

Why is frailty important in cancer?

By

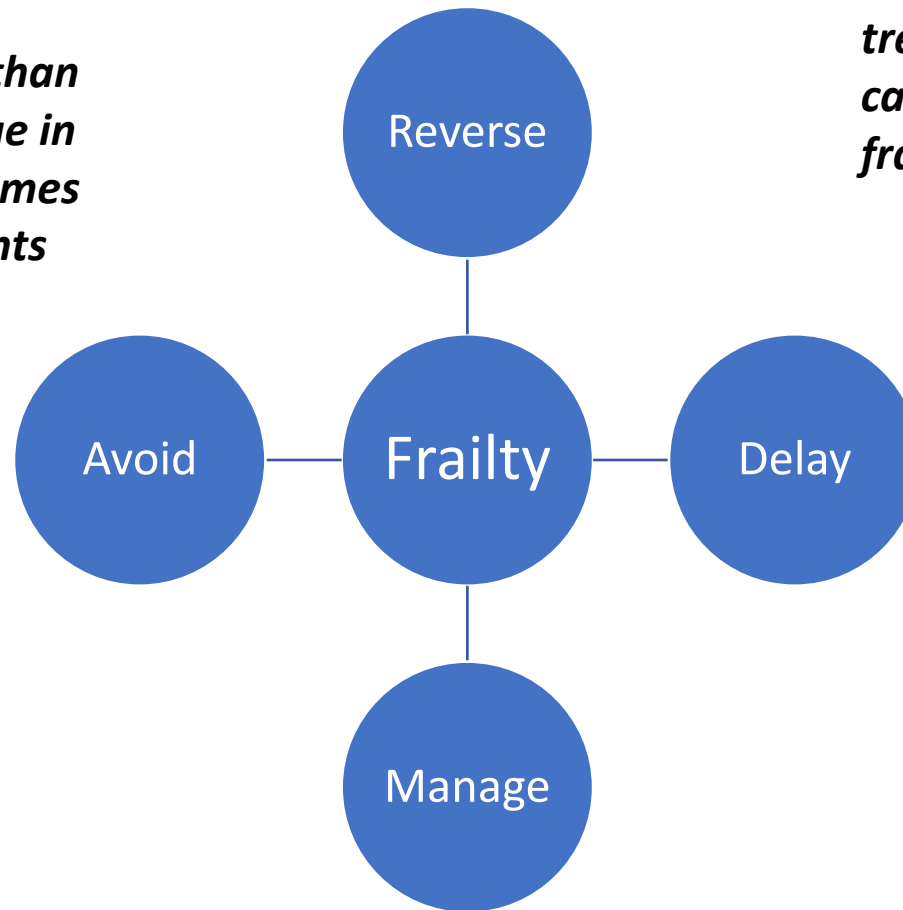
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Frailty is better than chronological age in predicting outcomes for cancer patients

Cancer and its treatments cause/accelerate frailty



Opportunities:

- Personalised care
- Optimisation
- Completion of treatment
- Improved outcomes

Reduce risks of:

- Undertreatment
- Overtreatment
- Unplanned admissions
- Morbidity
- Mortality



Table 4. Frailty prevalence

| Reference standard | Study | Frail (%) | Pre-frail (%) | Fit (%) |
|----------------------------|------------------------------|-----------|---------------|---------|
| CGA | Baitar et al. [18] | 64 | | 36 |
| | Clough-Gorr et al. [20, 21] | 22 | | 78 |
| | Kellen et al. [24] | 68 | | 32 |
| | Kristjansson et al. [25, 26] | 43 | 45 | 12 |
| | Luciani et al. [27] | 68 | | 32 |
| | Mangia et al. [28] | 7 | 21 | 72 |
| | Mohile et al. [29] | 60 | | 40 |
| | Molina-Garrido et al. [30] | 68 | | 32 |
| | Owusu et al. [31] | 43 | | 57 |
| | Puts et al. [32] | 42 | 24 | 34 |
| | Retornaz et al. [33] | 56 | 16 | 28 |
| | Singhal and Cheng [34] | 13 | 62 | 25 |
| | To et al. [36] | 13 | 60 | 28 |
| | Valero et al. [37] | 10 | 79 | 11 |
| | Wedding et al. [38] | 50 | 26 | 25 |
| Weltermann and Koller [39] | 34 | 42 | 24 | |

Median reported prevalence of:

- Frailty 42% (range 6-86%)
- Prefrailty 43% (range 13-79%)
- Fit 32% (range 11-78%)

The prevalence and outcomes of frailty in older cancer patients: a systematic review

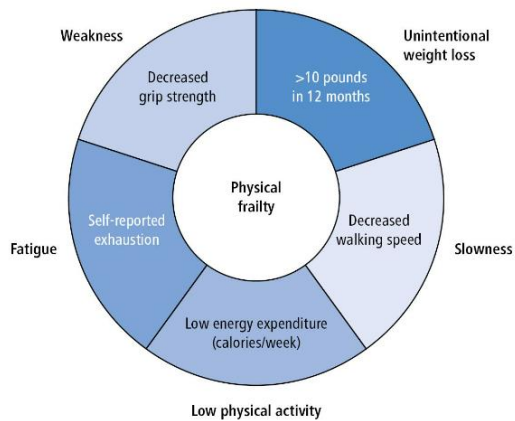
(Handforth et al 2015)



Studies using the phenotype model of frailty were more likely to find the cohorts to be fit

| Reference standard | Study | Frail (%) | Pre-frail (%) | Fit (%) |
|--------------------|------------------------------|-----------|---------------|---------|
| Phenotype model | Bylow et al. [19] | 6 | 44 | 49 |
| | Courtney-Brooks et al. [22] | 16 | 27 | 57 |
| | Degeys et al. [23] | 86 | | 14 |
| | Kristjansson et al. [25, 26] | 13 | 48 | 40 |
| | Tan et al. [35] | 28 | | 72 |

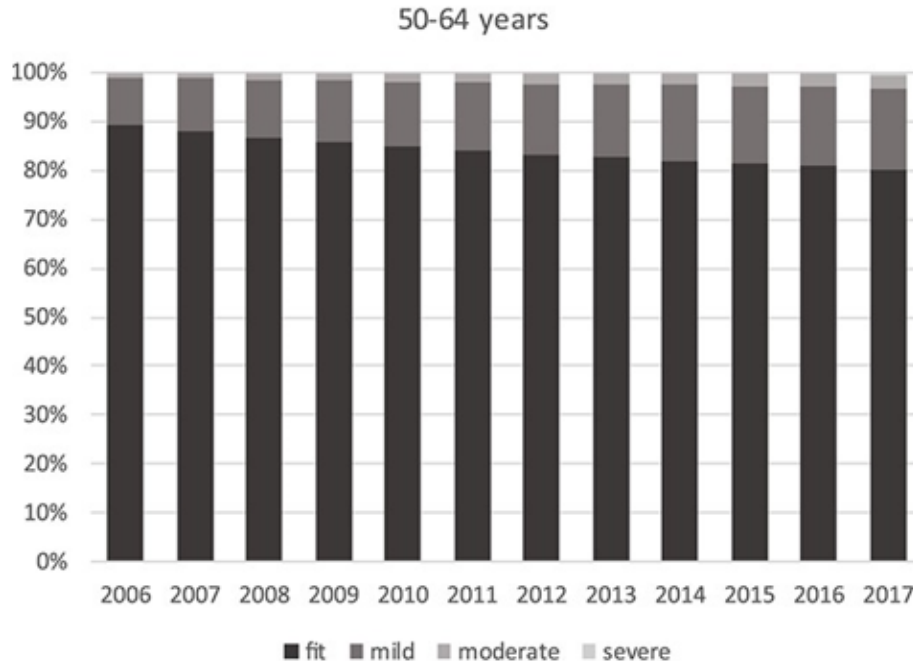
Physical frailty based on the Fried phenotype model. Adapted from *J Gerontol A Biol Sci Med Sci.* 2001 Mar;56(3):M146-56.





Young and Frail

Trend for 50-64 years
N=1,412,823



- Increasing frailty in the deficit cumulative model eFI

- 1 in 10 in 2006
- 1 in 5 in 2017

For all age groups frailty transitions are associated with increasing:

- age
- higher deprivation
- female sex
- Asian ethnicity
- urban dwelling

Adults aged 50-74 account for more than 4 in 10 (42%) of all cancer deaths (ONS)



Referral/Investigations

- A systematic review found that older age was linked with a preference for quality of life rather than length of life. Patients aged over 70 years have been shown to be less likely to want investigations for possible cancer symptoms and to accept a higher risk of cancer being undiagnosed.
- Older people want to be able to do the things they consider important for as long as possible; therefore, any investigation, referral, or treatment should **'add life to years, not years to life'**.
- The value to patients of having a diagnosis should be considered, and how a diagnosis may provide better access to palliative care, specialist nurses, and charitable support, which may improve symptomatic management and quality of life

(Investigating cancer symptoms in older people. BMJ 2020)



Cancer causes frailty

Prior studies demonstrate that cancer survivors frequently report:

- symptoms synonymous with frailty, which may persist for years after completion of treatment for cancer.
- -Treatment for cancer is hypothesized to accelerate the aging process.
- Cancer survivors are **46%** more likely to be frail compared to adults of similar age without a history of cancer.
- Given that cancer treatment is a transient exposure, frailty among cancer survivors may represent a unique entity with etiologies and trajectories distinct from those without a history of cancer.

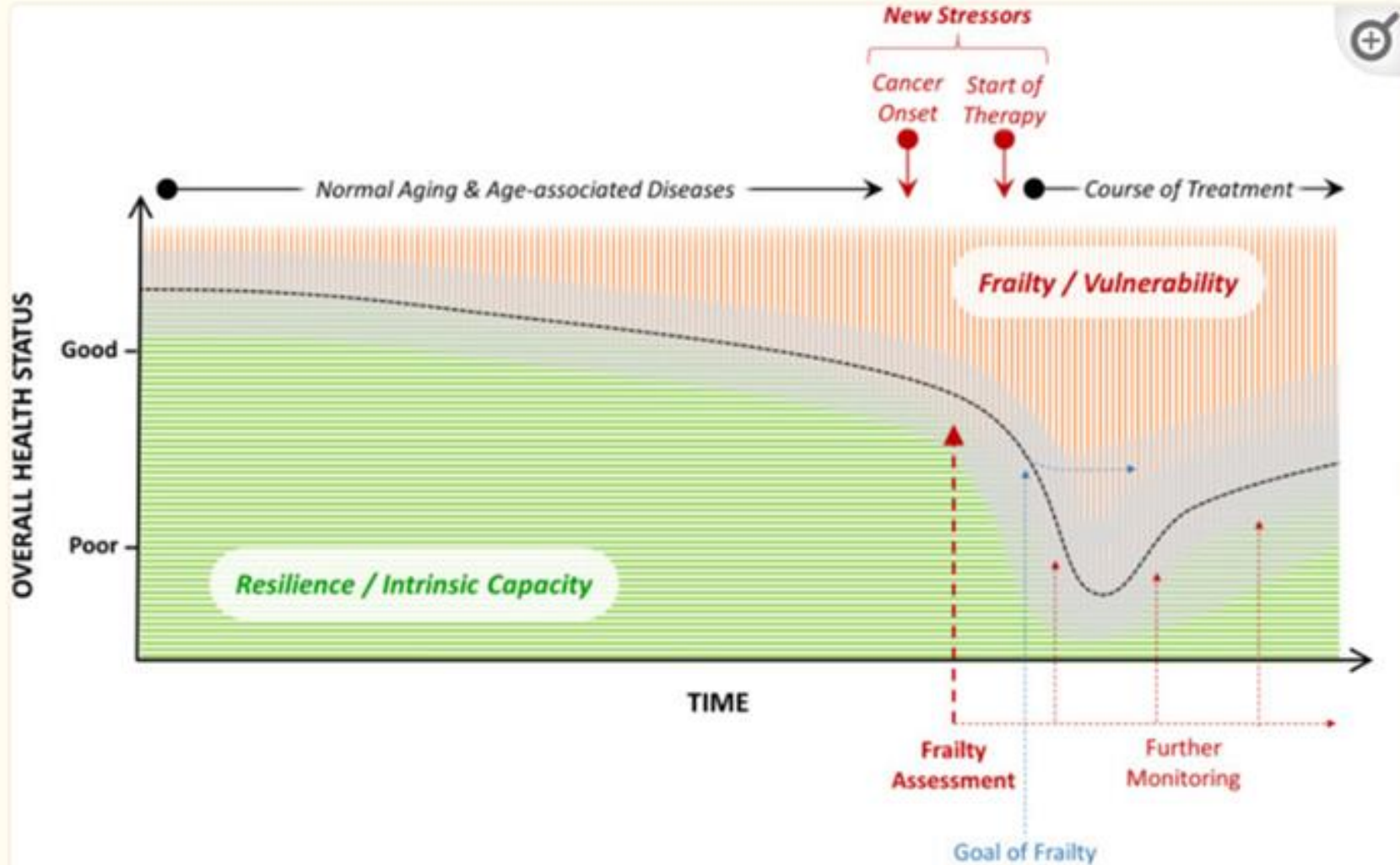
(Brown et al 2015)

- Frailty rates in survivors of adult cancers range from **9.1–59.0%**, often **double** and sometime nearly **quadruple** the rates of frailty in age, sex and race matched populations.

(Ness & Wogksch 2021)



Treatment



Age and Cancer Treatment Data (NCRAS 2013-20)

60% of 80+years do not have chemotherapy, radiation or surgery they receive other care.

(Other care represents the group of patients who had no record of chemotherapy, tumour resection, or radiotherapy in the time frame assessed. This may include patients who received other treatments (such as hormonal therapy or management of symptoms), treatment outside of the time frame assessed, treatment in a private setting, or there may be data missing from the datasets used.)

| Percentage other care (80+years) | 30-40% | 40-50% | 50-60% | 60-70% | 70-80% | 80-90% | 90-100% |
|----------------------------------|---------|----------|----------|--------|------------|----------|------------|
| Cancer Site | Rectum | Bladder | Breast | | Lung NSC | Kidney | Brain |
| | Testes | Cervical | Colon | | Oesophagus | Prostate | Liver |
| | Uterine | | Lung SCC | | | | Endocrine |
| | | | Ovary | | | | Pancreatic |

Prostate, Breast and Endocrine are more likely to be treated with hormonal therapy. However other cancers with high percentages not receiving treatment demonstrates possibility that cohort is frail and unsuitable for treatments. We know that 30% of those aged over 80 and 60 % of those over 90 are clinically frail in the normal distribution, this is higher in a cancer cohort.

Potential Adverse Outcomes Related to Frailty in Older Adults with Cancer (Goede 2023)

General Frailty Outcomes

- Early Death
- Care Dependency
- Nursing home admission
- Hospital Admission
- Permanent bedrest
- Falls
- Delerium
- Exacerbation/progression of chronic diseases
- Onset of acute illness
- Adverse drug interactions

Radiotherapy

- Increased toxicity
- Including late onset radiation damage
- Unplanned treatment interruption
- Premature treatment discontinuation
- Unplanned hospitalisation

Surgical Treatment

- Prolonged immobilisation
- Postoperative nutritional problems
- Postoperative delirium and depression
- post operative wound healing disorders
- Postoperative bleeding disorders
- Delayed recovery
- Other post operative complications including infections

Systemic drug treatment including chemotherapy

- Increase drug toxicity
- Including cytopenias infections organ toxicities
- Unplanned treatment interruption
- Premature treatment discontinuation
- Drug- drug interactions
- Unplanned hospitalisation

Unplanned Hospitalisation.

Prefrility/frailty were associated with a **2.5 fold** increased risk of hospital and a **1.9 fold** increased risk of long-term care admissions(Ness & Wogksch 2021)

What is the size of the problem?

Demand – Merseyside data from 2017 showed that mortality for 1950 people admitted acutely and referred to AO was 71% at 12 months

We asked trusts in 2022 - how many unplanned admissions with referral to AO team in did you have in 3 months (jan-march 2022) and what was their mortality at 12 months

Small trust

- Whittington 60 (mortality at 12 months 72%)

Larger trusts with cancer centre

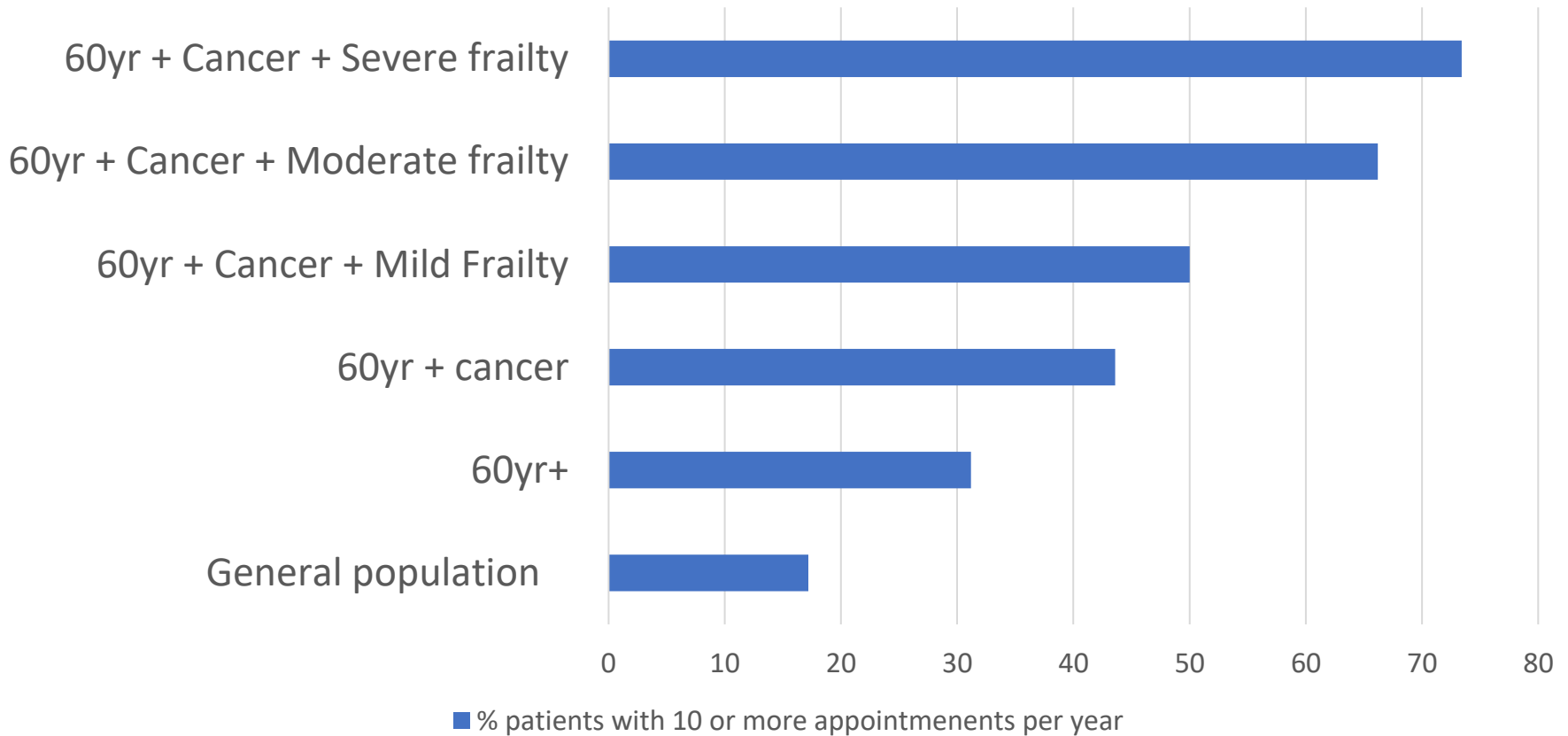
- Brighton 377 (mortality at 12 months 65.5%)
- Plymouth 365 (mortality at 12 months 79%)

Dr Ashling Lillis
Consultant in Acute Medicine
National Clinical Advisor
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DiiS – Primary Care High Intensity Users

% patients with 10 or more appointments per year



7% of the Dorset population have cancer coded

13% of appointments are with patients that have cancer coded

Comparisons of ED/MIU visits and admissions with frailty and cancer comorbidities coded

| | Total ED/MIU Visits | Total ED Admissions | Percentage admitted |
|------------------------------|---------------------|---------------------|---------------------|
| All | 81.3k | 24.5k | 30% |
| Cancer | 7619 | 4061 | 53% |
| Mild frailty | 11.8k | 4754 | 40% |
| Mild frailty + cancer | 2027 | 1088 | 53% |
| Moderate Frailty | 5737 | 3085 | 54% |
| Moderate frailty + cancer | 1397 | 801 | 57% |
| Severe Frailty | 4227 | 2660 | 63% |
| Severe frailty + cancer | 1337 | 852 | 64% |



Mild Frailty + cancer is an area that demonstrates differences in admissions that there may be opportunity to have impact.

Please note that anomalies within the A&E Secondary Users Services dataset has resulted in an overcount in ED/MIU visits.

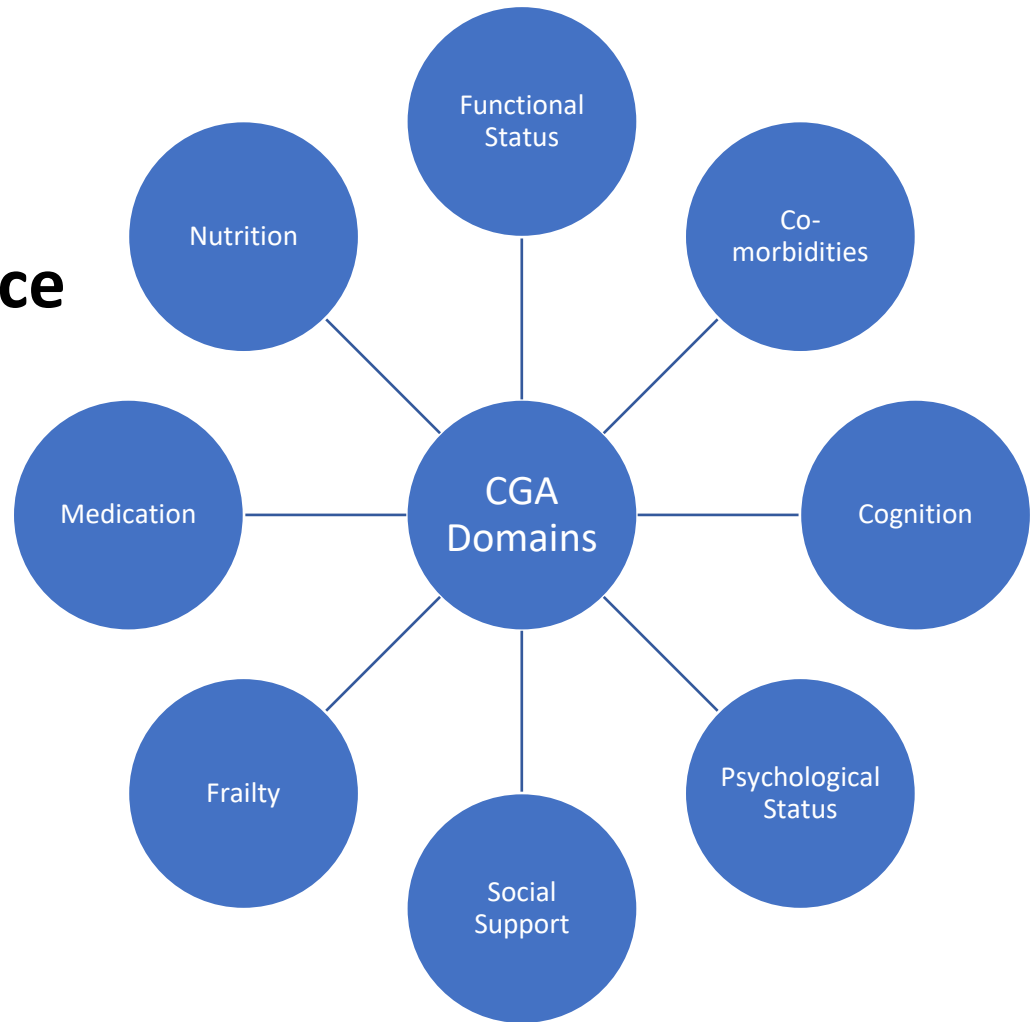


Components of the CGA and risks in older patients

‘Determining Chemotherapy Tolerance in Older Patients With Cancer’

Kim & Hurria (2013)

National Comprehensive Cancer Network. 11(12): 1494–1502.



Why optimisation is important? Using the CGA

Studies have linked depression to:

- hospitalizations,
- chemotherapy toxicity,
- decreased survival in older adults with cancer.

Problems performing IADLs are prognostic for

- severe chemotherapy toxicity
- poorer survival in older patients with cancer

Needing assistance with ADLs has been linked to:

- increased health care use
- shorter survival in geriatric patients.

Comorbidities predict early mortality in patients with cancer, independent of age and functional status.

Medical problems such as diabetes mellitus are associated with an increased risk of mortality in older adults with cancer

Organ dysfunction such as renal insufficiency is a risk factor for chemotherapy toxicity.

Close to one-third of patients with cancer take a combination of medications that are known to interact

Polypharmacy is an independent risk factor for overall survival in older patients with ovarian cancer.

older patients with lower baseline cognitive reserve may be at higher risk for further cognitive decline with chemotherapy.

Prospective studies have identified malnutrition as a risk factor for

- chemotherapy intolerance and
- decreased survival in older patients with cancer.

Social isolation has been linked to:
increased chemotherapy toxicity
decreased survival in patients with cancer.

Cognitive problems are associated with chemotherapy intolerance hospitalization in older adults with cancer.

Kim & Hurria 2013)



What is likely to be the problem?

A total of 234 geriatric patients aged ≥ 65 years with cancer receiving chemotherapy were enrolled during the study period of September 2016 to November 2018.

The prevalence of frailty was **58.1%**

On the CGA, common deficient dimensions were:

65.4% nutrition

38.5% comorbidity

24.8 % functional status

23.1% polypharmacy

17.5% Mood

13.2% falls

10.7% cognition

9.4% social support

Association of frailty and chemotherapy-related adverse outcomes in geriatric patients with cancer: a pilot observational study in Taiwan. Ho et al (2021)



Stop the clock

- Onco-Geriatricians often take patients off the fast-track pathway as it may not always be in the patient's best interest
- more time to ascertain fitness for treatments and reversibility leads to better overall care
- Time can also be taken to prehabilitate and optimise the patient



Reversibility

Frailty is a dynamic process it can be worsened or improved delayed and avoided.

- Inclusion criteria CFS = or < 5 Mild/prefrail
- Intervention: 3-month home-based exercise regime, emphasising strength, and dietary protein guidance (1.2 g/kg/day)
- Baseline: 17.7% of intervention and 16.9% of control participants were frail
- At follow-up, 6.3% and 18.2% were frail

Building resilience and reversing frailty: a randomised controlled trial of a primary care intervention for older adults. Travers et al (2023)



Prehabilitation Model

CFS scores - baseline to discharge from the programme



| CFS Difference | Total | As a % |
|---|------------|------------|
| Reduced by 2 (Managing Well to Mildly Frail) | 1 | Negligible |
| Reduced by 1 (maj. Managing Well to Vulnerable) | 26 | 3% |
| Maintained (mix of Managing Well & Vulnerable) | 345 | 36% |
| Improvement of 1 (Vulnerable to Managing Well, Managing Well to Well) | 452 | 47% |
| Improvement of 2 (Managing Well to Very Fit, Vulnerable to Well, Mildly Frail to Managing Well) | 119 | 12% |
| Improvement of 3 (See overleaf) | 13 | 1% |
| Improvement of 4 (See overleaf) | 4 | Negligible |
| Total Patients | 959 | |

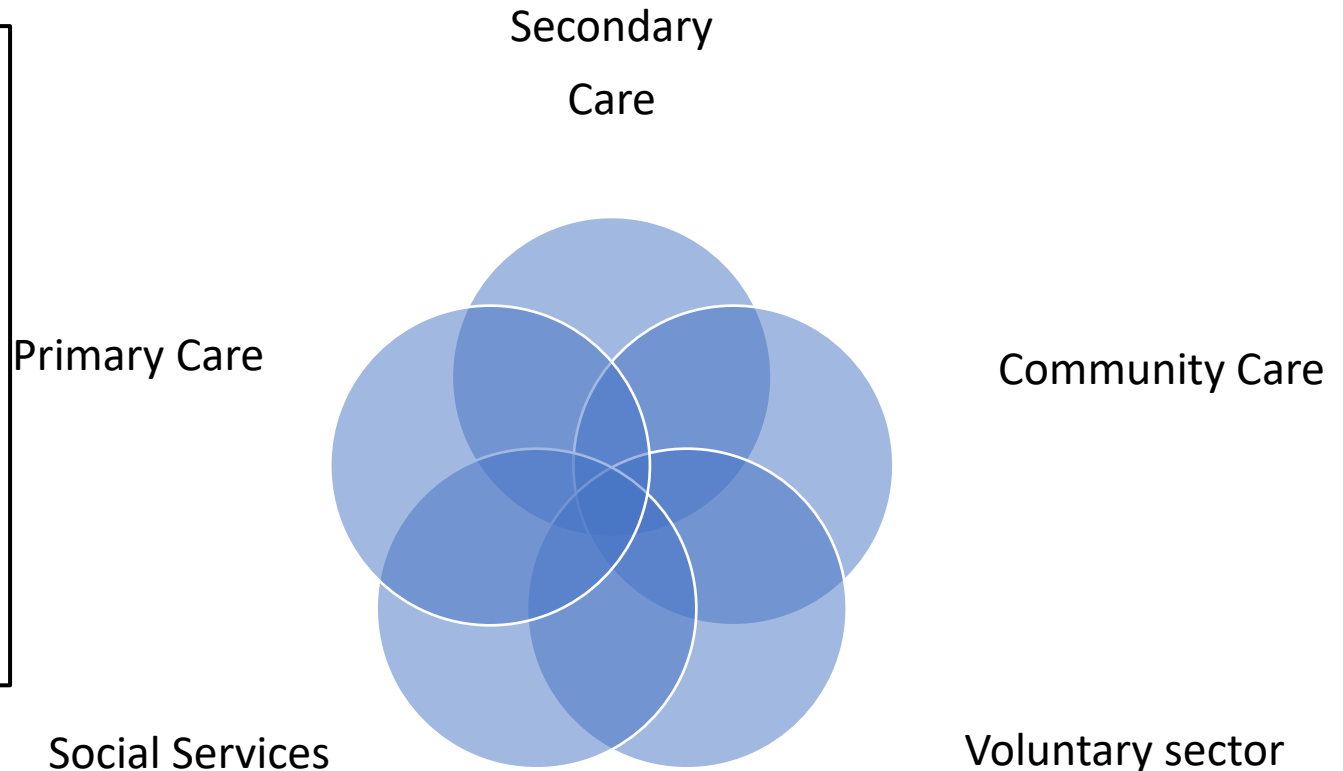
1 – Very Fit, 2 – Well, 3 – Managing Well, 4 – Vulnerable, 5 – Mildly Frail, 6 – Moderately Frail, 7 – Severely Frail



Whole System Approach

Who, what, where and when?

- Identification
- Assessment
- Personalised care
- Collaboration
- Monitor/Review
- Data collection





Guidelines and Supportive Documents



Implementing frailty assessment and management in oncology services

British Geriatrics Society
Improving healthcare for older people

BGS

Comprehensive Geriatric Assessment Toolkit for Primary Care Practitioners



NCCN GUIDELINES® INSIGHTS

CE

Older Adult Oncology, Version 1.2021

ABSTRACT

The NCCN Guidelines for Older Adult Oncology address specific issues related to the management of cancer in older adults, including screening and comprehensive geriatric assessment (CGA), assessing the risks and benefits of treatment, preventing or decreasing complications from therapy, and managing patients deemed to be at high risk for treatment-related toxicity. CGA is a multidisciplinary, in-depth evaluation that assesses the objective health of the older adult while evaluating multiple domains, which may affect cancer prognosis and treatment choices. These NCCN Guidelines Insights focus on recent updates to the NCCN Guidelines providing specific practical framework for the use of CGA when evaluating older adults with cancer.

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