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Risk Factors for Frailty and Prefrailty Among Cancer Patients Undergoing Chemotherapy: A Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - Unfunded.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 June 2025 and was last updated on 16 June 2025.

INTRODUCTION

eview question / Objective P (Population): Cancer patients undergoing chemotherapy; I (Exposure): Various potential risk factors; C (Comparison): Patients without these risk factors or in reference categories; O (Outcome): Presence of frailty or prefrailty, as assessed by validated measurement tools.

Rationale Frailty, as a critical clinical issue, is particularly prominent among cancer patients. Evidence suggests that cancer patients undergoing chemotherapy are more likely to develop frailty compared to cancer survivors not receiving chemotherapy or individuals without cancer.

Current research, both domestically and internationally, has predominantly focused on the prevalence of frailty and prefrailty across different cancer types, as well as their impact on chemotherapy toxicity and prognosis. However, systematic investigations specifically targeting the status of frailty and prefrailty during chemotherapy are relatively scarce, and most available studies are cross-sectional with limited sample sizes . Variability in frailty assessment tools and heterogeneity in cancer types across studies have led to inconsistent findings regarding the influencing factors of frailty and prefrailty. Considering the unique physiological stress associated with chemotherapy, the mechanisms and determinants of frailty during this treatment phase may differ from those in other stages of cancer care. Therefore, a systematic review and meta-analysis is urgently needed to synthesize existing evidence, summarize the influencing factors of frailty and prefrailty during chemotherapy based on large sample data, and provide an evidence-based foundation for early identification of high-risk patients, optimization of individualized treatment strategies, and the development of prehabilitation programs. This could help reduce chemotherapy-related adverse events and improve patients' quality of life and clinical outcomes.

Condition being studied Cancer is one of the major social, public health, and economic

challenges of the 21st century. According to the latest estimates from the International Agency for Research on Cancer (IARC), there were 20 million new cancer cases and 9.7 million cancer-related deaths worldwide in 2022. Cancer accounts for approximately 16.8% of all global deaths, significantly impacting life expectancy and imposing a substantial social and economic burden.

Frailty, as a critical clinical issue, is particularly prominent among cancer patients. It is defined as a decline in the physiological reserve and impaired ability to cope with stress due to dysregulation across multiple body systems. Evidence suggests that cancer patients undergoing chemotherapy are more likely to develop frailty compared to cancer survivors not receiving chemotherapy or individuals without cancer. Frailty is associated with an increased risk of treatment-related toxicity and poor clinical outcomes.

METHODS

Search strategy #1 ("Neoplasms"[MeSH Terms] OR "Cancer"[All Fields] OR "Tumors"[All Fields] OR "Neoplasia" [All Fields] OR "Malignant Neoplasm"[All Fields] OR "Malignancy"[All Fields]) #2 ("Drug Therapy"[MeSH Terms] OR "Antineoplastic Agents"[MeSH Terms] OR "Chemotherapy, Adjuvant"[All Fields] OR "chemotherapy" [All Fields] OR "Chemotherapies"[All Fields])

#3 ("Frailty"[MeSH Terms] OR "Frailty"[All Fields] OR "frailties"[All Fields] OR "frail"[All Fields] OR "frails"[All Fields] OR "frailness"[All Fields] OR "frailty syndrome"[All Fields] OR "Prefrailty"[All Fields] OR "Pre-frailty"[All Fields] OR "pre-frail"[All Fields] OR "pre frail"[All Fields] OR "prefrail"[All Fields])

#4 ("Risk Factors"[MeSH Terms] OR "risk factor"[All Fields] OR "risk factors"[All Fields] OR "Determinants"[All Fields] OR "associated factors"[All Fields] OR "influencing factors"[All Fields])

#5 #1 AND #2 AND #3 AND #4.

Participant or population The research subjects were patients aged 18 years or over who had been diagnosed with cancer through pathological examination and were undergoing chemotherapy as part of their treatment.

Intervention Not applicable.

Comparator Not applicable.

Study designs to be included Observational studies including cross-sectional, case-control, and cohort studies.

Eligibility criteria Inclusion criteria:(1) Study participants: patients aged ≥18 years, who have been diagnosed with malignant tumours through pathological examination and who require chemotherapy during treatment;

(2) Study tools: use of the relevant scales to assess the standard of frailty;

(3) Study type: cross-sectional studies, cohort studies or case-control studies;

(4) Outcome indicators: the incidence of frailty in cancer patients during chemotherapy and its influencing factors, with the requirement that the data can be extracted or converted for analysis.

Exclusion criteria: (1) case reports, reviews, and conference proceedings;

(2) literature for which the full text is unavailable or data are incomplete;

(3) literature with a Newcastle-Ottawa Scale (NOS) or Agency for Healthcare Research and Quality (AHRQ) recommended quality evaluation score of 0–3.

Information sources Relevant literature on the risk factors associated with frailty and prefrailty in cancer patients undergoing chemotherapy will be retrieved from the following databases: China National Knowledge Infrastructure (CNKI), Wanfang Database, VIP Database, PubMed, Web of Science, the Cochrane Library, EMBASE, and CINAHL.

Main outcome(s) Duplicate records were removed using noteExpress software, and then two researchers independently extracted data using a double-blind method. In case of disagreement, a third researcher was consulted to reach a consensus. The extracted data included first author, publication date, country, study type, tumor type, frailty assessment tool, inclusion age, mean age, number of frail individuals, total sample size, prevalence, and influencing factors.

Data management Data were imported into Excel and noteExpress. The data is entered by one person and verified by another.

Quality assessment / Risk of bias analysis Two researchers independently conducted the literature quality assessment. In cases of disagreement, a third researcher made the final decision to reach a consensus. Cross-sectional studies were evaluated using the quality assessment criteria recommended by the AHRQ, which include 11 items. A score of 1 was assigned for "yes," 0 for 'unclear' or "no," with 8–11 points indicating high quality, 4–7 points indicating moderate quality, and 6 points indicating high-quality literature.Use Stata software to draw a funnel plot and perform Egger's test and Begg's test to describe whether there is publication bias.

Strategy of data synthesis A meta-analysis of the prevalence of frailty and its influencing factors in cancer patients undergoing chemotherapy was conducted using Stata 15.1 software. The results were expressed as odds ratios (OR) and 95% confidence intervals (CI). The heterogeneity of the pooled data was primarily assessed using the chisquare test combined with the I² value. If $P \ge 0.10$ and $I^2 \leq 50\%$, indicating no significant heterogeneity among studies, the meta-analysis employed a fixed-effect model; otherwise, a random-effects model was selected. The sources of heterogeneity were further evaluated through sensitivity analysis or subgroup analysis. Factors that could not be combined were analyzed descriptively. Stata software was used to plot funnel plots and perform Egger's test and Begg's test to describe the presence of publication bias. The significance level was set at $\alpha = 0.05$.

Subgroup analysis Subgroup analysis by study type, frailty assessment tool, and age group included.

Sensitivity analysis To assess the robustness of the pooled incidence rate, a sensitivity analysis was conducted using a stepwise exclusion method. The results showed that excluding any single study did not result in a substantial change in the pooled incidence rate , suggesting that the results of this study are robust.

Sensitivity analysis of risk factors was performed using different effect models to analyze the test results, with no significant differences observed, indicating good stability of the results.

Language restriction Chinese.

Country(ies) involved China.

Keywords Malignant tumors; chemotherapy; frailty; pre-frailty; risk factors.

Contributions of each author

Author 1 - BingTing Wang - Conceived the study, developed the protocol, conducted the literature search, performed data extraction and analysis, and drafted themanuscript. Email: wbt00613@163.com Author 2 - cuiping Xu. Email: xucuiping775@sohu.com Author 3 - yinuo Wang - . Email: 363370409@qq.com