
Neither surgery nor chemotherapy	321	170	1	
Surgery only	801	427	1.32 (1.03–1.69)	0.03
Chemotherapy only	1906	1320	1.17 (0.94–1.46)	0.16
Both surgery and chemotherapy	7302	4528	1.12 (0.91–1.40)	0.29

[a] Odds ratios and 95% confidence intervals from a logistic regression model, adjusted for year of diagnosis and SEER registry.
[b] Mean (standard deviation). Odds ratios per single year (age) and each additional unit of Charlson Comorbidity Index.

Table 3
Association between frailty status and overall survival.

Frailty	Model with overall survival calculated from diagnosis		Model with overall survival calculated from 1 year post-diagnosis		Model with overall survival calculated from 2 years post-diagnosis		Model with overall survival calculated from 3 years post-diagnosis	
	HR (95% CI)[a]	p value	HR (95% CI)[b]	p value	HR (95% CI)[b]	*p* value	HR (95% CI)[b]	p value
Frailty at diagnosis								
Non-frail	1		1		1		1	
Pre-frail	1.10 (1.04–1.16)	0.001	0.99 (0.93–1.06)	0.81	0.97 (0.90–1.05)	0.45	0.94 (0.86–1.02)	0.16
Mildly frail	1.31 (1.23–1.40)	<0.001	1.07 (0.98–1.16)	0.13	1.00 (0.90–1.10)	0.95	0.92 (0.82–1.04)	0.19
Moderately frail	1.34 (1.22–1.47)	<0.001	1.10 (0.96–1.27)	0.18	1.07 (0.90–1.29)	0.44	0.90 (0.71–1.13)	0.36
Severely frail	1.51 (1.29–1.76)	<0.001	0.98 (0.74–1.30)	0.87	1.00 (0.71–1.41)	1.00	0.76 (0.47–1.21)	0.24
Current frailty								
Non-frail			1		1		1	
Pre-frail			1.23 (1.09–1.38)	0.001	1.53 (1.37–1.71)	<0.001	1.49 (1.30–1.69)	<0.001
Mildly frail			1.56 (1.38–1.76)	<0.001	2.24 (1.99–2.52)	<0.001	2.33 (2.02–2.67)	<0.001
Moderately frail			1.96 (1.71–2.23)	<0.001	2.83 (2.45–3.27)	<0.001	3.10 (2.61–3.68)	<0.001
Severely frail			2.26 (1.93–2.65)	<0.001	2.77 (2.27–3.39)	<0.001	3.70 (2.91–4.71)	<0.001

[a] Hazard ratios and 95% confidence intervals from a Cox proportional hazards model including frailty at diagnosis, adjusted for age at diagnosis, Charlson Comorbidity Index, tumor stage, histotype, race/ethnicity, Medicaid enrollment, types of treatment received, year of diagnosis, and SEER registry. Overall survival was calculated from diagnosis until death or last follow-up.

[b] Hazard ratios and 95% confidence intervals from a Cox proportional hazards model including both frailty at diagnosis and current frailty, adjusted for age at diagnosis, Charlson Comorbidity Index, tumor stage, histotype, race/ethnicity, Medicaid enrollment, types of treatment received, year of diagnosis, and SEER registry. Overall survival was calculated from 1, 2, and 3 years post-diagnosis until death or last follow-up.

assessment into prognostic models and clinical decision-making. Importantly, the ability to quantify frailty also creates opportunities for monitoring changes over time and evaluating interventions aimed at modifying frailty and improving outcomes.

Another strength of our study is the use of the CFI to quantify frailty. As noted above, clinical examination remains the gold standard for assessing frailty, but these assessments are not routinely documented in claims data. As a result, the CFI and other claims-based indices are designed to capture frailty through validated surrogates, which are diagnosis codes and health service billing codes that serve as proxies for the physiological state of frail older adults. The CFI has undergone extensive validation across multiple populations and settings. It demonstrates strong concordance with two of the most widely used and clinically validated frailty measures: the Frailty Phenotype and the Deficit Accumulation Frailty Index. Specifically, the CFI was strongly associated with the Frailty Phenotype (C-statistic = 0.78), which directly measures weakness, slowness, low activity, weight loss, and exhaustion. The CFI is also strongly correlated with the Deficit Accumulation Frailty Index (correlation = 0.59), which encompasses medical history (e.g., fall, memory-related disease), ability to perform activities of daily living (ADLs), objective performance tests (cognitive status, gait speed, and handgrip strength), and nutritional status (weight loss and body mass index) [32]. Additionally, the CFI has also been independently validated against clinical domains, including gait speed, grip strength, ADLs, and adverse health outcomes including death, disability, mobility impairment, recurrent falls, hospital days, and skilled nursing facility days [24]. Importantly, several studies have shown that the CFI outperforms other claims-based frailty indices when validated against gold-standard clinical frailty measures [32] and when predicting adverse outcomes in both the general Medicare population and subgroups [33]. In recognition of its performance and broad applicability, the Office of the Assistant Secretary for Planning and Evaluation (ASPE) and the Agency for Healthcare Research and Quality (AHRQ) recommended incorporating CFI scores into the Medicare data for use by researchers and other stakeholders [34].

The CFI calculates frailty using 93 diagnosis, procedure, and health utilization codes, which are routinely and consistently captured in administrative claims [23]. Thus, it enables repeated frailty assessment in such a large study population, which would not be feasible using clinical frailty assessment. Although the CFI is not designed to be used in clinical practice, clinicians have access to complementary validated measures, including clinical frailty assessment and EHR-based frailty indices as discussed above.

Our goal was to characterize dynamic changes in frailty following an ovarian cancer diagnosis, regardless of underlying cause. Accordingly, the CFI captures changes in physiological reserve arising from multiple factors, including aging, cancer progression, and cancer treatment. Conditions such as weight loss, fatigue, and anemia – whether attributable to the disease, its treatment, or other comorbid health conditions - are therefore appropriately reflected in the index. Rather than representing overinflation, inclusion of these factors aligns with our objective of measuring a patient's total frailty burden over time.

In this study, frailty was assessed at pre-defined annual landmarks (at diagnosis, 12, 24, and 36 months), rather than continuously over shorter intervals. We did not estimate the CFI at multiple time points within a given year. This is because frailty at each time point is calculated based on claims that occurred during a 12-month look-back period (per requirement by the algorithm developers) [27]. Calculating scores at more frequent intervals would result in substantial overlap, where the same diagnostic and procedure codes would contribute to frailty statuses at multiple adjacent time points, potentially complicating interpretation. Despite calculating frailty annually, our results clearly demonstrate that frailty is highly dynamic in this population. Future research should examine the dynamics of frailty over shorter intervals by employing clinical assessments or validated algorithms that support more frequent measurement.

Our study has some limitations. First, we restricted the analyses to patients aged 66+ and had continuous enrollment in Medicare fee-for-service for at least 12 months before and 36 months after diagnosis (or until death). This restriction may limit the generalizability of our findings to those without continuous enrollment in Medicare fee-for-service or those who enrolled in Medicare Part C. Additionally, our results may not extend to younger patients with ovarian cancer. Although frailty can occur in younger adults, its prevalence is substantially lower than in older populations [35]. Our study intentionally focused on older adults with cancer, who have a higher burden of frailty and for whom clinical guidelines recommend frailty assessment to guide care [14–16]. Further, our study included patients diagnosed over a wide range period (2000–2019). Thus, while the proportion of deaths and histology distribution in our study are consistent with large population-based studies [36–38], they may not reflect recent improvements in survival and histologic classification. Second, we lack information on other factors that can affect frailty status, such as rehabilitation services, symptoms, or disease recurrence. Prior research indicates that serous tumors often present acutely at advanced stages with a shorter period from symptom onset to diagnosis, while non-serous

tumors are often diagnosed at an early stage with a longer symptom duration [36]. This prolonged period of illness may contribute to a more significant cumulative decline in physiological reserves, partially explaining our finding that non-serous histotype was associated with higher odds of being frail at diagnosis compared to serous histotype. Regardless, the lack of these variables does not affect the main objectives of this study, which are to demonstrate the dynamic nature of frailty and the predictability of frailty over time. Similarly, the use of maintenance therapy, including poly [adenosine diphosphate (ADP)-ribose)] polymerase (PARP) inhibitors, is unlikely to affect our findings. This is because PARP inhibitors only received initial FDA approval for treatment of recurrent ovarian cancer in 2014 and first-line maintenance in 2018, while patients in our cohort were diagnosed between 2000 and 2019 [39]. Additionally, PARP inhibitors are currently approved for select patients with advanced or recurrent ovarian cancer, particularly those with BRCA mutations or homologous recombination deficiency. Thus, a significant portion of our cohort would not have been eligible for these agents. With the growth in PARP inhibitor use, future studies should examine how these agents affect the frailty dynamics. Third, our study only explored the association between frailty and overall survival; additional outcomes important to older adults with cancer, such as quality of life, cognition, and functional limitations, are not available in the dataset.

In conclusion, our study is the first to demonstrate that current frailty is more relevant to overall survival compared to frailty measured at diagnosis among older women with ovarian cancer. This is also the first study demonstrating the dynamic nature of post-diagnosis frailty in this population. Our findings highlight the importance of repeated frailty assessments to guide care for older women with ovarian cancer. We also found several factors associated with worsening in frailty, including chronological age, comorbidity, socioeconomic status, tumor stage, and baseline frailty. These factors can be incorporated into risk prediction models to identify patients with a high risk of frailty worsening, who need close management. Future studies should explore the association between frailty dynamics and other treatment outcomes among older women with ovarian cancer, such as quality of life, physical and cognitive functions. Future efforts that incorporate repeated frailty measurements in clinical practice are also warranted.

Declaration of generative AI use

The authors disclose the use of Microsoft Copilot and Google Gemini in the writing process to improve language clarity and readability. After using these tools, the authors thoroughly reviewed and edited the manuscript and take full responsibility for the content and accuracy of the published article.

CRediT authorship contribution statement

Minh Tung Phung: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Lisa M. Barroilhet:** Writing – review & editing, Funding acquisition, Conceptualization. **Neil Binkley:** Writing – review & editing, Funding acquisition. **Ronald E. Gangnon:** Writing – review & editing, Methodology, Funding acquisition. **Amy Trentham-Dietz:** Writing – review & editing, Funding acquisition, Conceptualization.

Funding sources

This project was supported by ACS grant IRG-19-146-54, funded by the American Cancer Society and the University of Wisconsin-Madison Carbone Cancer Center to Minh Tung Phung. Amy Trentham-Dietz received financial support by University of Wisconsin-Madison Carbone Cancer Center (P30CA014520). Minh Tung Phung was supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the Office of Research on Women's Health, Building Interdisciplinary Research Careers in Women's Health (BIRCWH) program, the Office of The Director, National Institutes of Health, and the National Cancer Institute, under Award Number K12AR084227 (2025–2030). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The funders had no roles in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Declaration of competing interest

The authors have no conflicts of interest to report.

Acknowledgments

The authors acknowledge the helpful assistance provided by the SEER-Medicare reviewers, Information Management System coordinator, and all patients whose valuable data contributed to this study. We also acknowledge the support from the Social Science Computing Cooperative at the University of Wisconsin-Madison. The collection of cancer incidence data used in this study was supported by the California Department of Public Health pursuant to California Health and Safety Code Section 103885; Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries, under cooperative agreement NU58DP007156; the National Cancer Institute's Surveillance, Epidemiology and End Results Program under contract HHSN261201800032I awarded to the University of California, San Francisco, contract HHSN261201800015I awarded to the University of Southern California, and contract HHSN261201800009I awarded to the Public Health Institute. The ideas and opinions expressed herein are those of the authors and do not necessarily reflect the opinions of the State of California, Department of Public Health, the National Cancer Institute, and the Centers for Disease Control and Prevention or their Contractors and Subcontractors.

Appendix A. Supplementary data

Supplementary tables to this article can be found online at https://doi.org/10.1016/j.ygyno.2026.04.019.

Data availability

The SEER-Medicare database is owned and managed by the National Cancer Institute. Information on how to obtain these data is available at https://healthcaredelivery.cancer.gov/seermedicare/obtain/.

References

[1] Explore Cancer Statistics. , Cancer Statistics Center, American Cancer Society, 2024.
[2] SEER*Explorer: An interactive website for SEER cancer statistics. April 16, 2025 ed, Surveillance Research Program, National Cancer Institute, 2025.
[3] J. Ferlay, M. Laversanne, M. Ervik, F. Lam, M. Colombet, L. Mery, et al., Global Cancer Observatory: Cancer Tomorrow (Version 1.1), International Agency for Research on Cancer, Lyon, France, 2024.
[4] J.E. Morley, B. Vellas, G.A. van Kan, S.D. Anker, J.M. Bauer, R. Bernabei, et al., Frailty consensus: a call to action, J. Am. Med. Dir. Assoc. 14 (2013) 392–397.
[5] C. Meernik, O.L. Osazuwa-Peters, L.E. Wilson, A. Joshi, M. Pisu, M.I. Liang, et al., Frailty in patients with ovarian cancer and the role of healthcare access, race, and ethnicity, Gynecol. Oncol. 190 (2024) 146–152.
[6] E.M. Cespedes Feliciano, C. Hohensee, A.E. Rosko, G.L. Anderson, E.D. Paskett, O. Zaslavsky, et al., Association of Prediagnostic Frailty, change in frailty status, and mortality after Cancer diagnosis in the Women's Health Initiative, JAMA Netw. Open 3 (2020), e2016747.
[7] D.M. Narasimhulu, M.E. McGree, A.L. Weaver, A. Jatoi, N.K. LeBrasseur, G.E. Glaser, et al., Frailty is a determinant of suboptimal chemotherapy in women with advanced ovarian cancer, Gynecol. Oncol. 158 (2020) 646–652.

[8] A. Kumar, C.L. Langstraat, S.R. DeJong, M.E. McGree, J.N. Bakkum-Gamez, A.L. Weaver, et al., Functional not chronologic age: frailty index predicts outcomes in advanced ovarian cancer, Gynecol. Oncol. 147 (2017) 104–109.
[9] V. Di Donato, G. Caruso, G. Bogani, A. Giannini, O. D'Oria, G. Perniola, et al., Preoperative frailty assessment in patients undergoing gynecologic oncology surgery: a systematic review, Gynecol. Oncol. 161 (2021) 11–19.
[10] J. Kelley, G. Smith, M. Yao, L. Chambers, R. DeBernardo, The modified 5-factor frailty index predicts postoperative outcomes in patients with ovarian cancer undergoing hyperthermic intraperitoneal chemotherapy, Surg. Oncol. 57 (2024), 102154.
[11] K. Li, R. Yin, Z. Li, Frailty and long-term survival of patients with ovarian cancer: a systematic review and meta-analysis, Front. Oncol. 12 (2022), 1007834.
[12] F.N. de Arruda, M.H.M. Oonk, M.J.E. Mourits, P. de Graeff, M. Jalving, G.H. de Bock, Determinants of health-related quality of life in elderly ovarian cancer patients: the role of frailty and dependence, Gynecol. Oncol. 153 (2019) 610–615.
[13] S. Man, X. Wu, H. Huang, J. Yu, L. Xia, Frailty in middle-aged and older adult postoperative patients with gynecological malignancies structural equation modeling, Front. Public Health 12 (2024), 1431048.
[14] M. Extermann, E. Brain, B. Canin, M.N. Cherian, K.L. Cheung, N. de Glas, et al., Priorities for the global advancement of care for older adults with cancer: an update of the International Society of Geriatric Oncology Priorities Initiative, Lancet Oncol. 22 (2021) e29–e36.
[15] J.A. Ledermann, X. Matias-Guiu, F. Amant, N. Concin, B. Davidson, C. Fotopoulou, et al., ESGO-ESMO-ESP consensus conference recommendations on ovarian cancer: pathology and molecular biology and early, advanced and recurrent disease, Ann. Oncol. 35 (2024) 248–266.
[16] V. Goede, Frailty and Cancer: current perspectives on assessment and monitoring, Clin. Interv. Aging 18 (2023) 505–521.
[17] A. Magnuson, L. Lei, N. Gilmore, A.S. Kleckner, F.V. Lin, R. Ferguson, et al., Longitudinal relationship between frailty and cognition in patients 50 years and older with breast Cancer, J. Am. Geriatr. Soc. 67 (2019) 928–936.
[18] E.D. Duchesneau, K. Reeder-Hayes, T. Stürmer, D.H. Kim, J.K. Edwards, J.L. Lund, Longitudinal trajectories of a claims-based frailty measure during adjuvant chemotherapy in women with stage I-III breast cancer, Oncologist 29 (2024) e1291-e301.
[19] H. Mian, T.M. Wildes, R. Vij, M.J. Pianko, A. Major, M.A. Fiala, Dynamic frailty risk assessment among older adults with multiple myeloma: a population-based cohort study, Blood Cancer J. 13 (2023) 76.
[20] J.S. Mandelblatt, X. Zhou, B.J. Small, J. Ahn, W. Zhai, T. Ahles, et al., Deficit accumulation frailty trajectories of older breast Cancer survivors and non-Cancer controls: the thinking and living with Cancer study, J. Natl. Cancer Inst. 113 (2021) 1053–1064.
[21] J. Pu, W. Zhou, W. Zeng, S. Shang, Long-term trajectories of frailty phenotype in older cancer survivors: a nationally representative longitudinal cohort study, Age Ageing 52 (2023).
[22] L. Enewold, H. Parsons, L. Zhao, D. Bott, D.R. Rivera, M.J. Barrett, et al., Updated overview of the SEER-Medicare data: enhanced content and applications, J. Natl. Cancer Inst. Monogr. 2020 (2020) 3–13.
[23] D.H. Kim, S. Schneeweiss, R.J. Glynn, L.A. Lipsitz, K. Rockwood, J. Avorn, Measuring frailty in Medicare data: development and validation of a claims-based frailty index, J. Gerontol. A Biol. Sci. Med. Sci. 73 (2018) 980–987.
[24] D.H. Kim, R.J. Glynn, J. Avorn, L.A. Lipsitz, K. Rockwood, A. Pawar, et al., Validation of a claims-based frailty index against physical performance and adverse health outcomes in the health and retirement study, J. Gerontol. A Biol. Sci. Med. Sci. 74 (2019) 1271–1276.
[25] W.P. Bensken, N.K. Schiltz, D.F. Warner, D.H. Kim, M.Y. Wei, A.R. Quiñones, et al., Comparing the association between multiple chronic conditions, multimorbidity, frailty, and survival among older patients with cancer, J Geriatr Oncol. 13 (2022) 1244–1252.
[26] R. Sachdev, G. Shearn-Nance, L. Vu, W.P. Bensken, S.L. Douglas, S.M. Koroukian, et al., Comparing the use of aggressive end-of life care among frail and non-frail patients with cancer using a claims-based frailty index, J Geriatr Oncol. 15 (2024), 101706.
[27] D. Bedell, R Program - Claims-Based Frailty Index, Harvard Dataverse, 2020.
[28] J.S. Gorzelitz, R. Brick, L. Deng, M. Mollica, N. Stout, S. Stoller, et al., Sociodemographic and clinical characteristics associated with rehabilitation services utilization in older women with early-stage breast cancer from SEER-Medicare 2009-2018, J. Cancer Surviv. 20 (1) (2026 Feb) 245–255.
[29] A. Clegg, J. Young, S. Iliffe, M.O. Rikkert, K. Rockwood, Frailty in elderly people, Lancet 381 (2013) 752–762.
[30] J. Luo, X. Liao, C. Zou, Q. Zhao, Y. Yao, X. Fang, et al., Identifying frail patients by using electronic health Records in Primary Care: current status and future directions, Front. Public Health 10 (2022), 901068.
[31] B. Kochar, D. Cheng, H.R. Lehto, N. Jain, E. Araka, C.S. Ritchie, et al., Application of an electronic frailty index to identify high-risk older adults using electronic health record data, J. Am. Geriatr. Soc. 73 (2025) 1491–1497.
[32] D.H. Kim, E. Patorno, A. Pawar, H. Lee, S. Schneeweiss, R.J. Glynn, Measuring frailty in administrative claims data: comparative performance of four claims-based frailty measures in the U.S. Medicare data, J. Gerontol. A Biol. Sci. Med. Sci. 75 (2020) 1120–1125.
[33] S.E. Heins, D. Agniel, J. Mann, M.E. Sorbero, Comparative performance of three claims-based frailty measures among Medicare beneficiaries, J. Appl. Gerontol. 43 (2024) 765–774.
[34] S.E. Heins, D. Agniel, J. Mann, M.E. Sorbero, Reviewing, Refining, and Validating Claims-Based Algorithms of Frailty and Functional Impairment, The Office of the Assistant Secretary for Planning and Evaluation (ASPE) at the U.S. Department of Health & Human Services, Santa Monica, California, 2023.
[35] G. Bai, Y. Wang, J.K.L. Mak, M. Ericsson, S. Hägg, J. Jylhävä, Is frailty different in younger adults compared to old? Prevalence, characteristics, and risk factors of early-life and late-life frailty in samples from Sweden and UK, Gerontology 69 (2023) 1385–1393.
[36] G. Lurie, L.R. Wilkens, P.J. Thompson, R.K. Matsuno, M.E. Carney, M.T. Goodman, Symptom presentation in invasive ovarian carcinoma by tumor histological type and grade in a multiethnic population: a case analysis, Gynecol. Oncol. 119 (2010) 278–284.
[37] H.E. Dinkelspiel, M. Champer, J. Hou, A. Tergas, W.M. Burke, Y. Huang, et al., Long-term mortality among women with epithelial ovarian cancer, Gynecol. Oncol. 138 (2015) 421–428.
[38] H.P. Yang, B. Trabert, M.A. Murphy, M.E. Sherman, J.N. Sampson, L.A. Brinton, et al., Ovarian cancer risk factors by histologic subtypes in the NIH-AARP diet and health study, Int. J. Cancer 131 (2012) 938–948.
[39] C. Walsh, Genetic implications for Cancer management: the changing landscape of poly (ADP-ribose) polymerase inhibitor indications in the treatment of ovarian Cancer, Clin. Obstet. Gynecol. 67 (2024) 711–719.