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Evaluating the Impact of Pharmacist Interventions in the Geriatric Oncology Setting

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B.Pharm M.Pharm MPSI

A thesis submitted to the National University of Ireland, Cork
for the degree of Doctor of Philosophy
in the School of Pharmacy

06/11/2025

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Declaration

This is to certify that the work I am submitting is my own and has not been submitted for another degree, either at University College Cork or elsewhere. All external references and sources are clearly acknowledged and identified within the contents. I have read and understood the regulations of University College Cork concerning plagiarism and intellectual property.

Signed:  **Date:** 06/01/2026

Darren Joseph Henry Breathnach (Walsh)

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Peer-reviewed publications

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- Walsh DJ, O'Driscoll M, Horgan AM, Tabb E, Hannan M, Morris C, Sahm LJ. Hospitalisation and adverse drug events in a geriatric oncology setting: A systematic review of the literature. Res Social Adm Pharm. 2024 Sep;20(9):820-827. doi: 10.1016/j.sapharm.2024.04.018. Epub 2024 May 1. PMID: 38705819.
- Walsh DJ, Sahm LJ, O'Driscoll M, Bolger B, Ameen H, Hannan M, et al. Hospitalisation due to adverse drug events in older adults with cancer, a retrospective analysis. J Geriatr Oncol. 2025;16(6). doi:10.1016/j.jgo.2025.102283

  Impact: As of October 2025, this article has been cited 4 times in peer-reviewed publications.
- Walsh DJ, O'Driscoll M, Sahm LJ, Meagher AM, Doblas P, McGowan E, Smith-Lehane G, Hannan M, Goggin C, Buckley C, Horgan AM. Ageing-related considerations for medication used in supportive care in cancer. J Geriatr Oncol. 2024 Jun;15(5):101760. doi: 10.1016/j.jgo.2024.101760. Epub 2024 Mar 30. PMID: 38556399.

  Impact: As of October 2025, this article has been cited 3 times in peer-reviewed publications.
- Walsh DJ, Sahm LJ, O'Driscoll M, Tabb E, Hannan M, Horgan AM. Comprehensive pharmacological geriatric assessment compared to usual care in an older adult with cancer in the absence of polypharmacy. Journal of Oncology Pharmacy Practice. 2023;0(0). doi:10.1177/10781552231182936

Presentations

Oral presentations

- Development of a medication review intervention in ambulatory older adults with cancer, International Society of Geriatric Oncology Annual Conference, Nursing and Allied Health Poster Walk Session, 21st November 2025
- Evaluating the Impact of Pharmacist Interventions in a Geriatric Oncology Outpatient Clinic, All Ireland Schools of Pharmacy Annual Research Conference 2025, Cork, 4th September 2025
- Evaluating the Impact of Pharmacist Interventions in the Geriatric Oncology Setting, UCC School of Pharmacy Monthly Clinical Seminar, Online, 12th May 2025
- Communication between Clinical Pharmacy and Aseptic Compounding in an era of Advanced Specialism, Hospital Pharmacist Association of Ireland Aseptic Services Specialist Interest Group Education Evening, 23rd January 2025
- Quality medicines management in prostate cancer patients, Mater Misericordiae University Hospital Education Event, 7th November 2024
- Principles of Geriatric Oncology and role of pharmacist, British Oncology Pharmacy Association Annual Symposium, 13th October 2024
- IN THE “WEED”S: Navigating herbal medicines in cancer care, Irish Association of Nurses in Oncology Annual Conference 2024, Kilkenny, 5th October 2024
- Quality medicines management in prostate cancer patients, Cork University Hospital Education Event, 3rd October 2024
- Opioids and other Miscellaneous Medications in Palliative Care, South East Palliative Care Centre, Palliative Care Journal Club, University Hospital Waterford, 25th July 2024
- Olanzapine in Advanced Cancer, Palliative Care Journal Club, South East Palliative Care Centre, Waterford, 9th May 2024

- Reducing potentially inappropriate medication use and patient harm in a dedicated geriatric oncology clinic – a cross-sectional study, Health Services Research and Pharmacy Practice (HSRPP) Conference 2024, Cork, 26th April 2024
- Role of Pharmacy Practitioners in Supporting Patients, Trinity College Dublin Oncology Masterclass, 17th April 2024
- Optimising communication for medication reviews in older adults with cancer, Irish Medication Safety Network PEARLS Finalist, Cork, 24th November 2023
- Updates in Chemotherapy Induced Nausea and Vomiting, Irish Pharmacy Haematology Oncology Society National Conference, Dublin, 18th November 2023
- Pharmacist Interventions in an ambulatory geriatric oncology clinic, UCC School of Pharmacy Monthly Clinical Seminar, Online, 19th September 2023
- Safe Prescribing of Chemotherapy, RCPI Safe Prescribing Course, Dublin, 20th July 2023
- Age-related considerations for Cancer Associated Thrombosis, Irish Association of Nursing in Oncology Education Evening, Waterford, 18th May 2023
- Polypharmacy and Potentially Inappropriate Medications in Older Adults with Cancer. National Cancer Control Programme, Geriatric Oncology Nursing Forum, Online, 27th March 2023
- Role of the Clinical Pharmacist in a Geriatric Oncology Clinic, RCPI Oncology Specialist Registrar Study Day, Waterford, 25th March 2023
- Evaluating the Impact of Pharmacist Interventions in a Geriatric Oncology Setting, UCC Cancer Trials Group, Online, 10th January 2023
- The Role of a Pharmacist in the Geriatric Oncology Clinic, Irish Pharmacy Haematology Oncology Society National Conference, Dublin, 12th November 2022

- Model of Integrated Pharmacological Care in Geriatric Oncology in Ireland. International Society of Geriatric Oncology Annual Conference, Geneva, 29th October 2022
- Evaluating the Impact of Pharmacist Interventions in a Geriatric Oncology Setting. UCC Cancer Research Seminar, Online, 17th January 2021
- Evaluating the Impact of Pharmacist Interventions in a Geriatric Oncology Setting, Irish Pharmacy Haematology Oncology Society Education Evening, Online, 25th November 2021

Poster presentations

- Walsh DJ, O'Driscoll M, Sahm LJ, Hannan M, Goggin C, Bambrick P, Barrett C, Horgan AM. Drug-related problems in ambulatory older adults with cancer; a retrospective analysis, Irish Geriatric Oncology Annual Meeting, Dublin, 5th April 2025
- Walsh DJ, Horgan AM, O'Driscoll M, Hannan M, Goggin C, Sahm LJ. Reducing potentially inappropriate medication use and patient harm in a dedicated geriatric oncology clinic: a cross-sectional study, *International Journal of Pharmacy Practice*, Volume 32, Issue Supplement_1, April 2024, Pages i19–i20, https://doi.org/10.1093/ijpp/riae013.024
- Penn S, Sahm LJ, O'Driscoll M, Horgan AM, Hannan M, Walsh DJ. Medication-Related Problems in Older Adults With Colorectal Cancer Compared to Lung Cancer: A Cross-Sectional Analysis, (2024), Abstracts. Pharmacoepidemiol Drug Saf, 33: e5859. https://doi.org/10.1002/pds.5859
- Walsh DJ, Horgan AM, Sahm LJ, Hannan M, Goggin C, Buckley C, Fennelly C, O'Driscoll M. Medication review in an outpatient Geriatric Oncology setting to improve the quality of available documentation in the event of unplanned hospitalisation, University Hospital Waterford Quality and Patient Safety Conference, Waterford, 10th November 2023
- Walsh DJ, O'Driscoll M, Sahm LJ, Goggin C, Hannan M, Buckley C, Fennelly C, Horgan AM. SIOG2023-5-P-351 - Proton Pump Inhibitor use in Older Adults with Cancer, Journal of Geriatric Oncology, Volume 14, Issue 8, S66

- Walsh DJ, Bolger B, Ameen H, Sahm LJ, McGowan E, Hannan M, O'Driscoll M, Horgan AM. Identifying the prevalence of polypharmacy in a cohort of older adults with cancer, BOPA 2022 – Abstract Book. Journal of Oncology Pharmacy Practice. 2023;29(1_suppl):S1-S94. doi:10.1177/10781552231153542
- Walsh DJ, Ameen H, Bolger B, Sahm LJ, McGowan E, Hannan M, O'Driscoll M, Horgan AM. The incidence of hospitalisation in older adults with cancer due to systemic anti-cancer therapy (SACT) toxicity, BOPA 2022 – Abstract Book. Journal of Oncology Pharmacy Practice. 2023;29(1_suppl):S1-S94. doi:10.1177/10781552231153542
- Evaluating the Impact of Pharmacist Interventions in a Geriatric Oncology Outpatient Clinic, Showcase of Employment-based PhD Scholars, Bright Futures: Celebrating our Researchers! Cork, 26th April 2023 (Video abstract)
- Walsh DJ, Sahm LJ, O'Driscoll M, Hannan M, Horgan A.M. SIOG2022-0106 - Length of Acute Hospital Stay in an Older and Younger Oncology Population, Journal of Geriatric Oncology, Volume 13, Issue 8, Supplement 1, 2022, Page S57, ISSN 1879-4068, https://doi.org/10.1016/S1879-4068(22)00380-0. (https://www.sciencedirect.com/science/article/pii/S1879406822003800)
- Walsh DJ, Hamid M, Hannan M, Tabb E, Dunne E, Horgan AM, Lynch P, MyoOo N, O'Connor M, Calvert P, Jordan E. SIOG2022-0129 - Impact of Cancer Treatment on Polypharmacy Status and Subsequent Hospitalisation due to Toxicity in Older Adults with Cancer, Journal of Geriatric Oncology, Volume 13, Issue 8, Supplement 1, 2022, Page S62, ISSN 1879-4068, https://doi.org/10.1016/S1879-4068(22)00390-3. (https://www.sciencedirect.com/science/article/pii/S1879406822003903)

PhD Education and Training

Postgraduate taught modules completed

Total: 15 European Credits Transfer System (ECTS) credits

- PG6030 Reproducible Research Practices using R

  ECTS credit weighting: 5

- PG6003 Teaching and Learning for Graduate Studies

  ECTS credit weighting: 5

- IP6013 Pharmacotherapeutics in Palliative Care

  ECTS credit weighting: 5

Other training completed

- ICH GCP (R2) Investigator Site Training, FIRECREST

  13th July 2022

- Research Integrity, Second Edition from Oxford University Press/Epigeum

  14th June 2022

- How to get published in a scholarly journal: Top Tips from a Publisher, Elsevier

  9th May 2022

- The fundamentals of GDPR, HSELand

  3rd February 2022

List of Abbreviations

- ACB – Anticholinergic burden
- ACEi – Angiotensin converting enzyme inhibitor
- ADE – Adverse drug events
- ADL – Activities of daily living
- ADR – Adverse drug reaction
- AGS – American GeriatricS Society
- AKI – Acute kidney injury
- ALT – Alanine transaminase
- APINCH – Anti-infective, Potassium and other electrolytes, Insulin, Narcotics, Chemotherapeutic agents, Heparin and anticoagulants
- ARB – Angiotensin receptor blocker
- ASCO – American Society of Clinical Oncology
- AST – Aspartate aminotransferase
- BSA – Body surface area
- BSC – Best supportive care
- CARG – Cancer in Ageing Research Group
- CAT – Cancer-associated thrombosis
- CGA – Comprehensive geriatric assessment
- CGPA – Comprehensive geriatric pharmacological assessment
- CI – Confidence interval
- CINV – Chemotherapy-induced nausea and vomiting
- CNS – Central nervous system
- COPD – Chronic obstructive pulmonary disease
- CRIDECO – CRIbado de DEterioro COgnitivo para promover ciudades neuroprotegidas
- CTCAE – Common Terminology Criteria for Adverse Events
- CUH – Cork University Hospital
- DDI – Drug-drug interactions
- DRP – Drug-related problem
- EAHP – European Association of Hospital Pharmacy
- ECOG – Eastern Cooperative Oncology Group
- EDQM – European Directorate for the Quality of Medicines & HealthCare
- ESC – European Society of Cardiology
- ESCP – European Society of Clinical Pharmacy
- ESMO – European Society of Medical Oncology
- EuGMS – European Geriatric Medicine Society
- FDA – Food and drug administration
- FIP – International Pharmaceutical Federation
- FRIDs – Falls Risk Inducing Drugs
- GAIN – Geriatric Assessment-Driven Intervention
- GOAL – Geriatric Oncology Assessment and Liaison
- GO-PIMS – Geriatric oncology potentially inappropriate medication
- GP – General Practitioner

- GRADE – Grading of Recommendations, Assessment, Development, and Evaluations
- H – Histamine
- HSE – Health Service Executive
- HPAI – Hospital Pharmacists Association of Ireland
- IGRIMUP – International Group for Reducing Inappropriate Medication Use and Polypharmacy
- IIOP – Irish Institute of Pharmacy
- iPMS - Integrated patient management system
- ISTH – International Society on Thrombosis and Haemostasis
- IV – Intravenous bolus
- IVI – Intravenous infusion
- JBDS – Joint British Diabetes Societies
- JGO – Journal of Geriatric Oncology
- LOS – Length of stay
- LUTS – Lower urinary tract symptoms
- MDT – Multidisciplinary team
- MMAT – Mixed Methods Appraisal Tool
- MSKCC – Memorial Sloan Kettering Cancer Centre
- NAHS – Nursing, Allied Health and Scientists
- NCCN – National Comprehensive Cancer Network
- NCCP – National Cancer Control Programme
- NHS – National Health Service
- NSAIDs – Non-Steroidal Anti-inflammatory Drugs
- OAM – Oral anticancer medication
- OECD – Organisation for Economic Co-operation and Development
- OPD – Outpatients department
- OPERAM – Optimising Therapy to Prevent Avoidable Hospital Admissions in Multimorbid Older Adults
- OR – Odds ratio
- OTC – Over-the-counter
- PCNE – Pharmaceutical Care Network Europe
- PCRS – Primary Care Reimbursement System
- PDI – Potential drug interactions
- PICOST – Patient population, Intervention, Comparator, Outcome, Setting, Timing
- PIM – Potentially Inappropriate Medications
- PO – Per oral
- POM – Potentially Omitted Medications
- PPIs – Proton pump inhibitors
- PRISMA - Preferred Reporting Items for Systematic Reviews and Meta-Analyses
- PRN – Pro re nata
- RCT – Randomised controlled trial
- RR – Relative risk

- SACT – Systemic anticancer therapy
- SIG – Specialist Interest Group
- SIOG – International Society of Geriatric Oncology
- SPC – Summary of Product Characteristics
- SSRIs – Selective Serotonin Re-uptake Inhibitors
- STOPP – Screening Tool of Older Person's Prescriptions
- START – Screening Tool to Alert doctors to Right Treatment
- UHW – University Hospital Waterford
- USA – United States of America
- WHO – World Health Organisation
- WICOP – Waterford Integrated Care for Older People

Acknowledgments

It feels necessary to start this section by stating that it is impossible to include everybody who has positively influenced and impacted this thesis. Years of collaborative practice-based work means leaning on so many people and crossing so many paths. Thank you to everyone.

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Daire, the apple of my eye, I wrote most of this thesis with you on a baby monitor next to the computer screen! I could write a second thesis on how much I love you. If the time and effort that has gone into this work makes your life a fraction better, it was all worth it.

Éist le fuaim na habhann agus gheobhaidh tú breac.

Thesis Abstract

Introduction

Older adults can have increasingly complex care needs, especially in the presence of multimorbidity and/or frailty. The addition of a cancer diagnosis, and the prospect of treating cancer, either with surgery, radiotherapy or systemic therapy (any pharmacological therapy) adds to the healthcare burden placed upon patients. Older adults with cancer are at an increased risk of systemic anticancer therapy toxicity (SACT). An integrated approach to managing the complex healthcare needs of older adults is part of national policy in Ireland, through the National Integrated Care Framework for Older Persons in community healthcare, and the emergence of rapid-access frailty services in acute care. In the field of medical oncology, the growing specialty of geriatric oncology incorporates a comprehensive geriatric assessment (CGA), and multidisciplinary approach, with a view to assessing, and overcoming, potential barriers to optimal cancer care. Nationally, there is strategic ambition to enhance care for older adults with cancer, as evidenced in the National Cancer Strategy 2017-2026. The role of the pharmacist in this setting has yet to be extensively explored, and the potential impact of integrating a pharmacist into the geriatric oncology multidisciplinary team is yet unknown.

Aim

To assess the impact of the integration of a pharmacist into the Geriatric Oncology Assessment and Liaison (GOAL) Clinic in University Hospital Waterford (UHW), as measured by the incidence of unplanned hospitalisation due to adverse drug events (ADE) in patients who attend the clinic.

Methods

A systematic review of the literature was undertaken to identify the incidence of unplanned hospitalisation due to ADE in older adults with cancer. This was followed by an assessment of the impact of SACT on polypharmacy status and unplanned hospitalisation, and the length of hospital stay in older adults with cancer compared to the general population. A retrospective analysis of older patients (aged ≥70 years) who attended a medical oncology outpatient appointment was undertaken to determine the incidence of (i) unplanned hospitalisation and (ii) unplanned hospitalisation due to ADE. A novel intervention, using a pragmatic adaptive iterative process, was employed to design and implement a comprehensive intervention, comprising of a patient-centred medication review process, delivered by the pharmacist in the GOAL clinic. Post intervention, a prospective study assessing the incidence of (i) unplanned hospitalisation and (ii) unplanned hospitalisation due to ADE was then conducted. The results of the retrospective and prospective studies were compared.

Results

The systematic review found a paucity of published literature focused on unplanned hospitalisation due to ADE in the older adult population with cancer. The average length of stay for an older adult with cancer was approximately double that of the general population. SACT increased unplanned hospitalisation when it contributed to a change in polypharmacy status. In the retrospective analysis of 174 patients, 43% (n=75) had an unplanned hospitalisation, with 24% (n=42) having an unplanned hospitalisation due to ADE. Polychemotherapy was the only statistically significant

independent predictor of unplanned hospitalisation due ADE. In the prospective interventional study (n=240), after a structured medication review, CGA and multidisciplinary team (MDT) input, 39% of patients (n=93) had an unplanned hospitalisation, with 10% of patients (n=24) having an unplanned hospitalisation due to ADE. Polychemotherapy, performance status, and potentially inappropriate medication (PIM) were independent predictors of unplanned hospitalisation due to ADE. There was a statistically significant 65% risk reduction ($p<0.001$) between unplanned hospitalisation due to ADE in the prospective study in comparison to the retrospective study.

Conclusion

A pharmacist as an integrated member of a geriatric oncology MDT, and delivering a comprehensive medication review, can effectively identify potential medication related problems in older adults with cancer. This can lead to a significant reduction in the incidence of unplanned hospitalisation due to ADE.

Chapter 1 – Introduction

1.1 Background

1.1.1 Older adults

Older adults (typically defined as ≥65 years of age) are recognised as being particularly vulnerable to ADE (1, 2). Increasing age is associated with physiological changes that can affect the pharmacokinetics and pharmacodynamics of medications (3, 4), and older adults have a higher prevalence of comorbidities (5). This in turn can lead to polypharmacy (typically defined as the co-prescribing of ≥5 medications) (6), a greater likelihood of PIM (7, 8), drug-drug interactions (DDI) (9) and, subsequent ADE.

Older adults are often under-represented in clinical trials, where the proportion of older adult participation does not reflect the proportion of older adults in the real-world setting. This means data regarding the safety and efficacy of medications can be difficult to correlate to an older adult, particularly in the presence of frailty (the inability to recover functionality from an external stressor, such as an unplanned hospitalisation) (10). Supporting this, are the findings of Gosselin *et al*., who noted that 78% of clinical trials for common medications used in community dwelling older adults in Canada, did not report efficacy or safety data specific to older adults, and that approximately half of drug monographs available to healthcare professionals contain insufficient or limited data regarding older adults (11).

The impact of an unplanned hospitalisation on an older adult can be profound. Older adults are more likely to have complex comorbidities when presenting for admission (12). An unplanned hospitalisation can exacerbate geriatric syndromes, which may

inhibit the patient returning to their baseline functional status, in the absence of appropriate safeguarding and intervention (13) (Figure 1).

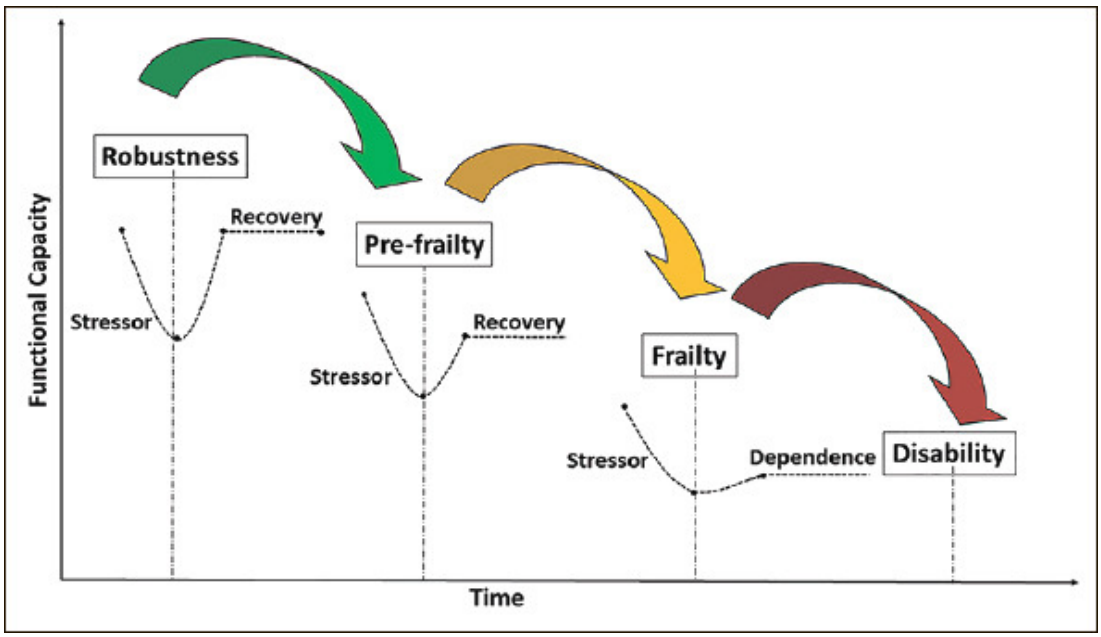


Figure 1: The cascade of functional decline in older adults from independence, through to frailty and disability (in the absence of intervention), reproduced with permission from Dent et al. (13)

As the number of chronic illnesses increases, so too does the risk of frailty (14).

Attempting to address these concerns in the inpatient setting has led to some degree of success in the field of geriatric medicine (15). The development of a 10-step integrated care framework for older people in Ireland has resulted in increased access to specialist geriatrician and interdisciplinary care in the community setting (16) (Figure 2). This has introduced a coordinated approach in the management of geriatric syndromes and associated potential complications, as older adults transition between primary and secondary care. This involves rapid access frailty teams in the acute hospital setting and primary care teams actively managing syndromes such as frailty (17). This can decrease the risk of further functional decline, once the patient

has recovered to an ambulatory status to avoid readmission and frailty-related mortality (18).

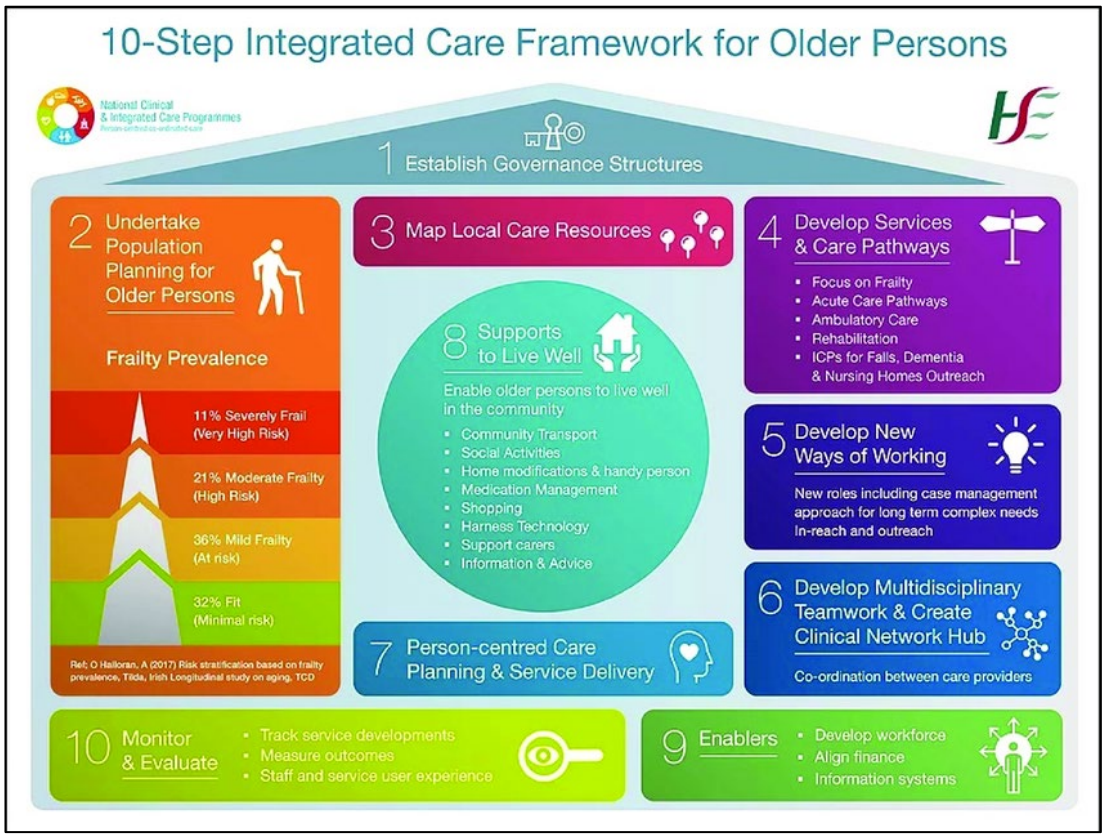


Figure 2: The 10-step integrated care framework for older persons, reproduced with permission from Barry et al. (16)

The role of geriatric interventions in ambulatory older adults, essentially providing a CGA as a form of prophylaxis, is growing, and has been recognised as the gold standard model of care for older adults with frailty (19). A CGA is the organised approach to assessment designed to determine an older person's medical conditions, mental health, functional capacity and social circumstances (17). The World Health Organisation (WHO) have developed best practice guidelines on comprehensive assessment of older adults in the community setting (20).

The practice of CGA within community services in primary care have become more common in the Irish healthcare system (17). Integrated teams such as the Waterford

Integrated Care for Older People (WICOP) aim to support older adults living in their own homes, maintaining independence further into life, following the 10-step integrated care framework for older persons development (Figure 2) (16).

One of the main drivers of intervening in older adult care prior to an unplanned hospitalisation is to avoid the impact that such an event, or stressor as described in Figure 1, has on a patient's frailty (21). Frailty is associated with an increased mortality risk and can be compounded by other undesirable health outcomes such as falls, fractures and decreased functional capacity (22). Preventing an unplanned hospitalisation in an older adult with, or at risk of, frailty can improve quality of life, prevent institutionalisation and decrease healthcare usage as well as healthcare-related expenses (23).

1.1.2 Older adults with cancer

Unplanned hospitalisation can significantly impact all older adults with frailty, however the concurrent impact of a cancer diagnosis, and the prospect of cancer treatment can complicate this further (21). Cancer on its own can impact functional status (24). The addition of cancer treatment modalities, in the form of SACT, radiotherapy and surgery can increase the likelihood of an unplanned hospitalisation, with an increased risk of functional decline as a result (24). This is highlighted in the outline of integrated care for older adults with cancer developed by Kheng Soo *et al.* (Figure 3) (25).

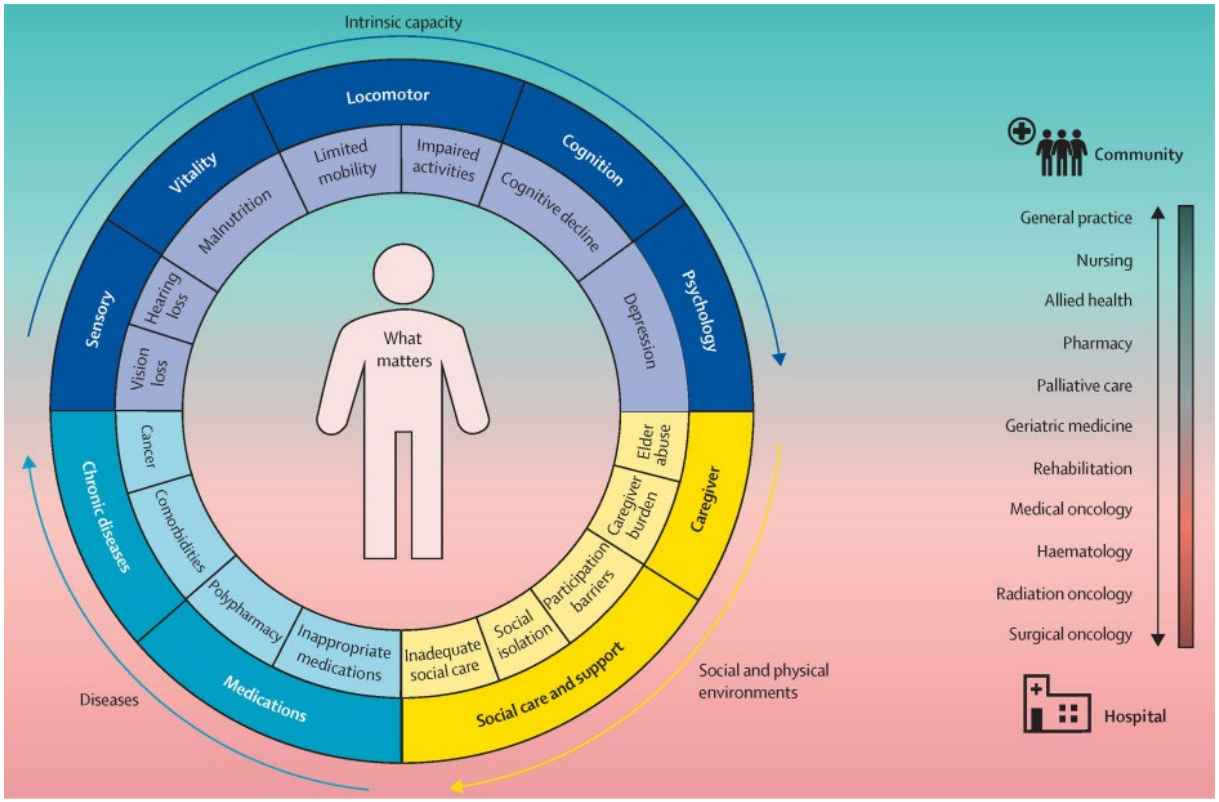


Figure 3: Integrated care for older people with cancer, reproduced with permission from Kheng Soo et al. (25)

Ageing has been associated with cancer, primarily via three non-exclusive mechanisms: carcinogenesis, molecular changes and environmental phenomena (26). The proportion of adults diagnosed with cancer aged ≥65 years is projected to account for 70% of all diagnoses by 2030 (26).

Outlaw *et al.* (27), expanded on a concept opined by Jolly *et al.* (28), that drivers of cancer care in older adults resemble an iceberg (Figure 4). Patient demographics, such as performance status, age and gender are apparent, as are tumour characteristics, such as primary tumour site, staging, histopathology and targetable genetic mutations. What is often hidden, to a treating surgeon, medical oncologist or radiation oncologist, are other drivers of poor outcomes. These drivers have inspired the theoretical and practical development of the multidisciplinary geriatric oncology field.

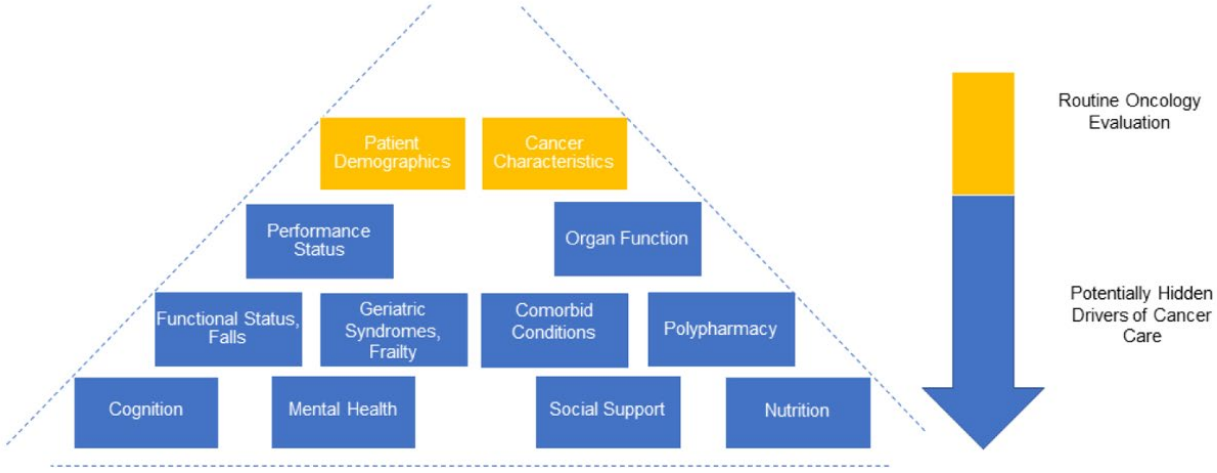


Figure 4: The "Iceberg" concept of cancer care for older adults, reproduced with permission from Outlaw et al. (27). This concept illuminates factors that may not be apparent to the oncology team with routine assessment

The emergence of geriatric oncology as a discipline began in earnest in 1983 with The Cancer in the Elderly conference hosted by Rosemary Yancik and Paul Carbone. Over the following decades, milestones in the emerging field included the American Geriatrics Society (AGS) Special Interest Group (SIG) development in 1991, the founding of the International Society of Geriatric Oncology (SIOG) in 2000, and the establishment of the Journal of Geriatric Oncology (JGO) in 2010 (Figure 5) (27).

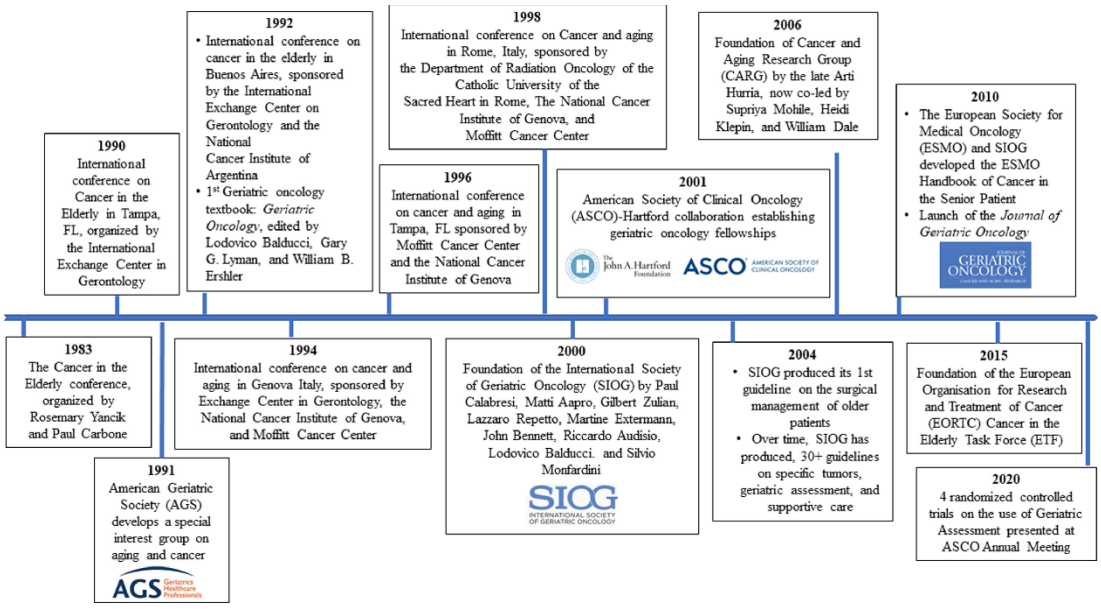


Figure 5: A history of geriatric oncology from the 1980's to the turn of this decade, reproduced with permission from Outlaw et al. (27)

Despite this progress, a complication of the pharmacological management of older adults with cancer is the lack of access to clinical trials. The lack of representation of older adults in clinical trials makes it challenging to translate best evidence to the real-world setting. A clear example of this has been the historical use of chronological age for patient stratification when considering access to clinical trials (29). This is not in line with the evidence, which suggests that biological age and functional status are far better predictors of patient outcomes (30).

Sedrak *et al*. identified twenty-three barriers to older adult inclusion in cancer clinical trials, categorising them as system, provider, patient, and caregiver-related factors (Table 1) (29).

Table 1. Barriers to older adult participation in cancer clinical trials, adapted from Sedrak et al (2021) (29).

Category	**Barrier**
System	Eligibility criteria
	Consent form language
	Trial availability
Provider	Concern for toxicity
	Concern for patient age
	Time/burden
	Preference for another treatment
	Unaware of available trials
Patient	Knowledge
	Transportation
	Time/burden
	Concern about efficacy and toxicity
	Against experimentation
	Treatment preferences
	Finances
	Age (believing they are too old)
	Emotional burden
Care-giver	Preferences
	Burden

Given this mismatch of evidence versus clinical practice, the European Geriatric Medicine Society (EuGMS) Pharmacology SIG highlight the field of geriatric oncology as a key area of focus for research due to the lack of safety and efficacy data from

clinical trials and drug product literature, leaving them exposed to treatments with a poorer evidence base, and thus potentially greater harm (31).

1.2 Geriatric oncology versus standard of care

The practice of geriatric oncology typically refers to adults aged ≥65 with cancer but can be extended to patients with established frailty and cancer, without strict chronological age cutoffs. This has been extensively discussed in the literature, with SIOG first producing guidelines on CGA (32), surgery (33), and chemotherapy toxicity in older adults with cancer over 15 years ago (34). The multidisciplinary nature of performing a CGA in older adults with cancer has been outlined in several reports of geriatric oncology models of care (35, 36).

With the emergence of evidence-based guidance from SIOG (32, 37), and the American Society of Clinical Oncology (ASCO) on screening and assessment tools in older adults with cancer (38), the transition from standard care to a more comprehensive model, that proactively identifies issues and intervenes in these domains is underway. The patient journey from diagnosis to treatment in standard oncological care is outlined in Figure 6(a), and the patient journey from diagnosis to treatment in the geriatric oncology setting is outlined in Figure 6(b) for comparison.

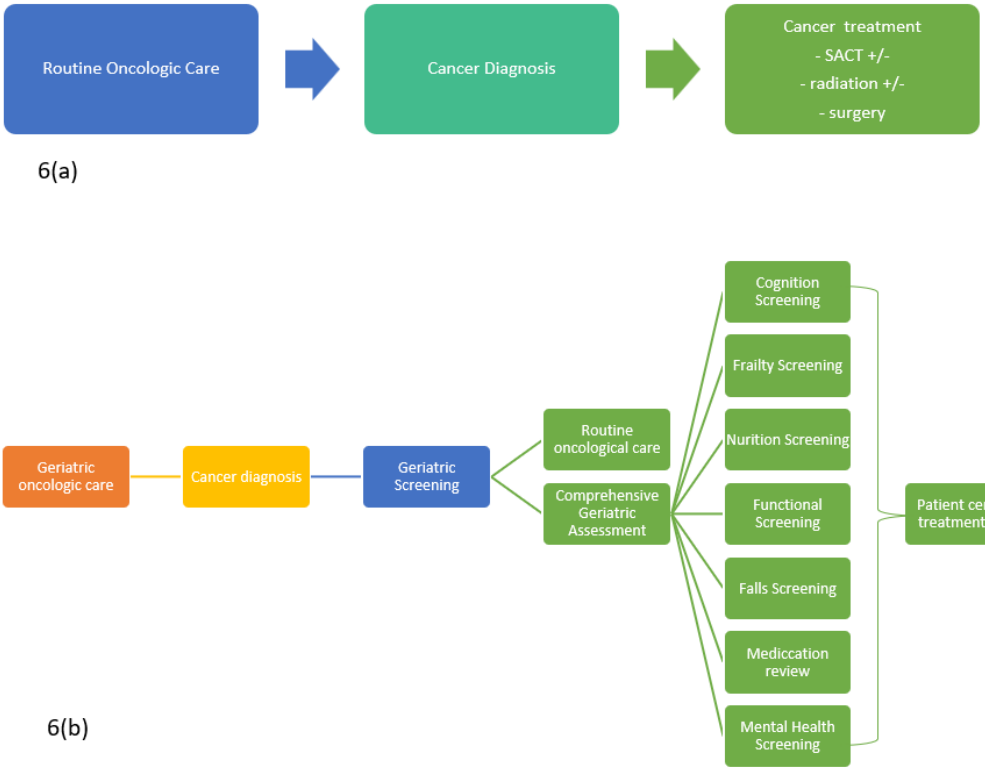


Figure 6(a) routine oncologic care and Figure 6(b) geriatric oncologic care

Key: SACT – systemic anticancer therapy

1.2.1 Geriatric oncology models of care

The geriatric oncology model of care has demonstrated benefits in randomised controlled trials (RCT) in terms of decreased SACT toxicity (39, 40), and improved health-related quality of life (41). There are multiple models of care used in clinical practice, with Chapman *et al.* outlining the benefits and barriers of different models of care in the Journal of Clinical Oncology in 2021 (35) (Figure 7).

Model	Description	Advantages	Disadvantages
Screen and refer model	Screen with a validated tool and refer for GA if screen positive	Less time and resource intensive May be able to refer to complete needed domains	Need to have knowledge and availability of community resources Patient may need to see multiple providers/ appointments
Shared care model	Medical management divided between primary care provider and oncologist	Relationship often exists already	Requires good communication and may lack a geriatric focus
Multidisciplinary consultative model	Patient referred and GA performed by the multidisciplinary team	Can evaluate and influence a large number of patients	Outcomes may be limited by a primary oncologist after recommendations, most patients not followed longitudinally
Geriatric driven/embedded consultative Model	A geriatrician or geriatric-trained CRNP/PA embedded in oncology clinic	Can follow and be available longitudinally as issues arise	May be limited to the specific clinic they are embedded in Limited by the availability of geriatric-trained provider
Geriatric oncologist as a primary provider	A dual-trained geriatric oncology physician assumes all care of the patient	More control over outcomes as one provider manages all the care	Limited by the number of dual-trained physicians
Self-administered geriatric assessment	Patient completed questionnaire with several variables completed by trained staff	Fewer resources needed	Expertise needed to interpret assessment May be limited by the availability of resources if needs are identified

Abbreviations: CRNP, Certified Registered Nurse Practitioner; GA, geriatric assessment; PA, physician assistant.

Figure 7: Models of Delivery for Geriatric Oncology Care outlined by Chapman et al (35), reproduced with permission.

The Irish government published the National Cancer Strategy 2017-2026 in July 2017 (42). This was one of the first national cancer strategies in the world to identify geriatric oncology as a specific focus within cancer care. Section 10.8 of the strategy outlines the key requirements for optimising care for older adults with cancer, focusing on the areas of education, clinical practice and research (42). Recommendation 28 of the National Cancer Strategy 2017 – 2026 states that *"Links between cancer services and geriatric services will be strengthened, facilitated by the appointment of a National Clinical Lead in Geriatric Oncology in the NCCP."* (42). In 2024 Dr. Anne Horgan, a consultant medical oncologist from UHW, and Dr. Amanda Lavan, a consultant geriatrician from St. James's Hospital in Dublin, were appointed as joint-clinical leaders in geriatric oncology by the National Cancer Control Programme (NCCP) in Ireland, a directorate within the HSE, responsible for the implementation of Ireland's national cancer strategies. In 2025 the NCCP established

a National Geriatric Oncology Steering Group, which is tasked with developing a national model of care for the Irish public healthcare system.

1.2.2 Geriatric oncology in Ireland

Ireland's first geriatric oncology clinic was founded in UHW under the clinical supervision and leadership of Dr. Anne Horgan in 2017. The GOAL clinic has a dynamic model, that has grown from 2017 until now, blending and incorporating elements of the "screen and refer" model, the "shared care" model, and the "multidisciplinary consultative" model described previously in Figure 7 (35).

In 2017, the clinic was piloted using a MDT, with remote, *ad-hoc* pharmacist input. Data collated from the GOAL clinic between 2018 and 2021 (43), showed a comparable incidence of unplanned hospitalisation due to SACT toxicity, relative to the intervention arms of two randomized controlled trials assessing the impact of CGA driven care in older adults with cancer, ie the GAP70+ and the Geriatric Assessment-Driven Intervention (GAIN) study (39, 40). In 2022, new members of the MDT joined the GOAL clinic, an occupational therapist, and a pharmacist. By 2024 the MDT had expanded to include a second medical oncologist, a geriatrician and a palliative care consultant (Figure 8).

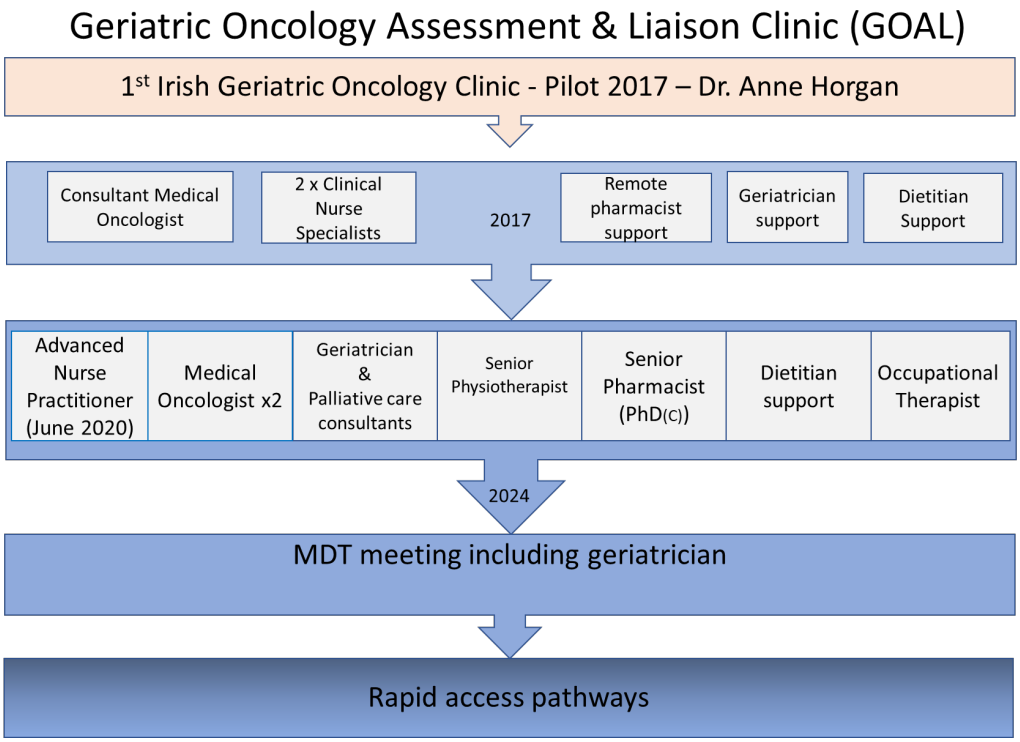


Figure 8: The evolution of the Geriatric Oncology Assessment and Liaison (GOAL) clinic in University Hospital Waterford, between 2017 and 2024. The GOAL clinic is Ireland's first geriatric oncology clinic. Key: (c) - candidate

Patients with a cancer diagnosis aged ≥70 years, scheduled to attend an outpatient medical oncology clinic in UHW are screened using the G8 screening tool to assess the potential benefit from a CGA (44). The G8 screening tool assesses aspects of geriatric domains that may help clinicians identify older cancer patients who may benefit from a CGA (45). Patients who have a positive screen are offered an appointment at the GOAL clinic. Patients who attend the GOAL clinic then receive a CGA, and the outcomes of the assessment are discussed at a weekly GOAL MDT meeting, which includes all members of the core team and a consultant geriatrician. The MDT outcomes inform the patient's discussion with their medical oncologist, where the risk-benefit ratio of SACT options is weighed and their treatment plan made. The MDT also communicates the outcomes of the meeting to other key stakeholders such as, but not limited to, the patient's General Practitioner (GP),

community pharmacy, other consultants involved in their care, medical social workers, and specialist older adult services such as the WICOP memory clinic, or the urology lower urinary tract symptoms (LUTS) assessment clinic, for example. The patient journey through the GOAL MDT is outlined in Figure 9.

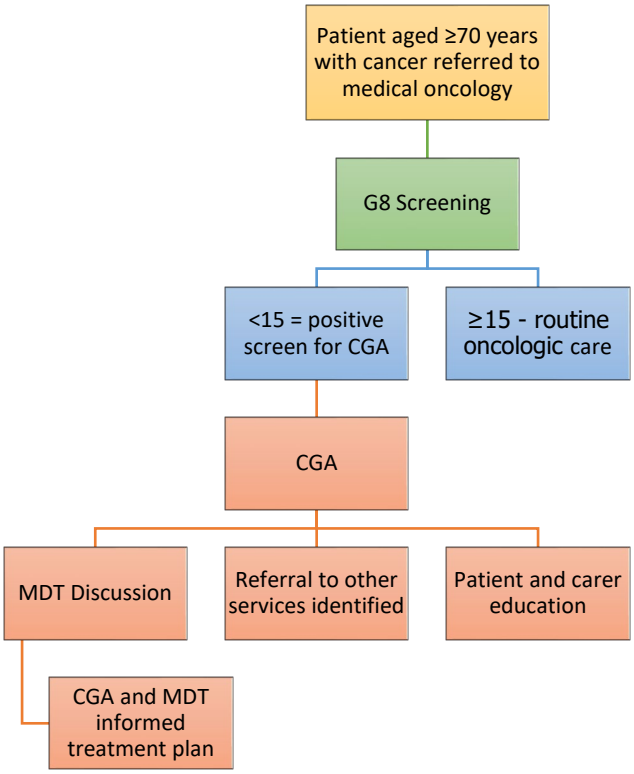


Figure 9: The patient journey through the GOAL Clinic.

1.2.3 Pharmacists as members of the geriatric oncology multidisciplinary team

The inclusion of a pharmacist in the geriatric oncology MDT is not universal. This is surprising, given the presence of polypharmacy as a recognised geriatric domain (32, 46), and the inclusion of "*medication use*" in SIOG consensus guidelines for conducting a CGA (32). The literature consistently shows the associations between polypharmacy, DDI, or PIM and adverse outcomes in older adults with cancer (9, 47-49). These include, but are not limited to, ADE, frailty, falls, cognitive impairment, chemotherapy toxicity, postoperative complications, unplanned hospitalisations,

and mortality. Pharmacists have shown their value in the fields of oncology (50, 51) and geriatrics (52). Pharmacists improve medication safety (53), reduce inappropriate medication use (54), and contribute significantly to improved medication-related outcomes at transitions of care between primary and secondary/tertiary care (55).

Given the complexity of SACT protocols, and the additional medication burden associated with prescribing SACT, the inclusion of a pharmacist as part of a geriatric oncology MDT would be considered rational, yet to-date there is a paucity of published literature to support this. The ASCO guideline for conducting a CGA on older adults with cancer, recommends a formal medication review, as part of the CGA process, prior to initiating SACT in an older adult with cancer (38). A subgroup of SIOG, Young SIOG, comprising medical oncologists, geriatricians, pharmacists, nurses, dieticians, occupational therapists, physiotherapists, oncology psychiatrists, epidemiologists, speech and language therapists, and administrators from all over the world produced guidance for conducting medication reviews in older adults with cancer (56). This contains key components that are referred to by both SIOG, and the National Comprehensive Cancer Network (NCCN) in the United States of America (USA) guidelines on CGA (32, 57). This guidance outlines the fundamentals of conducting a medication review in this patient population. These are *"assessing medication indication and dose appropriateness, assessing polypharmacy and PIM, evaluating adherence and DDI, and discontinuing inappropriate or unnecessary medication*." (56).

SACT describes all systemic therapies that are prescribed to treat cancer with curative or palliative intent. SACT can be prescribed in the neoadjuvant (prior to surgery), adjuvant (postoperatively), palliative setting, or concomitantly with radiotherapy in certain cases with curative intent. Supportive care medications refer to all medications that are used prophylactically to prevent SACT toxicity, in the treatment of SACT toxicity, and/or physiological complications from progressive cancer.

SACT adds to a patient's medication burden and introduces high-risk medications that have potentially severe toxicity profiles in older adults with cancer. In addition, the concomitant prescribing of prophylactic supportive care medications such as antiemetics, antihistamines and corticosteroids can create further challenges in optimising care as many of these medications are high risk PIM in older adults in general (7, 8, 58). Further, these complex regimens independently increase the risk of DDI and non-adherence (59). The medication review process described by Young SIOG is outlined in Figure 10 (56).

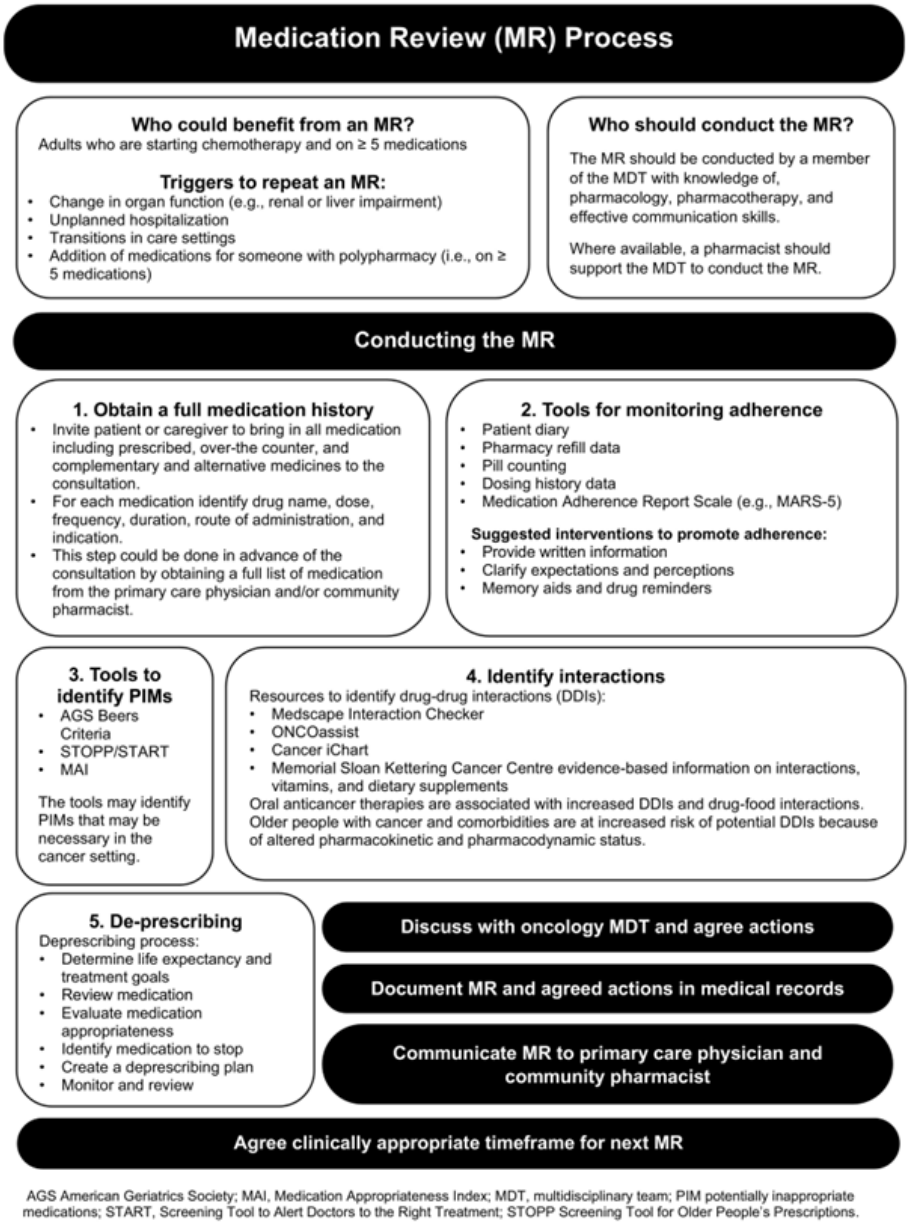


Figure 10: Medication review process in older adults with cancer, reproduced with permission from Kantilal et al. (56)

Whilst this guide provides an excellent baseline structure for designing a medication review for a geriatric oncology clinic, in clinical practice reviewing medications in this patient cohort is complex and challenging. This framework forms the basis for a pharmacist role in a geriatric oncology MDT. The introduction of a pharmacist to the

GOAL clinic in UHW provided the basis to evaluate the effectiveness of conducting a medication review in this clinical setting.

Since there are no published data on outpatient pharmacist involvement in geriatric oncology MDT to date, this thesis aspires to provide a foundation, upon which future research in this field can be built.

1.3 Addressing medication-related issues in geriatric oncology

Medication-related issues in older adults with cancer are outlined by a position paper published by the SIOG Nursing, Allied Health and Scientists (NAHS) interest group in 2016 (12). SIOG NAHS is a group comprised of nurses, pharmacists, dieticians, occupational therapists, physiotherapist, speech and language therapists, scientists and epidemiologists who provide expertise and research in caring for older adults with cancer. This paper highlights the value of a comprehensive medication assessment as part of a CGA.

While there is evidence to show the benefits of interventions to reduce the use of inappropriate medications in the general geriatric population (60-62), consensus guidance on the effective management of polypharmacy and PIM in older adults with cancer, is still outstanding. Studies have demonstrated that there is widespread polypharmacy and PIM prevalence in the geriatric oncology population (63, 64), however data are lacking on interventional studies aimed at addressing these issues.

Medication-related issues in older adults with cancer can be categorised into three distinct subgroups: 1) chronic medications, 2) SACT and, 3) supportive care medications. These represent the groups of pharmacological treatments that patients are prescribed throughout their cancer journey.

1.3.1 Chronic medications

Chronic medications can be taken regularly or as required [pro re nata (PRN)]. These medications are used to manage chronic conditions that the patient has had prior to their cancer diagnosis or identified during their cancer journey. Examples include antihypertensive agents, anti-diabetic agents, and gastric acid suppressants.

In older adults with cancer, medication-related problems can arise with chronic medications for several reasons including:

i. Poor prognosis due to cancer, thus making a medication an additional risk rather than a benefit (65).
ii. The necessity to treat a chronic condition may no longer be present in a patient with cancer compared to a patient without cancer, due to altered prognosis.

A patient with metastatic cancer and a poor prognosis, for example, may no longer need tight glycaemic control in type-2 diabetes mellitus as the risk of hypoglycaemia may outweigh the benefit of antihyperglycemic therapy, and therefore de-intensification of pharmacological management may be appropriate (66).

1.3.2 SACT

The risk of SACT toxicity is significant for all cancer patients however in older adults (67), particularly those with established frailty, this risk is even greater (34). The Cancer in Ageing Research Group (CARG), an international consortium of geriatric oncology investigators, have developed a validated toxicity calculator that can assist healthcare professionals in quantifying the risk of an older adult experiencing toxicity to mono- or poly-chemotherapy that would be severe enough to warrant an

unplanned hospitalisation (68). The CARG toxicity calculator is validated for conventional cytotoxic chemotherapy, however, other modalities of SACT such as hormone therapy, targeted therapies, and immunotherapy are yet to be validated. Toxicity risks for immunotherapy seem to be similar in older and younger patients (69). There are exceptions, with pneumonitis and myocarditis appearing to occur in older adults more frequently. Severe adverse events in patients treated with immunotherapy occurs more frequently in younger patients, whereas mortality and length of hospitalisation is more frequently associated with older patients (69). SACT is also affected by age-related changes to pharmacokinetics and pharmacodynamics (3). Age-related changes in particular to renal and hepatic impairment can require significant alteration to standard SACT regimens to prevent significant toxicity (70).

1.3.3 Supportive care

Many drug classes used in supportive care are used based on limited evidence and for unlicenced indications, e.g. the use of the second-generation atypical antipsychotics for cancer-related anorexia (71). Medications used as first-line options for supportive cancer care are frequently identified as PIM in older adults. Table 2 lists medications that are recommended in selected clinical practice guidelines for supportive and palliative care published by the European Society of Medical Oncology (ESMO) that appear in Screening Tool of Older Person's Prescriptions (STOPP)/Screening Tool to Alert doctors to Right Treatment (START) version 3 or the 2023 AGS Beer's criteria, commonly used tools to identify PIM (7, 8).

Table 2: Alphabetical list of medications recommended in selected clinical practice guidelines for supportive and palliative care published by the European Society of Medical Oncology (ESMO) that are identified as potentially inappropriate medications by STOPP/START v3 and/or the American Geriatrics Society Beer's criteria (7, 8).

Medication	**Indication**	**STOPP/ START v3 (7)**	**2023 Beer's Criteria (8)**
Angiotensin converting enzyme inhibitor (ACEi) or Angiotensin receptor blocker (ARB)	Prophylaxis against left ventricular dysfunction in patients commencing cardiotoxic SACT (72)	Yes	Yes
Antihistamines	Grade 2 drug-induced pruritis (73)	Yes	Yes
	Immune mediated skin toxicity (74)		
Amitriptyline	Neuropathic pain (75)	Yes	Yes
Aripriprazole	Hyperactive delirium (76)	Yes	Yes
Benzodiazepines	Anxiety (77)	Yes	Yes
	Insomnia (78)		
	Refractory breathlessness (79)		
Beta Blockers	Prophylaxis against left ventricular dysfunction in patients commencing cardiotoxic SACT (72)	Yes	No
	Immune-related cardio-toxicity (74)		
Bisphosphonates	Bone metastasis (80)	Yes	No
Colchicine	Uncomplicated immune-related pericarditis (74)	Yes	Yes
Corticosteroids	Appetite (81)	Yes	Yes
	Control of cancer-related fatigue (82)		
	Refractory breathlessness (79)		
	Grade 2 palmar-plantar erythrodysaesthesia syndrome from doxorubicin, pegylated-doxorubicin or taxanes (73)		
	Grade ≥ 3 (or intolerable grade 2) palmar-plantar erythrodysaesthesia syndrome from doxorubicin, pegylated-doxorubicin or taxanes (73)		
	Immune related adverse events (74)		

Medication	Indication	STOPP/ START v3 (7)	2023 Beer's Criteria (8)
	Prevention or treatment of chemotherapy- and radiotherapy-induced nausea and vomiting (83)		
Co-trimoxazole	Immune-related pulmonary toxicity (74)	No	Yes
Diltiazem	Rectal tenesmus (84)	Yes	Yes
Duloxetine	Neuropathic pain (75)	Yes	Yes
Factor *Xa* Inhibitors	Prevention and treatment of cancer-associated thrombosis (CAT) (85)	Yes	Yes
Gabapentanoids	Neuropathic pain (75)	Yes	Yes
	Grade 2 drug-induced pruritis (73)		
	Grade ≥3 (or intolerable grade 2) drug-induced pruritic (73)		
Hypnotics	Insomnia (78)	Yes	Yes
Insulin	Immune-related diabetes (74)	No	Yes
Levothyroxine	Immune-related hypothyroidism (74)	Yes	No
	Immune-related hypophysitis (74)		
Metoclopramide	Prevention or treatment of chemotherapy- and radiotherapy-induced nausea and vomiting (83)	Yes	Yes
Methotrexate	Immune-related rheumatological toxicity (74)	Yes	No
Nifedipine	Rectal tenesmus (84)	No	Yes
Non-Steroidal Anti-inflammatory Drugs (NSAIDs)	Mild pain(86)	Yes	Yes
	Palmar-plantar erythrodysaesthesia syndrome prevention with capecitabine (Celecoxib) (73)		
	Immune-related rheumatological toxicity (74)		
Olanzapine	Appetite and chronic nausea (81)	Yes	Yes
	Prevention or treatment of chemotherapy- and radiotherapy-induced nausea and vomiting (83)		
	Hyperactive delirium (76)		
Opioids	Severe chronic breathlessness (79)	Yes	Yes

Medication	Indication	STOPP/ START v3 (7)	2023 Beer's Criteria (8)
	Cough (84)		
Quetiapine	Hyperactive delirium (76)	Yes	Yes
Selective Serotonin Re-uptake Inhibitors (SSRIs)	Depression (77)	Yes	Yes
Strong opioids	Moderate to severe pain (86)	Yes	Yes
	Neuropathic pain (75)		
	Pain due to oral mucositis in patients undergoing haematopoietic stem cell transplantation (87)		
	Pain due to oral mucositis in patients receiving conventional or high-dose chemotherapy, with or without total body irradiation (87)		
Venlafaxine	Neuropathic pain (75)	Yes	Yes
Warfarin	Prevention and treatment of CAT (85)	Yes	Yes
Weak opioids	Mild to moderate pain (86)	Yes	Yes

Note: Medications recommended but which do not appear in either STOPP/START version 3 or the 2023 updated Beer's criteria are omitted.

Key: STOPP - Screening Tool of Older Person's Prescriptions; START - Screening Tool to Alert doctors to Right Treatment; ACEi - Angiotensin converting enzyme inhibitor; ARB - Angiotensin receptor blocker; SACT – Systemic anticancer therapy; NSAIDs - Non-Steroidal Anti-inflammatory Drugs; SSRIs - Selective Serotonin Re-uptake Inhibitors

While STOPP/START version 3 (7) and the Beer's criteria (8) are not designed to be used in the context of advanced cancer or palliative care, consideration should be given to the concerns raised by the application of these tools on an individual patient level, and to the risk-benefit ratio of these medications in the context of advanced cancer. Alternative therapy should be considered, and its efficacy weighed against the risk of the first line option. Patients who have advanced cancer and have a poor prognosis (< 12 months life expectancy), the presence of established severe irreversible frailty, and impaired activities of daily living (ADL) meet the inclusion criteria for the STOPPFrail deprescribing tool (88), which primarily includes medications used to treat chronic conditions, or medications used in the setting of primary prevention.

1.3.4 Patient-specific factors

There are also patient-specific factors that can lead to medication-related problems.

Allergy status

Having a well-documented allergy status in oncology is important due, for example, to the risk of neutropenic sepsis in those receiving SACT (89), which requires prompt administration of empirical intravenous antimicrobials. Patients with a history of known drug allergies specific to antimicrobials require careful consideration for escalated prophylactic regimens to prevent infusion related reactions. This can involve the administration of histamine $(H)_1$ antagonists, H_2 antagonists and high doses of corticosteroids prophylactically, which, as outlined in Table 2, can be problematic in older adults (90).

Infusion-related reactions

The risk of a severe, life-threatening infusion-related reaction to medications such as monoclonal antibodies, taxanes, or platinum agents, must be weighed against the potential risk of a fall or acute cognitive decline using medications with strong anticholinergic properties (score ≥3) such as first-generation antihistamines, for example chlorphenamine or diphenhydramine (91). H_2 antagonists are associated with altered mental status in older adults (92), and prolonged exposure to corticosteroids can lead to musculoskeletal, metabolic, endocrine, infective, cardiovascular, dermatological, ophthalmological, gastrointestinal and neuropsychiatric adverse effects (93).

Dysphagia

Many cancers are also associated with dysphagia, in particular head and neck cancers, gastroesophageal cancers, and gastric cancers that can result in oesophageal or gastric outlet obstruction and thus an inability to swallow solid oral dosage forms (94). Lymphadenopathy associated with lung cancer, and metastatic breast cancer can also significantly impact swallow, as can tumours of the central nervous system (CNS) (94, 95). Assessing swallow and outlining strategies to manage medication dosage forms and patients progress through different states of dysphagia is an important consideration to prevent a reduction in medication efficacy and thus quality of life (96, 97).

Adherence

Assessing patient adherence is another patient-specific medication related problem. Tools have been developed to formally assess medication adherence (98). Guidance on conducting medication reviews in older adults acknowledge these can be onerous

in the clinical setting, and that simple questions related to adherence may suffice (56). The identification of poor adherence to medications can help healthcare professionals tailor and adapt SACT and supportive care plans to minimise the risk of poor adherence by choosing treatment options that are managed in supervised settings, such as an oncology day ward, or specialised clinic such as an oral anticancer medication (OAM) clinic. Assessing non-adherence can also help clinical pharmacists discuss adherence aids, such as pillboxes, blister packs and using caregivers to assist in the safe and effective administration of medications (99).

1.4 The role of the pharmacist

The pharmacist in a geriatric oncology setting plays a key role in the safe and effective pharmacological treatment of patients. It requires an extensive general knowledge of medications used to treat chronic conditions, and a specialist knowledge of pharmacotherapy used in gerontology and in clinical oncology (51, 52, 100). This involves managing many of the potentially hidden drivers of cancer care outlined in Figure 4. While addressing polypharmacy is a domain in which pharmacists have a clear competency in, other domains are also areas worthy of discussion.

1.4.1 Organ function

Pharmacists can assist in identifying medications that have the potential to adversely affect organ function (101, 102). They can recommend dose adjustments of SACT in renal and hepatic impairment (70), and advise on adequate supportive care precautions to be taken to prevent organ specific toxicities of SACT. For example, reducing the risk of post-renal acute kidney injury (AKI) secondary to haemorrhagic

cystitis with alkylating agents by advising on an appropriate regimen of prophylactic mesna to prevent acreolin accumulation in the bladder (103).

1.4.2 Falls

Pharmacists can help optimise functional status by identifying Falls Risk Inducing Drugs (FRIDs) in older adults with cancer (104). Whilst many tools can help healthcare professionals identify medications that may increase the risk of falls, such as STOPPFall (105), the literature shows that deprescribing FRIDs alone is seldom sufficient in significantly reducing falls in older adults (104). Therefore the pharmacist is an additional support to nursing colleagues identifying other risk factors for falls, such as orthostatic hypotension (106), sarcopenia (107), and malnutrition (108). The pharmacist also supports (i) occupational therapy colleagues in providing tailored modifications in the home to prevent falls risks (109), (ii) physiotherapist colleagues (110), and, (iii) dietician colleagues in providing nutritional assessments to prevent falls (111).

1.4.3 Frailty

Frailty in older adults with cancer can be difficult to reverse (21). The domains of frailty, comorbidity and polypharmacy are closely interconnected (14), with increasing comorbidity and polypharmacy important risk factors for frailty in older adults with cancer. Increasing burden of comorbidities is associated with prescribing cascades, exacerbating polypharmacy and compounding frailty, which can significantly affect older adults (112-114). The pharmacist has the optimal skillset to assess polypharmacy, identify prescribing cascades and assist in rationalising medications (48, 51, 115).

1.4.4 Cognitive impairment

Cognitive impairment in older adults with cancer can be multifactorial. Age-related changes in cerebral vasculature can naturally result in a decline in cognitive function over time (116). Excessive exposure to medications with CNS activity (8), or exposure to significant anticholinergic activity can adversely affect cognition (91, 117). Pharmacists can recommend modifications to pharmacological therapies to reduce anticholinergic burden (ACB) in patients, with the aim of improving cognitive function and reducing further cognitive decline (118).

1.4.5 Mental health

In patients with pre-existing mental health issues, pharmacists can recommend appropriate modifications to those medications that may predispose patients to adverse effects. An example would be the presence of a tumour that increases bleeding risk in a patient prescribed an antidepressant with antiplatelet activity such as SSRIs (119), or using a steroid-sparing antiemetic regimen in patients with a history of steroid induced psychosis (83). In patients who develop anxiety and/or depression during their cancer journey, pharmacists can liaise with psycho-oncology teams to individualise pharmacological interventions (77).

1.4.6 Malnutrition

The role of the pharmacist in malnutrition varies, depending on the root cause of malnourishment. When a patient is malnourished due to dysphagia, whether intrinsically in cancers that directly affect swallow, or extrinsically via external pressure on the oesophagus, pharmacists can assist the facilitation of appropriate medication selection via non-solid oral dosage forms or enteral feeding tubes (97).

Where malnutrition is identified because of cancer or SACT, pharmacists can help identify optimal pharmacological interventions to minimise the impact and duration of malnutrition and if present, anorexia (71). Pharmacists can also collaborate with dieticians to ensure that optimal nutritional supplements are selected for malnourished patients, particularly advising around feeding times relative to medication administration to reduce potential interactions (120).

1.4.7 Pharmacists as specialists

The NCCP Oncology Medication Safety Review Report (121) notes that there is currently no Irish accredited training course for pharmacists in Oncology/Haematology in general. The role of the pharmacist in the setting of cancer care is outlined by the NCCP National Competency Framework for Pharmacists working in Cancer Care (122). This competency framework, developed by a working group of pharmacy representatives from (i) the NCCP, (ii) Irish Institute of Pharmacy (IIOP), (iii) the Irish Pharmacy Union, (iv) hospital oncology pharmacy and (v) community pharmacy can be used to inform the development and provision of training and education for pharmacists working in cancer care, and to be a standard against which a pharmacist may benchmark themselves. It outlines the core competencies required for pharmacists working in cancer care to practice at a basic level, a specialist level, and an advanced specialist level.

Medication review guidance published by Young SIOG identifies the pharmacist as the optimal member of the MDT to conduct medication reviews (56). The role of oncology pharmacists in medication management of older adults with cancer is outlined by Whitman *et al*. (51), concluding that a pharmacist-led medication review

should be standard of care when aligning medication management and anticancer treatment decisions.

Pharmacists can perform structured medication reviews in geriatric oncology settings that follow a clear process outlined by Kantilal *et al* (56). Common challenges faced by clinical pharmacists working in the geriatric oncology setting have been described (56, 123). These primarily refer to challenges relating to clarity regarding the pharmacist role, opportunities for pharmacists to join specialist MDTs in the absence of structured workforce planning, the feasibility of implementing pharmacist recommendations across a range of disciplines, and a lack of training opportunities for pharmacists to upskill in a dual-specialist service.

Pharmacists working in geriatric oncology settings needs to have clinical expertise in age-related pharmacokinetics and pharmacodynamics, pharmacotherapy in older adults, clinical oncology/haematology, deprescribing, and risk assessment. They also need communication skills that enable them to communicate complex interventions and processes with patients, carers, primary care physicians, community pharmacists and other members of the geriatric oncology MDT. They need to be sensitive to best practices in health literacy, to ensure that information is given using plain English and avoiding medical jargon (124).

The pharmacist must combine best practice guidance for a myriad of conditions, apply them to the patient specific oncological scenario and provide advanced-level care plans to be implemented with the goal of optimal pharmacotherapy and quality of life for patients, regardless of the intent of their anticancer treatment. It is imperative that in clinical settings and MDT meetings where a pharmacist is not a

prescriber, that they provide the prescriber with the information required to enable shared decision making between the clinician and the patient.

1.5 Thesis hypothesis, aim and objectives

1.5.1 Hypothesis

Based on the rationale outlined in sections 1.3 and 1.4, we hypothesize that a comprehensive geriatric pharmacological assessment (CGPA) as part of a CGA, conducted by a pharmacist, with knowledge of medication management and clinical oncology, will reduce the incidence of unplanned hospitalisation due to ADE in a large tertiary cancer centre in Ireland.

1.5.2 Aim

To assess the impact of the integration of a pharmacist into the GOAL Clinic, as measured by the incidence of unplanned hospitalisation due to ADE.

1.5.3 Objectives

To achieve these aims, four objectives have been identified:

1. To identify and critically appraise the current literature regarding ADE in older adults with cancer.
2. To identify the incidence of polypharmacy, unplanned hospitalisation, and unplanned hospitalisation due to ADE in UHW prior to pharmacist presence in the GOAL clinic.
3. To conduct a CGPA in patients to optimise therapy and quantify the incidence of polypharmacy, unplanned hospitalisation, and unplanned hospitalisation in University Hospital Waterford after pharmacist introduction to the GOAL clinic.

4. To assess the impact of a CGPA upon unplanned hospitalisation due to ADE in older adults with cancer.

1.6 Thesis outline and methodological justification

This thesis consists of seven chapters, which provide a comprehensive and detailed overview of the impact of clinical pharmacist input into a geriatric oncology MDT. Figure 11 provides an overview of the thesis and elucidates the approaches taken to ensure that the aims and objectives of the thesis are addressed by the individual studies conducted during this doctoral research.

To meet the aims and objectives outlines in section 1.5.2 and 1.5.3, the following methodological approach has been undertaken:

Chapter 1: This chapter introduces the research topic, outlines the potential role for clinical pharmacy in geriatric oncology and defines the aims and objectives of the thesis.

Chapter 2: This comprises a quantitative systematic review of the literature to assess the current evidence in relation to ADE in older adults with cancer.

The aim of this chapter is to identify and critically appraise the current literature regarding adverse drug events in older adults with cancer (Paper 1).

Chapter 3: Chapter 3 presents the findings of a baseline evaluation of the geriatric oncology population in UHW and the HSE South-East cancer region, and a macro-economic analysis of unplanned hospitalisation in older adults with cancer.

This is a quantitative retrospective analysis of data to assess the length of stay of older adults with cancer relative to the general population, and the impact of SACT

and supportive care on polypharmacy status and the subsequent impact on unplanned hospitalisation. The aim of this chapter to assess the extent of the current burden of polypharmacy and hospital stay on older adults with cancer.

Chapter 4: Chapter 4 presents the findings of a quantitative retrospective chart review of ambulatory oncology patients aged ≥70 years who attended an outpatient oncology appointment between January and March 2018 inclusive.

The aim of this chapter is to assess SACT, supportive care and chronic medications, to identify if ADE occur in absence of polypharmacy and to assess if unplanned hospitalisation due to ADE occurs in non-SACT medications (Paper 2).

Chapter 5: This chapter details the methodology used in the interventional study reported in Chapter 6.

The primary intervention in Chapter 6 is the integration of a pharmacist into the GOAL clinic. Other than integration of the pharmacist into the service to work with stakeholders to develop solutions for a different and emerging model of care, we did not pre-specify the approaches to be taken in developing these solutions prior to the study but instead, allowed for actions and approaches to be co-created and developed in real time with stakeholders to respond to the evolving and dynamic needs of the service with a complex multimorbid population, utilising the principles of pragmatic clinical research (Paper 3).

Chapter 6: This chapter outlines a prospective interventional quantitative study using iterative adaptive methodology to analyse the impact of a complex intervention by a pharmacist in older adults with cancer.

The aim of this chapter is to conduct a CGPA in patients to optimise therapy and quantify the incidence of polypharmacy, unplanned hospitalisation, and unplanned hospitalisation due to ADE in UHW after pharmacist introduction to the GOAL clinic (Papers 4 and 5).

Chapter 7: Chapter 7 summarises the findings of the research conducted in UHW during the process of the doctoral research and outlines areas of future research needs, and opportunities for clinical pharmacists in geriatric oncology.

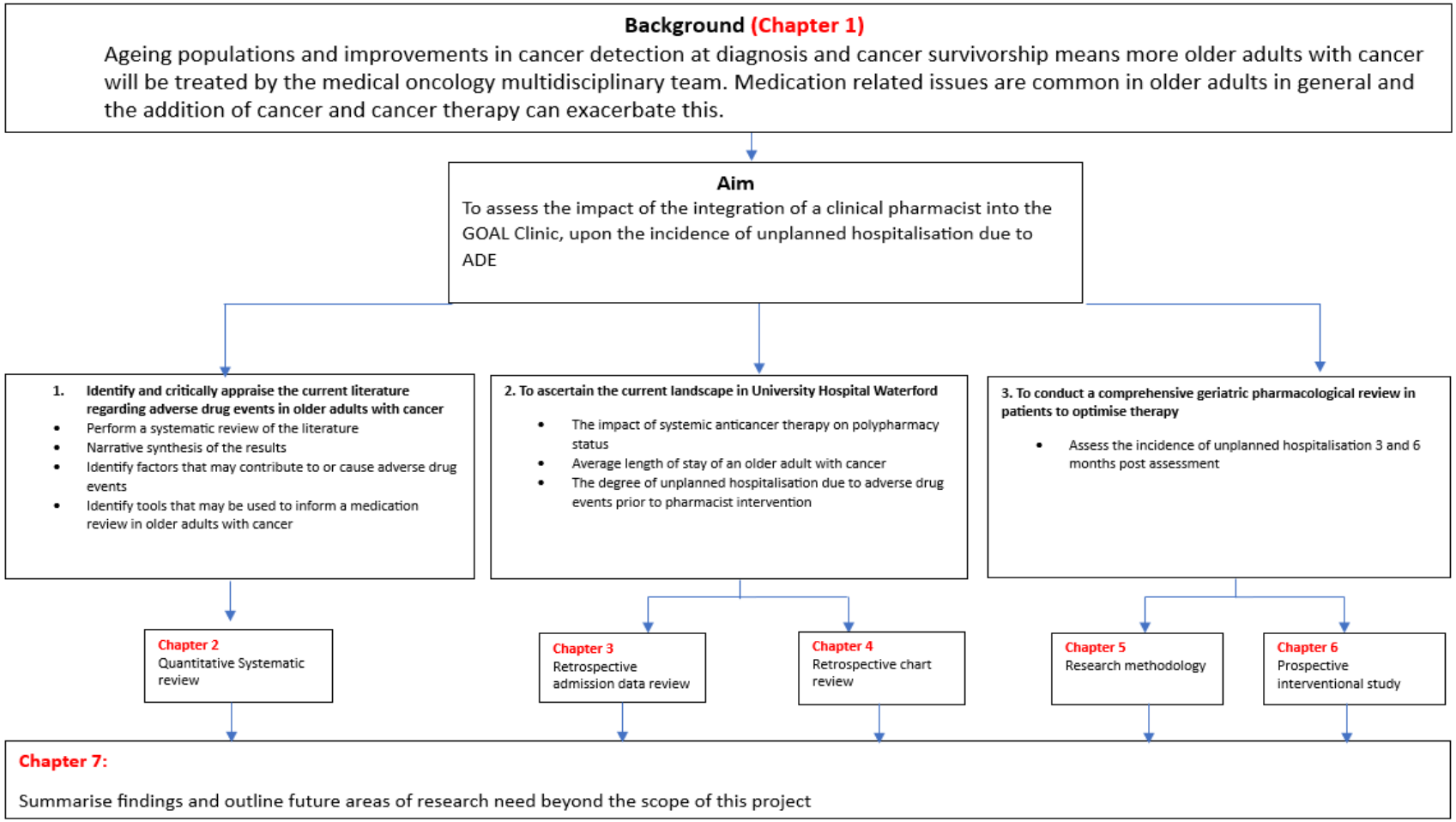


Figure 11: Thesis outline

Chapter 2 – Hospitalisation and Adverse Drug Events in a Geriatric Oncology Setting: A Systematic Review of the Literature

Systematic review registration

Walsh DJ, Sahm LJ, O'Driscoll M, Tabb E, Hannan M, Morris C, Horgan AM. Hospitalisation and Adverse Drug Events in a Geriatric Oncology Setting: A Systematic Review of the Literature. PROSPERO 2022 CRD42022307356 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022307356



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Hospitalisation and Adverse Drug Events in a Geriatric Oncology Setting: A Systematic Review of the Literature

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Review methods were amended after registration. Please see the revision notes and previous versions for detail.

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Hospitalisation and adverse drug events in a geriatric oncology setting: A systematic review of the literature

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ABSTRACT

Background: Geriatric Oncology is a specialty where a multidisciplinary approach can address the unmet needs of older adults with cancer. Older adults are at increased risk of adverse drug events (ADE) due to age-related changes in pharmacokinetics and pharmacodynamics, increasing treatment complexity, and medication burden.
Objectives: To review the literature to determine the incidence of unplanned hospitalisation due to ADE for all medications, both systemic anticancer therapy (SACT) and non-SACT medications.
Methods: A systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The search included the following databases: PubMed, CINAHL, and Embase. A manual search of Scopus was then performed. Study quality was assessed using the Cochrane Handbook for Systematic Reviews of Interventions, Mixed Methods Appraisal Tool (MMAT) and Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework.
Results: Overall, three studies were included. One observational study reported 19 % of unplanned hospital admissions due to ADE in patients aged ≥70 years with cancer. The first retrospective study reported 24 % of unplanned hospital admissions are due to ADE in patients aged ≥70 years with cancer, and the second retrospective study reported 26 % of patients with metastatic melanoma treated with immune checkpoint inhibitors had an unplanned hospital admission due to an ADE.
Conclusion: There is a paucity of studies assessing unplanned hospitalisation due to ADE in older adults with cancer. Future studies are needed and should account for the reporting of potential ADE relative to supportive care, ancillary medications, and indeed chronic medications used to treat long-standing comorbidities.

Author Contributions:

Writing – original draft: DJW, MO'D, AMH, LJS

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Methodology: DJW, MO'D, AMH, LJS. Ms. Shauna Barret, Medical Librarian in Cork University Hospital was consulted in generating the search strategy.

Data extraction: DJW, MO'D, AMH, LJS, ET, MH, CM

Data analysis: DJW, MO'D, AMH, LJS, ET, MH, CM

2.1 Abstract

Introduction

Geriatric Oncology is a specialty where a multidisciplinary approach can address the unmet needs of older adults with cancer. Older adults are at increased risk of ADE due to age-related changes in pharmacokinetics and pharmacodynamics, increasing treatment complexity, and medication burden.

Aim

To review the literature to determine the incidence of unplanned hospitalisation due to ADE for all medications, both SACT and non-SACT medications.

Methods

A systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines. The search included the following databases: PubMed, CINAHL, and Embase. A manual search of Scopus was then performed. Study quality was assessed using the Cochrane Handbook for Systematic Reviews of Interventions, Mixed Methods Appraisal Tool (MMAT) and Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework.

Results

Overall, two studies were included. One observational study reported 19% of unplanned hospital admissions due to ADE in patients aged ≥70 years with cancer. One retrospective study reported 26% of patients with metastatic melanoma treated with immune checkpoint inhibitors had an unplanned hospital admission due to an ADE.

Conclusion

There is a paucity of studies assessing unplanned hospitalisation due to ADE in older adults with cancer. Future studies are needed and should account for the reporting of potential ADE relative to supportive care, ancillary medications, and indeed chronic medications used to treat long-standing comorbidities.

2.2 Introduction

Geriatric Oncology, as outlined in Chapter 1, is a specialty where a multidisciplinary approach can address the unmet needs of older adults with cancer (39, 41, 125). SIOG published recommendations in 2005 recommending the use of a CGA in older adults with cancer (126). These recommendations were updated in 2014 (32), and in 2018 ASCO introduced guidelines for patients receiving chemotherapy (38). This was followed by the NCCN in the USA introducing their guidelines for Older Adult Oncology in 2021 (57). The ESMO/SIOG Cancer in the Elderly Working Group produced a position paper in 2024 supporting this approach (127).

This provides the justification for targeting this patient population for interventions that may reduce unplanned hospitalisation. The literature to date contains published RCT which reports the impact of a CGA on unplanned hospitalisation due to SACT toxicity (39, 40), and health related quality of life (41). The aim of this chapter is to assess the literature for publications that relate to ADE due to all medications, including SACT, supportive care and regular medications, in older adults with cancer.

In 2018 the International Group for Reducing Inappropriate Medication Use and Polypharmacy (IGRIMUP) issued a position statement that said, *"polypharmacy is an urgent issue that requires a coordinated global effort to provide medical care systems that better serve patients with multimorbidity"* (1). This need has been recognised by practitioners for over a decade. Scott *et al.* in 2009 called *"for concerted action in accordance with the principles of evidence-based medicine and good gerontologic practice"* in relation to addressing polypharmacy (128).

Older adults are at increased risk of ADE, defined as *"noxious and unintended responses to drugs occurring at doses normally used in man for the prophylaxis, diagnosis or therapy of*

disease, or for modification of physiological function" (129). This is commonly due to age-related changes in pharmacokinetics and pharmacodynamics, increasing treatment complexity, and medication burden (130). PIM in older adults, are medications in which the risks of harm and/or ADE potentially outweigh the benefits in the clinical context of an older adult (8), and that the avoidance of, or deprescribing of these medications may prevent ADE (7).

The prevalence of medication related hospitalisation in the general older adult population appears to be in the region of 7.2% - 12.8% of the population (131). Approximately half of ADE reported are hypothesised as being preventable (132). Older adults with cancer are particularly vulnerable to ADE, with the prevalence of SACT toxicity leading to a hospital visit of 51% in those receiving a CGA, and 71% in those receiving standard of care, in the GAP70+ trial (39). Hence, we see higher rates of medication-related toxicity in older adults with cancer receiving systemic therapy, compared to the general older adult population.

There is a recognized need for medication optimisation in older adults in general (7, 128). The addition of a cancer diagnosis further complicates this. Treatment modalities for cancer, such as SACT, surgery, and radiotherapy all require supportive care medications for the treatment of cancer and cancer-related issues (133). This may increase the prevalence of polypharmacy and PIM prescribing, in the absence of a structured medication review. Optimisation of medication prior to, and during treatment, may offset some of this medication related risk. It is recognised in the literature that ageing-related changes in pharmacokinetics and pharmacodynamics can have a significant impact on SACT efficacy and toxicity, as well as pharmacological interventions to help prevent and manage SACT toxicities (3, 134). In addition to ageing; tumour site, surgical resection of tumours, and radiotherapy can impact

pharmacokinetics, thus predisposing older adults with cancer to a higher risk of developing ADE (135, 136).

There is data showing the benefit of a CGA in older adults with cancer. The GAP70+ study demonstrated reduced rates of unplanned hospitalisation due to SACT in patients who underwent a CGA prior to starting treatment, compared to patients who received standard of care (39), however, it did not examine ADE related to non-SACT medications (all medications taken by the patient that are not direct anticancer agents, including ancillary medications to SACT protocols, medications for non-malignant chronic conditions, over-the-counter medications, and herbal remedies). Healthcare professionals encounter a cohort of patients who have unplanned hospitalisations due to non-oncological and non-SACT related issues, which may be exacerbated by non-SACT medications, including medications used in supportive cancer care.

A sub analysis of this trial identified polypharmacy, and DDI as independent risk factors for adverse outcomes in older adults with cancer receiving SACT (49). The prevalence of polypharmacy and PIM is increased in older adults (137). The presence of ≥8 medications and PIM in patients aged ≥70 years with cancer has been associated with physical function impairments (48). It was found that 71% of patients received five or more medications at baseline, with 62% of patients having at least one PIM (47). Polypharmacy and PIM are both associated with increased adverse outcomes, including unplanned hospitalisation.

2.3 Aim

This literature review sought to identify and evaluate studies that assessed unplanned hospitalisation due to ADE in older adults with cancer, including supportive care medication, and long-term medication related admissions.

2.4 Methods

2.4.1 Search strategy

This systematic review was conducted according to the PRISMA 2020 guidelines (138). A completed PRISMA checklist is provided in Appendix 1. The study protocol (139) was registered on PROSPERO (Ref: CRD42022307356) (140).

The search strategy was developed, and search terms identified, in consultation with a medical librarian and the search was conducted on Embase, PubMed and CINAHL (Appendix 2). All publication types were included in the initial search strategy, without language, geographical region, or date restrictions. The inclusion criteria were identified by using a Patient population, Intervention, Comparator, Outcome, Setting, Timing (PICOST) table (Appendix 3).

2.4.2 Inclusion Criteria

Studies that included older adults with cancer (can be defined as either ≥65 years or ≥70 years dependent upon definition of study authors) were deemed eligible for inclusion. To be included studies had to report ADE for both SACT and non-SACT medications. Studies that assessed both preventable and unpreventable ADE were included.

The exclusion criteria comprised of (i) case reports, (ii) RCT examining investigational medicinal products, (iii) studies that only included haematological malignancies, (iv) studies that reported unplanned hospitalisations, but where the proportion due to ADE was unclear, (v) studies that did not have a full text or an English language version available, (vi) studies that only reported SACT toxicity and did not report non-SACT toxicity , and (vi) emergency department visits without hospitalisation.

2.4.3 Study selection and data extraction

The results of the search were combined and uploaded into Rayyan (141). Duplicates were detected and excluded, and the remaining studies underwent title and abstract review, followed by full text review of those papers deemed eligible. The primary author (DW) reviewed all papers, and the papers were then divided up between the other authors to complete an independent and blind review. In the case of conflicts, the two reviewers discussed, and where consensus was not possible, the decision of a third author was sought, at each stage of the process. Authors who were involved in more than one of the papers that were accepted after title and abstract review then had their bibliography hand searched on SCOPUS.

Studies identified as meeting the inclusion criteria had their data extracted using the Cochrane data collection form for RCT adapted for our systematic review (142). Data were extracted by DW and verified by a second author.

2.4.4 Assessment of methodological quality

Chapter 8 and chapter 25 of the Cochrane Handbook for Systematic Reviews of Interventions was used as a guide to identify bias in included studies (143), and the risk of bias was identified as low, high or unclear. DW assessed the bias of each included study, and a second reviewer for each included paper independently assessed the primary author's assessment.

When synthesizing the study data from each included study, attrition rate – defined as an attrition ≥5% of the study population at baseline was identified as having a high risk of attrition bias (144), due to incomplete data on the entire study population being present. Study quality was assessed using the MMAT for quantitative non-randomized studies (Table 4) (145).

Certainty assessment on each study was carried out using the GRADE framework (146) . As GRADE is a subjective ranking, the primary author performed a ranking, and this was independently assessed by a second author. A third author resolved any conflict.

For the incidence of hospitalisation due to ADE, whether statistical significance (p value) was attributed to the effect in the study was assessed. Reported odds ratio (OR) relative risk (RR) and the confidence intervals (CI) were also noted. Information on the statistical methods used to calculate these effects in each included study are provided in the adapted Cochrane data collection and risk of bias form.

2.4.5 Data Synthesis

The adapted Cochrane data collection tool (Appendix 4) was used to define outcomes sought (142). Study characteristics were then assessed. These included the type of study, the participants involved, the types of interventions, comparisons made in the study and the outcomes measured.

The following characteristics of included studies were collated:

Methods:

Aim of study, design, unit of allocation (study subjects), start date, end date, duration of participation, ethical approval.

Participants:

Population description, setting, inclusion criteria, exclusion criteria, method of recruitment, informed consent obtained, total population, clusters (if applicable), baseline laboratory results, withdrawals and exclusions, age, sex, ethnicity, severity of illness, comorbidities, other relevant sociodemographic details, where available.

Outcomes:

Outcome name, time point measured, time points reported, outcome definition, person measuring/reporting outcomes, unit of measurement, upper and lower limits, validation of outcome tool, imputation of missing data, assume risk estimate, power, all where appropriate.

Data and analysis:

Comparison, outcome, subgroup, time point, results, any other results reported, number of missing participants, reasons missing, reasons moved, unit of analysis, statistical methods used, if reanalysis required, if reanalysis possible, reanalysed results, all where available and appropriate.

Other information:

Key conclusions of study authors, reference to other relevant studies, correspondence required for further study information, reviewer notes.

The data from the included studies were tabulated, with relevant information to the primary research question populated.

2.5 Results

The search was conducted on 10.03.2022, updated on 09.02.2023, and 27.10.23.

A total of 6,225 records were identified using the search strategy, of which 432 were identified as duplicates using Rayyan duplication detection (141), and manual screening. The resulting 5,793 records were screened to assess the title and abstract for possible inclusion. This process resulted in the exclusion of 5,681 results. Of the 114 papers remaining, two were not available as full text. Assessment of the 112 available full texts was conducted, of which

two were deemed to have met the inclusion criteria. Reasons for exclusion of other papers are outlined in Figure 12.

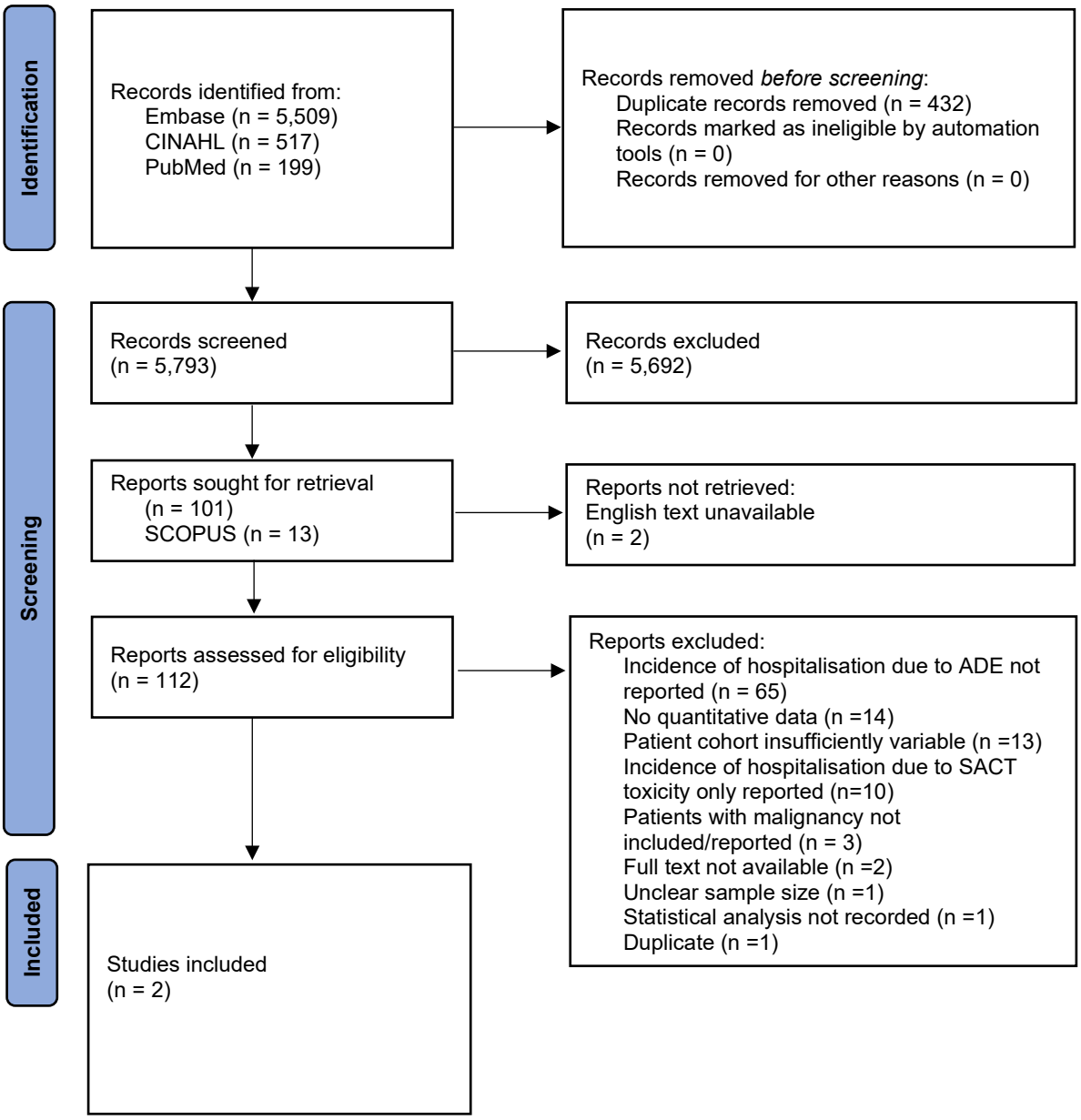


Figure 12: PRISMA flow chart outlining the identification, screening, and subsequent inclusion of relevant papers.

Across the two studies, 2,337 older adults with cancer were included. One study was conducted in the Republic of Ireland (n=121)(64), one study was conducted in the Netherlands (n= 2,216) (147). Table 3 summarizes studies that reported all ADEs.

Table 3: Papers that reported all ADE in older adults with cancer.

Title	Author	Study type	Tumour Type	Total Number in Group (n)	Hospitalisation due to ADE (%)	Findings	Conclusions
Adverse Drug Reactions in an Oncological Population: Prevalence, Predictability, and Preventability (64)	Lavan *et al.* 2019	• Prospective observational study • Older adults were defined as ≥70 years	All carcinoma	121/350	19	• Many ADR*s in patients with cancer in this study were not caused by SACT • ADRs occurred in similar frequencies in older and younger patients secondary to SACT (8.3% vs. 13.1%, p =0 .295), non-SACT (10.7% vs. 8.3%, p = .107), and a combination of both (0% vs. 1.3%, p = .240). • Twenty-two ADRs (29.3%) were definitely avoidable, 25 (33.3%) possibly avoidable, and 28 (37.4%) unavoidable	• This study shows that multimorbidity, polypharmacy, and ADE are highly prevalent in patients with cancer • ADE caused by SACT and non-cancer medications are a significant cause of acute hospitalisation in oncology patients. • Patients may benefit from Comprehensive Geriatric Assessment and specialist medication evaluation at this time
Toxicity, Response and Survival in Older Patients with Metastatic Melanoma Treated with Checkpoint Inhibitors (147)	De Glas *et al.* 2021	• Retrospective registry analysis • Older adults were defined as ≥65 years	Melanoma	2216	26	• Unplanned hospitalisation occurred in 24.2% of patients due to toxicity from immune checkpoint inhibitors and 1.8% of patients due to toxicity from other treatment.	• Future studies should investigate aging-related predictors and quality of life in older patients treated with checkpoint inhibitors. • The authors did not have a conclusion in relation to unplanned hospitalisation due to ADE.

**Note: Lavan et al use the phrase Adverse Drug Reaction (ADR) in a manner interchangeable with our use of Adverse Drug Event (ADE)*

Key: ADE – Adverse Drug Event; ADR – Adverse Drug Reaction; CGA – Comprehensive Geriatric Assessment; NSAIDs – Non-Steroidal Inflammatory Drugs; SACT – Systemic Anti-Cancer Therapy

Our search strategy revealed two papers that report the incidence of unplanned hospitalisation due to ADEs in their respective study populations. Lavan *et al.* report 19% of unplanned hospital admissions are due to ADE in patients aged ≥70 years with cancer (64). De Glas *et al.* report 26% of patients with metastatic melanoma treated with immune checkpoint inhibitors had an unplanned hospitalisation due to an ADE (147).

Risk of bias was assessed using the MMAT for quantitative non-randomized studies (145). As all studies were quantitative non-randomized studies, one being prospective observational, and one being a retrospective registry database analysis this was deemed an appropriate assessment. The risk of bias assessment in both studies can be found in Table 4.

Table 4: MMAT assessment for included studies using the Mixed Methods Appraisal Tool (MMAT) version 2018 for information professionals and researchers (143)

Lavan *et al.* (64)					
Category of study designs	**Methodological quality criteria**	**Responses**			
		Yes	**No**	**Can't tell**	**Comment**
Screening questions	S1. Are there clear research questions?	X			
	2. Do the collected data allow to address the research questions?	X			
Quantitative non-randomized	3.1. Are the participants representative of the target population?	X			
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?	X			
	3.3. Are there complete outcome data?	X			
	3.4. Are the confounders accounted for in the design and analysis?	X			
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?			X	
De Glas *et al.* (147)					
Category of study designs	**Methodological quality criteria**	**Responses**			
		Yes	**No**	**Can't tell**	**Comment**
Screening questions	S1. Are there clear research questions?	X			
	2. Do the collected data allow to address the research questions?	X			
Quantitative non-randomized	3.1. Are the participants representative of the target population?	X			
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?	X			
	3.3. Are there complete outcome data?	X			
	3.4. Are the confounders accounted for in the design and analysis?			X	
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?			X	

Bias was found to be low in all studies, with sound methodological approaches for the study type, with some uncertainty about outcomes, due to no discernible comparator in Lavan *et al.* (64), and a lack of clarity surrounding the assessment of confounders for non-treatment toxicity in De Glas *et al.* (147).

The GRADE tool was used to assess each paper for certainty of evidence and to establish the quality of evidence in the literature (148). In total it was found that one paper ranked very low certainty, when grading them for certainty of evidence relative to the research question, and one paper ranked moderate certainty. The baseline certainty for one study was low, as it was a retrospective study. One study was upgraded because the sample size was deemed significant (64), and the reported outcome matched the research question. A summary of the GRADE assessment can be found in Table 5.

Table 5: Reporting biases and certainty of evidence for included studies.

Study	GRADE Assessment							
	Baseline Certainty	**Risk of Bias**	**Imprecision**	**Inconsistency**	**Indirectness**	**Publication Bias**	**Reason for Ranking Up**	**GRADE Rating**
Lavan *et al.* (64)	Low – Observational Study	N/A	N/A	N/A	N/A	N/A	A sample of 333 patients was required to detect an ADR rate of 7% with a margin of error of 2% at 95% confidence. Incidence of ADR was 19% in older adults, total population sample size was 350.	Moderate quality
De Glas *et al.* (147)	Low – retrospective study not representative of entire oncology patient cohort	Selective reporting bias relative to our research question	N/A	N/A	N/A	N/A	N/A	Very low

2.6 Discussion

2.6.1 Summary of evidence

This review was the first, to our knowledge, to systematically review and analyse the literature regarding the incidence of hospitalisation due to ADE in the geriatric oncology setting, encompassing SACT and non-SACT medication. A paucity of studies relating to this outcome was identified. Our systematic review only found one paper that reported the prevalence in patients once hospitalized (64), and one paper that reported the incidence, confined to patients with metastatic melanoma receiving immune checkpoint inhibitors (147). One paper reported the preventability of ADE (62.7%) (64).

These findings, however, show that hospitalisation due to ADE in older adults with cancer is prevalent, largely predictable and in many cases potentially avoidable, thus supporting the integration of a comprehensive geriatric assessment, complete with medicines review in line with SIOG guidelines (56). Studies that have identified SACT toxicity as a primary outcome have been designed to demonstrate that a CGA is beneficial in reducing SACT toxicity (39, 41, 43, 125). These papers also excluded older adults who are either unfit for SACT or elect not to receive SACT. These trials have contributed significantly to the literature but were not designed to answer our research question. GAP70+ and GAIN demonstrated a reduction in Grade 3-5 SACT toxicity (39, 125), and INTEGERATE demonstrated reduced rates of functional decline in patients who receive a CGA (41), however non-SACT related hospitalisations were not examined in these papers. Lavan *et al.* and De Glas *et al.* have demonstrated that older adults with cancer experienced unplanned hospitalisation due to ADE caused

by non-SACT medication (64,147), in addition to that caused by SACT toxicity. Prospective interventional studies may help to support these findings.

De Glas *et al.* does differ from the other studies (147), in respect to patient cohort. As this study included patients with metastatic melanoma, being treated with immune checkpoint inhibitors, it is difficult to compare the findings of this study to the other papers discussed in this review. A recent meta-analysis found that performance status and organ function were predictors of immune checkpoint inhibitor toxicity, independently of increasing age (149). The higher rates of Grade 1 and Grade 2 toxicities in older adults in this study, may not have resulted in hospitalisation, however, the impact of these toxicities on quality of life needs to be further understood, and the clinical significance of non-hospitalisation toxicities is beyond the scope of this review.

Nightingale *et al.* demonstrated that a pharmacist led comprehensive medication assessment is effective in identifying high rates of patients with polypharmacy (5-9 medications), hyperpolypharmacy (≥10 medications) and PIM using a combination of tools (115, 150-152). Turner *et al.* supports this approach (153) showing multimorbidity in patients with cancer can lead to ADE, polypharmacy, prescribing of PIM and potential drug-drug interactions. Of note, the protocol of a single-blinded, randomized, controlled trial assessing the optimisation of polypharmacy in geriatric oncology (the OPTIMAL study) has been published and is underway (154).

Medication optimisation should be considered for all older adults with cancer, where feasible. The role of the clinical pharmacist, with oncological and gerontological expertise could potentially ameliorate some risk in this patient population. Guidance

on conducting medication reviews in older adults with cancer have been published (56) and current clinical pharmacist practices have been reported (123).

Opportunities to optimise medications used to treat chronic conditions in older adults with cancer, and cancer survivors, in primary healthcare settings may further reduce hospitalisation in older adults with cancer and cancer survivors. Medication optimisation in primary care settings have shown efficacy in improving deprescribing of PIM, in older adults in a general practice setting(155). High rates of PIM and polypharmacy have also been observed in long-term care facilities and these can be addressed by the multidisciplinary primary care team (156).

Education and research opportunities for clinical pharmacists in the field of geriatric oncology are scarce at present. Expanding teams and creating educational resources so that pharmacists in oncology roles can expand their geriatric knowledge, and pharmacists involved in the care of the older adults can expand their oncology knowledge, should be a consideration for teaching institutes, cancer centres and national cancer control programmes to ensure appropriate measures are taken to optimise medications in older adults with cancer (157, 158).

2.6.2 Limitations and strengths

This review was limited by the consideration of English language papers only, and the small number of studies included, which had methodological limitations. Not all full texts were readily available. A meta-analysis was deemed unfeasible due to the limited and heterogenous nature of the data available in the literature.

A strength of this review is that the review process was guided by a medical librarian in building a comprehensive search strategy. The data collection, extraction and

analysis were conducted by a research group with a diverse background in clinical pharmacy, academic pharmacy, medical oncology, and oncology nursing, enabling a broad knowledge base to be applied to the narrative discussion.

2.6.3 Implications for future research

Future research is needed to identify the incidence of hospitalisation due to ADE in the wider geriatric oncology population. RCT to date have utilised SACT toxicity as a primary objective, however, we have identified a lack of prospective studies that analyses all hospitalisations due to ADE. We have also identified a lack of studies that include patients on supportive care, or active surveillance who are still under the care of medical oncology specialties.

Research investigating methods to optimise medications in older adults with cancer, both those who are receiving SACT and those who do not, are needed to assess the impact of effective medication management in this high-risk patient population (123). Studies should account for the reporting of potential ADE relative to supportive care, and indeed chronic medications used to treat long-standing comorbidities.

2.7 Conclusion

In conclusion, multidisciplinary efforts to prevent ADE is an unmet need of older adults with cancer. The CGA process has been shown to reduce the incidence of SACT toxicity (39, 125), however, the impact of this on non-SACT related ADE is at present unknown. Our review supports these findings, where drug related issues are under-represented in the literature. The relevance and clinical significance of non-SACT toxicity is yet to be determined, despite well devised studies evaluating SACT toxicity.

In addition, there is an absence of studies evaluating ADE in patients on best supportive care strategies. Data are also lacking in patients under active surveillance who have undergone curative treatment, despite the increasingly growing number of patients who fall under the umbrella of cancer survivorship.

Chapter 3 – Hospitalisation, polypharmacy, and length of stay in older adults with cancer

Author Contributions:

Writing – original draft: DJW,

Writing – review & editing: DJW, MO'D, AMH, LJS

Methodology: DJW, MO'D, AMH, LJS

Data extraction: DJW

Data analysis: DJW

3.1 Abstract

Introduction

This chapter will examine the baseline statistics in UHW for key variables relevant to older adults with cancer, such as length of stay for unplanned hospitalisation and the impact of SACT treatment on polypharmacy status, prior to the introduction of a pharmacist to the GOAL clinic.

Young SIOG recommend medication review for all older adults on ≥5 medications receiving SACT (56). Many older adults receive SACT therapy that involves more than one chemotherapeutic agent (polychemotherapy), and at least one, if not more, supportive care medications. It was important to establish the impact of SACT on polypharmacy status, to identify if this affected the prevalence of unplanned hospitalisation in this cohort.

Aim

To determine mean length of stay for older adults with cancer, and to assess the impact of cancer treatment on drug burden/polypharmacy status in older adults, and to determine the macroeconomic impact of hospital stays in this cohort.

Methods

Inpatient management software was used to identify patients who had been admitted as an inpatient under the care of a medical oncologist to UHW over a 6-month period (October 2021 to March 2022). Patients who were admitted for elective procedures were excluded. The total number of bed days was then counted, and the mean determined.

Simultaneously, patients who had attended the GOAL Clinic over a 30-month period were assessed using the GOAL Clinic database. Here, the total number of medications per patient was recorded, in addition to their SACT treatment plan.

The total number of SACT medications, and the total number of supportive care medications were added to the total number of medications at baseline. Patients were categorised as having non-polypharmacy (<5 medications), polypharmacy (5-9 medications) and hyperpolypharmacy (≥10 medications) at (i) baseline and (ii) upon commencement of SACT. The impact of SACT on this status and subsequent treatment toxicity was then analysed.

The macroeconomic impact of an unplanned hospitalisation was determined using the average cost of a bed day in a HSE hospital, and the average length of stay for (i) the general population, and (ii) older adults with cancer.

Results

Older adults with cancer admitted to UHW had a mean length of stay of approximately 11 bed-days, compared to approximately 6 days in the general population.

Approximately 29% of patients without polypharmacy pre- or post-SACT had an unplanned hospitalisation, 57% of patients who transitioned from non-polypharmacy to polypharmacy upon commencement of SACT were hospitalised, 20% of patients who transitioned from non-polypharmacy to hyperpolypharmacy upon commencement of SACT were hospitalised, 39% of patients who had polypharmacy pre- or post-SACT had an unplanned hospitalisation and 50% of patients who

transitioned from polypharmacy to hyperpolypharmacy upon commencement of SACT were hospitalised.

Older adults with cancer had a 184% increased cost in unplanned hospitalisation, compared to the general population.

Conclusion

The mean length of stay for an inpatient in an acute public hospital in Ireland has been between 5.4 and 6.0 days (159). We identified older adults with cancer as having approximately double the length of stay of the national average (12 days). Considering a longer length of stay is associated with declining performance status, increased frailty, and a reduction of baseline functional status (160), targeted measures to reduce unplanned hospitalisations in this patient population may have significant benefits.

It is also clear that patients commencing SACT have a significant incidence of hospitalisation due to toxicity, and this increases sharply when polypharmacy status escalates upon initiation of SACT and supportive care medications.

3.2 Introduction

3.2.1 SACT toxicity and unplanned hospitalisation

Phase III clinical trials for chemotherapy, and for immunotherapy have underrepresented older adults with cancer, and outcomes in older adult cohorts in these trials have been underreported in the literature (161, 162). The inadequate detailing of treatment efficacy, adverse effects, and impact on quality of life in these studies leads to a challenge in making informed treatment decisions for older adults with cancer, in whom systemic therapy is recommended by clinical practice guidelines. In addition, a review of Food and Drug Administration (FDA) registered clinical trials on immunotherapy found that no study protocols included a baseline CGA in older adults enrolled in studies (162).

The impact of a CGA on treatment decision making, and treatment outcomes is well established in the literature. A systematic review published by Hamaker *et al*. in 2022 examined 65 publications from 61 studies. It found that a CGA resulted in an altered treatment plan in a median of 31% of patients (range 7-56%) (163). The degree of change increased with increased MDT input, and that non-oncologic interventions were recommended in over 70% of patients, showcasing a marked degree of deficiencies at baseline in geriatric domains. CGA directed therapy reduced the rates of SACT toxicity, increased treatment completion rates and led to an increased in overall patient functionality and quality of life. Therefore, when considering SACT in older adults with cancer, a CGA is strongly recommended.

The GAP70+ study demonstrated the benefit of a CGA on significant (Grade 3-5) SACT toxicity in older adults with cancer. In this RCT, 50.1% of patients who received a CGA

prior to treatment initiation experienced grade 3-5 toxicity, compared with 71.2% of patients who received routine oncological care, with an adjusted relative risk of 0.74 (95% CI: 0·64–0·86; p<0·001) (39).

In the GAIN study, patients received a geriatric assessment, and an MDT interventional approach to implementing CGA results was compared to sending the CGA results to a treating oncologist. Grade 3-5 toxicity to chemotherapy was observed in 50.5% of the intervention arm, and 60.6% of the standard of care arm, a significant 10.1% reduction (95% CI, −1.5 to −18.2%; p = 0.02). There was, however, no statistically significant difference between the arms in terms of emergency department visits, or unplanned hospitalisation.

Previous research from the GOAL clinic in UHW shows that older adults receiving a CGA prior to receiving SACT results in toxicity that leads to unplanned hospitalisation in 36% of patients, with 42% of patients discontinuing treatment early due to adverse effects (43). This study evaluated data over a 30-month period to April 2021, a period a pharmacist was not a member of the MDT, and a structured medication review did not routinely take place.

It is evident from the literature assessing the impact of CGA in older adults with cancer that unplanned hospitalisation due to SACT toxicity can significantly decrease when a CGA is performed at baseline and SACT regimes are adjusted, accounting for the potential for geriatric syndromes to impact patient outcomes (39).

3.2.2 Polypharmacy and medication-related problems

As comorbidity increases, medication usage increases also. This can increase the risk of drug interactions, medication related adverse events, and promote exacerbation

of geriatric syndromes, such as falls (164). Polypharmacy prior to older adults starting SACT is abundant, with Lu-Yao *et al.* finding the presence of polypharmacy in up to 80% of patients (165).

One of the challenges in assessing polypharmacy is the variation of definitions in the literature, with the most common definition, and the one used by Young SIOG as taking ≥5 or more medications (56). Turner *et al*. found that no single polypharmacy cut-off point is optimal for predicting multiple adverse events in older people with cancer (166). With increasing polypharmacy, the presence of prescribing cascades makes medication reviews challenging, and often strategies to reduce polypharmacy need to be done in a step-wise fashion to reverse cascades and ensure withdrawal syndromes are avoided (113, 167).

Polypharmacy is associated with adverse outcomes in older adults with advanced cancer being treated with SACT. The GAP70+ study identified that patients in the intervention arm had more medications discontinued, leading to reduced polypharmacy (39). A secondary analysis of GAP70+ assessed the association of polypharmacy (defined in this study as ≥8 medications) and potential DDI with adverse treatment outcomes (59). This study found that polypharmacy at baseline was associated with a statistically significant increase in grade ≥2 and grade ≥3 toxicities. In addition, major potential drug interactions (PDI) (defined as drug interactions in which treatment modification or the avoidance of combination therapy is recommended) were statistically significantly associated with early treatment discontinuation.

The added complexity in older adults with cancer relative to the general older adult population is the capacity for impairments to overlap. This leads to adverse events that are multi-factorial, where a patient may experience an adverse event due to cancer-related, medication-related or ageing/frailty-related impairment (14). Identifying a root cause of an adverse event and deciphering if a medication was responsible for, or contributed to, the adverse event is difficult. In the presence of polypharmacy, where multiple medications may be contributing, ascertaining which medication to target for intervention can be challenging.

An example of this in an older adult with cancer is reduced renal function. This can be caused by a cancer-related impairment such as an obstructive tumour, paraprotein calcification or tumour-lysis syndrome. It can also occur through drug-induced kidney injury, such as is observed with the anticancer platinum agents, nephrotoxins such as ACEi, NSAIDs or loop diuretics, and some antimicrobials used in neutropenic sepsis such as amikacin or gentamicin. Reduced renal function is associated with increasing age in the cancer population (168, 169). Table 6 outlines risk factors and aetiologies of acute kidney injury in critically ill patients with cancer (169).

Table 6: Risk factors and aetiologies of acute kidney injury in critically ill patients with cancer adapted from Rosner et al (169).

Patient-specific risk factors	Cancer-related risk factors
Age > 65 years	Neutropenia and resulting sepsis
Underlying CKD	Post-nephrectomy for RCC
Diabetes mellitus	Haematological cancers
Potential nephrotoxin medications (NSAIDs, ACEi, ARBs)	Urinary tract obstruction
	Post- hematopoietic stem cell transplant
Comorbid conditions (such as cirrhosis, heart failure, nephrotic syndrome)	Thrombotic microangiopathy
	Tumour lysis syndrome
	Hypercalcemia
	Paraneoplastic glomerular diseases
	Chemotherapy toxicities

Key: ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; CKD, chronic kidney disease; NSAIDs, non-steroidal anti-inflammatory drugs; RCC, renal cell cancer.

Many older adults with cancer are frail, or pre-frail, at baseline, which leads to poorer tolerance of SACT and increased postoperative complications, both of which result in prolonged hospitalisation (170). Indeed, advanced cancer itself is a disease with a known association with frailty, whereas locally advanced or curable cancer can still be detected in older adults with pre-existing frailty (170). Common diseases, and conditions associated with frailty are outlined in Table 7 (14).

Table 7: Diseases and conditions associated with frailty (14)

Diseases known to increase the risk of frailty	**Conditions caused by frailty**
Congestive heart failure	Hip fractures
End stage renal disease	Pressure ulcers and chronic wounds
Diabetes	Sarcopenia
	Weight loss/malnutrition
Dementia	Decreased strength, exercise tolerance
	Slow gait speed, poor mobility
Depression	Slow motor processing
	Decreased balance
Advanced cancer	Low physical activity
	Cumulative illness
Chronic obstructive pulmonary disease (COPD)	Cognitive impairment
	Increased vulnerability to stressors
Acquired Immunodeficiency Syndrome, Tuberculosis and other chronic infections	Psychosocial stressors

It is therefore important to understand the impact polypharmacy can potentially have on an older adult with cancer, particularly in the presence of frailty, and the implications for problematic polypharmacy in this population. It is imperative to consider the impact that SACT and supportive care medications will have on the medication burden of a patient and to consider whether this may contribute to, or cause, unplanned hospitalisation in older adults with cancer and frailty. The degree of impact depends upon the SACT regimen that a patient commences. The medication burden of SACT, routine prophylaxis and PRN supportive care medications of selected different regimens are shown in Table 8.

Table 8: Medication burden impact of various SACT regimens indicated in older adults with cancer

Regimen	**Indication***	**SACT**			**Routine pre-SACT prophylaxis**	**PRN Supportive Care**	**Total number of medicines**
		Medication	**Route**	**Frequency**			
Capecitabine	Breast cancer Colorectal cancer	Capecitabine	PO	Twice daily for 14 days followed by a 7-day break	None	Metoclopramide **or** Cyclizine	2
AC	Breast cancer	Doxorubicin Cyclophosphamide	IV IVI	Every 14 **or** 21 days	Palonosetron Netupitant Dexamethasone	Metoclopramide **or** Cyclizine	6
mFOLFIRINOX	Pancreatic cancer	Fluorouracil Oxaliplatin Irinotecan	IV IVI IVI	Every 14 days	Palonosetron Netupitant Dexamethasone Atropine Loperamide Folinic acid	Metoclopramide **or** Cyclizine and Loperamide	10
Carboplatin/ Paclitaxel	Ovarian cancer Peritoneal cancer Fallopian tube cancer Cancer of unknown primary	Carboplatin Paclitaxel	IVI IVI	Every 21 days	Palonosetron Netupitant Dexamethasone Chlorphenamine Famotidine	Metoclopramide **or** Cyclizine	8

*As per NCCP protocols available at https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/ (Accessed February 2025)

Key: SACT – Systemic Anticancer Therapy; AC- doxorubicin and cyclophosphamide; mFOLFIRINOX -modified folinic acid, fluorouracil, irinotecan and oxaliplatin, PO – per oral; IV – Intravenous bolus; IVI – Intravenous infusion

Finally, assessing the length of time an older adult with cancer spends hospitalised during an unplanned admission is important, as this will cause, worsen and potentially instil permanent aspects of frailty (21).

3.2.3 Economic impact of unplanned hospitalisation

The economic impact of unplanned hospitalisation in patients who have an ADE compared to those that have not has been examined by Bennett *et al*. in a prospective cohort study (171). Medication-related adverse events were associated with an increased cost of €2047, with preventable events and severe events accounting for further increase in cost (€2559 and €3580 respectively).

Medication-related problems have been strongly linked to increased length of stay and increased healthcare utilisation, with the risk increasing by the addition of each medication by a hazard ratio of 1.14 (95% CI 1.09, 1.20), and length of stay directly increased in over a quarter of patients (172).

This chapter focuses on the impact SACT, and cancer-related medication burden has on polypharmacy status, it's role in SACT toxicity and what a resulting unplanned hospitalisation might mean for an older adult with cancer, as well as the potential economic impact.

3.3 Aim

The aim of this baseline work was threefold:

(i) to establish the length of hospital stay in older adults with cancer relative to the general population

(ii) to evaluate the impact of polypharmacy status on SACT toxicity in older adults resulting in an unplanned hospitalisation.

(iii) to determine the macroeconomic impact of hospital stays in this cohort

3.4 Methods

3.4.1 Determining length of stay for unplanned hospitalisation

A study on length of stay in patients acutely admitted under a medical oncologist in UWH between October 2021 and March 2022 inclusive was conducted. Data were gathered by identifying patients admitted under the four practicing medical oncologists in UHW using the integrated patient management system (iPMS) software. Patients with haematological malignancies, including non-Hodgkin's and Hodgkin's lymphoma were excluded as they are treated by clinical haematologists in UHW and do not have a referral pathway to the GOAL clinic. Baseline descriptive data collected included: (i) patient age, (ii) gender, (iii) primary cancer diagnosis, (iv) cancer staging, (v) length of acute hospital admission, and (vi) pre-chemotherapy G8 score (a score of <15 indicates possible frailty, and a potential benefit form a CGA). Patients were stratified into two groups. Those ≥70 years old and those <70 years old. The average length of stay was then calculated from the inpatient report as total number of bed days the patients were admitted for and the two groups compared. This was then compared to the national average for all adults.

3.4.2 Assessing the impact of SACT on polypharmacy status and unplanned hospitalisation due to SACT toxicity

Data were collected and analysed from the GOAL Clinic database. Patients who attended for a CGA had the following variables collected: (i) gender, (ii) cancer staging, (iii) SACT treatment plan, (iv) number of medications before and (v) after starting SACT, and (vi) subsequent unplanned hospitalisation. Patients were categorised into their pre-treatment polypharmacy status as having (i) non-polypharmacy (<5 medications), (ii) polypharmacy (5-9 medications), or (iii) hyperpolypharmacy (≥10 medications) pre-treatment. The total number of medications contained in the standard treatment protocol for the patients, and upfront prophylactic supportive care medications were then added to the patient's total number of medications in line with the algorithm shown in Table 8. Patients were then assigned a post-treatment polypharmacy status. The incidence of unplanned hospitalisation due to SACT toxicity for each patient group using their combined polypharmacy status pre- and post-treatment was compared.

3.4.3 Assessing the macro-economic impact of unplanned hospitalisation

Initially, national patient data from 2015-2023 were collated from the Department of Health National Healthcare Statistics Report (173) and the Organisation for Economic Co-operation and Development (OECD) data explorer (174) to determine the average length of stay of an adult due to an unplanned hospitalisation. The HSE Spending Review for 2022 was then assessed to determine the economic cost of an unplanned hospital admission in the Irish context (175).

3.5 Results

3.5.1 Length of hospital stay in older adults with cancer

Data on 89 patients were examined, with a median age of 62 (range 32- 84); 24(27%) were ≥70 years old and 52(58%) were female. The most common cancers were gastrointestinal, n=24(27%) and breast, n=11(12%). Fifty-seven patients (64%) had stage IV disease; with 64(72%) receiving SACT at admission. G8 scores were calculated for 19/24 of those aged ≥70 years, 18(95%) of whom scored ≤14 (potentially benefiting from a CGA). The average length of stay for patients aged ≥70 years was 11.25 days versus 12.44 days for those <70 years (p=0.76).

3.5.2 The impact of polypharmacy status on SACT toxicity in older adults resulting in an unplanned hospitalisation

In relation to assessing the impact of SACT on polypharmacy status and subsequent hospitalisation due to toxicity in older adults with cancer, 162 patients were screened. Patient demographics are outlined in Table 9. Ninety-four (58%) were male. Sixty-five patients (40%) had stage IV disease. Ninety-nine (61%) had treatment, of whom, 42 (42%) were hospitalised. Seventeen patients were in the non-polypharmacy category prior to and after starting treatment. Twenty-three of these patients (55%) were hospitalised due to toxicity.

Table 9: Demographic details of patients

Demographic (n = 162)	**n (%)**
Gender	
Male	94 (58)
Female	68 (42)
Stage	
I	6 (4)
II	21 (13)
III	71 (44)
IV	65 (40)
SACT	
Yes	99 (61)
No	63 (39)
Unplanned hospitalisation (n=99)	
Yes	42 (42)
No	57 (58)
Unplanned hospitalisation due to SACT toxicity (n=42)	
Yes	23 (55)
No	19 (45)

Key: SACT – Systemic Anticancer Therapy

Twenty-one went from non-polypharmacy prior to treatment to polypharmacy after starting treatment, with 57.1% of these were hospitalised due to toxicity. Five patients went from non-polypharmacy to hyperpolypharmacy, with 20% of these hospitalised due to toxicity. Twenty-three had polypharmacy before and after treatment, with 39% of these hospitalised due to toxicity. Twenty patients went from polypharmacy to hyperpolypharmacy, with 50% of these hospitalised due to toxicity. Thirteen had hyperpolypharmacy at baseline before starting treatment, with 38% of these hospitalised due to toxicity. Polypharmacy status and toxicity rate is summarised in Table 10.

Table 10: Pre- and post-treatment polypharmacy status and associated rate of unplanned hospitalisation due to SACT toxicity.

Pre-treatment status	Post-treatment status	Toxicity Rate
Non-polypharmacy	Non-polypharmacy	29%
Non-polypharmacy	Polypharmacy	57%
Non-polypharmacy	Hyperpolypharmacy	20%
Polypharmacy	Polypharmacy	39%
Polypharmacy	Hyperpolypharmacy	50%
Hyperpolypharmacy	Hyperpolypharmacy	39%

3.5.3 The macro-economic impact of unplanned hospitalisation in older adults with cancer

According to Department of Health National Healthcare Statistics Report the average length of stay for all inpatient admissions between 2015 and 2023 was 6.1 days. The average length of stay for all causes according to the OECD between 2015 and 2023 was 5.9 days (Table 11).

Table 11: Average length of stay according to the OECD

Time period / **Diagnostic category**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**Average**
All causes	5.7	5.7	5.7	5.8	5.9	5.9	5.8	6.2	6.2	5.9
Neoplasms	9.7	9.9	9.8	9.6	10	9.9	9.6	10.2	10	9.9

The average length of stay for all patients with a cancer diagnosis, categorised as neoplasms, according to the OECD was 9.9 days (Figure 13).

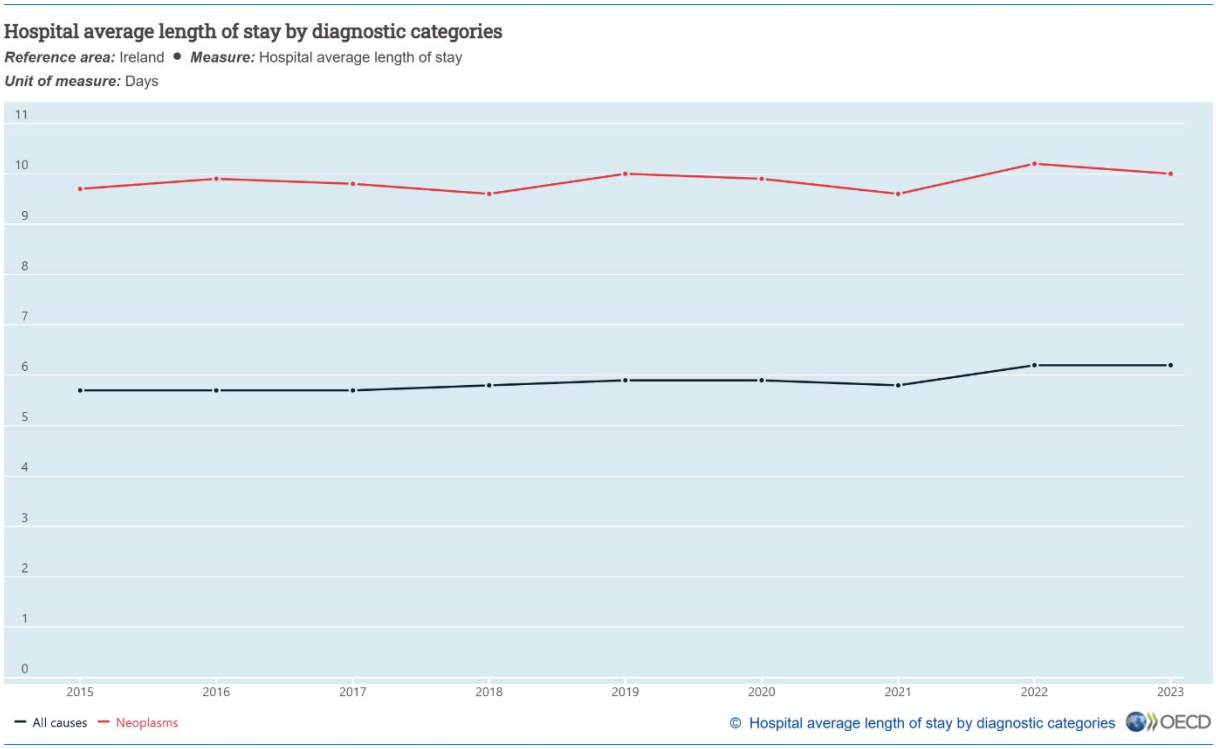


Figure 13: Average length of stay for patients of all causes, and patients with a diagnosed neoplasm in the acute public hospital sector in Ireland between 2015 and 2023 (source OECD data explorer)

The HSE Spending Review for 2022 determined that the absorbed cost of a hospital bed in an acute public hospital in Ireland in 2021 was €7,203 per week, equating to €1,029 per day of admission. Therefore, the approximate cost of an admission for all causes is between €5,968.20 and €6,276.90, accounting for the difference between the OECD and Department of Health data. The approximate cost of a hospital admission for a patient with cancer was €10,084.20 according to OECD data.

Using a cost of €1,029 per day of admission, we can therefore estimate that an unplanned hospitalisation in an older adult with cancer to UHW is €11,576.25 and for those aged <70 years is €12,800.76. The costs of a hospital admission are summarised in Table 12.

Table 12: Length of stay and associated health-economic cost for all adults, all adults with a cancer diagnosis, and adults with an unplanned hospitalisation in the Irish setting.

Source	**Department of Health (Ireland)**		**Organisation for Economic Co-operation and Development (OECD)**		**University Hospital Waterford Inpatient Data**	
	Length of stay (days)	**Economic cost (€)**	**Length of stay (days)**	**Economic cost (€)**	**Length of stay (days)**	**Economic cost (€)**
All causes	6.1	6,276.90	5.9	5,968.20		
All cancer patients			9.8	10,084.20		
Unplanned hospitalisation –solid tumours (≥70 years)					11.25	11,576.25
Unplanned hospitalisation –solid tumours (<70 years)					12.44	12,800.76

3.6 Discussion

The purpose of this chapter was to determine the impact of polypharmacy and polypharmacy status on SACT toxicity resulting in an unplanned hospitalisation, as well as identify the average length of stay, and the economic burden of an unplanned hospitalisation in older adults with cancer relative to the general population.

3.6.1 Impact of polypharmacy status on SACT toxicity

We have shown that polypharmacy status can be linked to unplanned hospitalisation, and where SACT causes a transition in polypharmacy status the incidence increases sharply. The findings associated with SACT toxicity suggest that the treatment burden of SACT and supportive care may have a greater impact on hospitalisation than baseline polypharmacy status, with SACT and supportive care creating a transition of polypharmacy status being associated with greater incidence of unplanned hospitalisation due to toxicity. This suggests that complex SACT regimens, or supportive care regimens that contain PIM may be greater drivers of toxicity than the total number of medications taken. Therefore, medication reviews should take into account treatment complexity and prophylactic supportive care medications, and not solely be focused on medications for chronic conditions, defined in tools such as STOPP/START and the Beer's criteria (7, 8).

The treatment regimens outlined in Table 8 give an indication of the complexity associated with some SACT protocols. The protocol for modified FOLFIRINOX alone confers an ACB score of 5 for just the supportive care medications alone (Figure 14). This has potentially huge clinical significance as an ACB score ≥3 confers an increased risk of falls, cognitive impairment and mortality. This regimen also accounts for the

routine prescribing of at least ten medications as standard, many of which are high risk, as defined by international medication safety standards (176). The challenge associated with managing this risk lies in the clinical complexity of the individual patient circumstances. This protocol is typically used in the curative setting, and all three anticholinergic medications described in Figure 14 are key supportive care medications, without suitable alternatives.

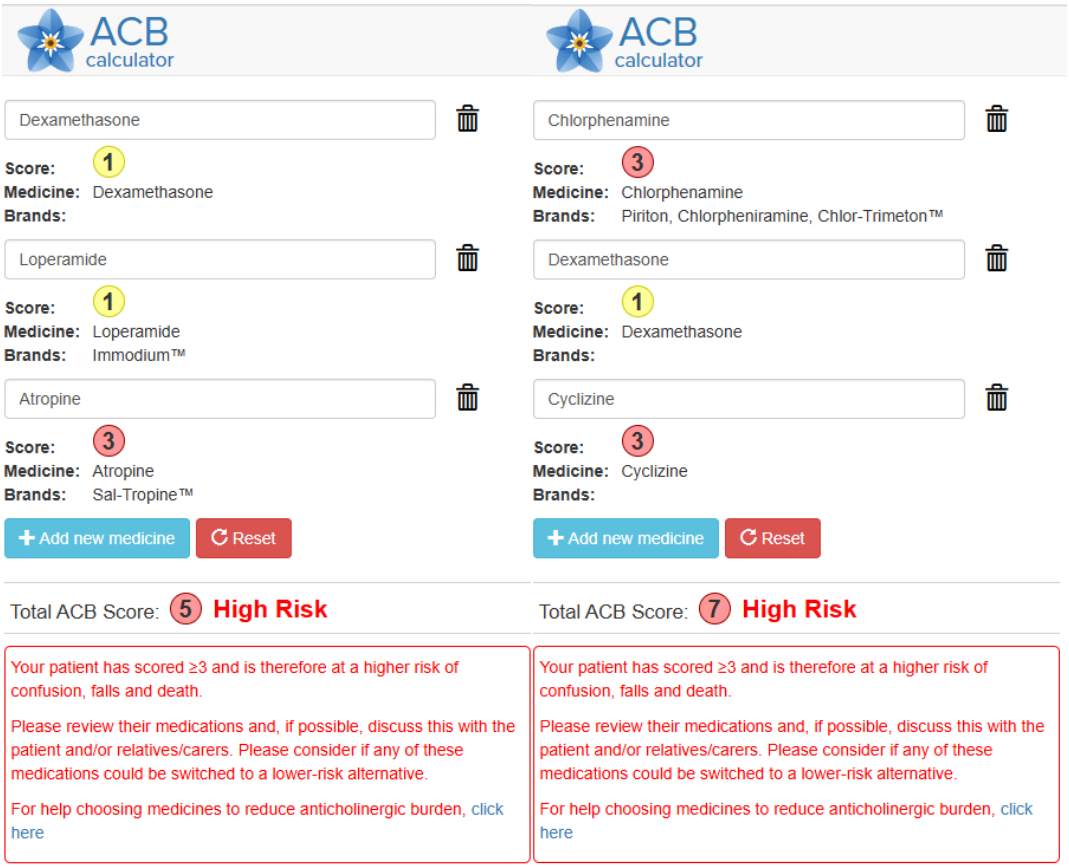


Figure 14: Anticholinergic burden score of supportive care medications used as standard prophylaxis for the modified FOLFIRINOX protocol and Carboplatin/Paclitaxel (screenshot taken from https://www.acbcalc.com/) (177)

Atropine and loperamide play a key role in the prevention of cholinergic syndrome, a potentially life-threatening acute toxicity associated with irinotecan therapy (178). Dexamethasone is a key antiemetic, as the protocol is highly emetogenic, however corticosteroid sparing approaches can be taken to reduce cumulative dexamethasone exposure (179-181). Similarly, carboplatin, in combination with

paclitaxel, can have an ACB score of 7 associated with its prophylactic supportive care. This occurs using first-generation antihistamines and dexamethasone, which are used to reduce the risk of an infusion-related reaction. Cyclizine is frequently used in place of metoclopramide for breakthrough chemotherapy-induced nausea and vomiting (CINV), as metoclopramide can be contraindicated in patients with brain metastasis, who have had a seizure (182). These may be essential, unavoidable medications, that carry a significant risk of ADE in older adults themselves.

The NCCN Older Adult Oncology guideline outlines commonly used supportive care medications that may be problematic in older adults with cancer (90). This resource contains potentially suitable alternatives, and research assessing the efficacy of second-generation antihistamines as prophylaxis against infusion-related reactions in older adults with cancer, could provide a safer alternative to first-generation antihistamines, with lower risk of falls, and cognitive decline.

3.6.2 Length of hospital stay in cancer patients

We used macro-epidemiological data to ascertain average length of stay for the broader population in the Irish context using openly published epidemiological data from the Department of Health and the OECD. This data is incredibly useful to outline the current additional burden a hospital admission has on a cancer patient, compared to the general population, and to estimate the additional economic cost of an unplanned hospitalisation in this setting. It is important, however, to acknowledge some of the limitations of this data.

The data for patients with neoplasms in the OECD database does not distinguish between unplanned hospital admission, hospital admission for diagnostic work up

and elective admissions for anticancer therapy. Therefore, it was important to use local data to filter out all admissions that were not unplanned, to get a more accurate determination of the impact an unplanned hospitalisation has both in terms of length of stay, and economic impact.

This explains the discrepancy between the OECD data and the data from the Department of Health for all diagnosis, and between the OECD and UHW for cancer patients. Elective admissions, for systemic therapy, for example, are typically short inpatient stays where a patient may be admitted for a short number of days to receive a cycle of systemic therapy and be discharged upon completion. This contrasts with an unplanned hospitalisation due to toxicity, such as neutropenic sepsis, which may require a prolonged course of intravenous antimicrobials, or chemotherapy induced nausea and vomiting which may require prolonged symptom control, rehydration, and electrolyte replacement. Therefore, the inclusion of elective admissions for systemic therapy in macro-epidemiological data, or short investigative stays, will reduce the average length of stay data and not truly reflect the impact an unplanned hospitalisation has.

While length of stay does not differ significantly between older and younger adults with cancer, targeting older adults for medication reviews is logical where resources are limited due to the association between increasing age and complex comorbidity, frailty and polypharmacy as outlined in Chapter 1. Therefore, for patients being considered for SACT, we have shown that consideration should be given to the patient's baseline pharmacological burden, and the potential impact SACT and supportive care may have on this.

3.6.3 Macro-economic impact of unplanned hospitalisation

Our analysis in UHW found that the average length of stay for an older adult with cancer was 11.25 days. Using data from the HSE Spending Review 2022, we extrapolated that to an estimated average cost of €11,576.25 per patient. This was compared to the average length of stay documented in the Department of Health National Healthcare Statistics Report for all adult inpatients, at 6.1 days, which had an estimated cost of €6,276.90. We can extrapolate a 184% increased cost per hospital admission in older adults with cancer, compared to the general population.

The macro-economic burden of unplanned hospitalisation in older adults with cancer is quite difficult to determine. The HSE Annual Report and Financial Statements 2024 highlights a 37% increase in the number of people aged ≥65 years compared to 2015 in Ireland, with an anticipated 165% projected increase in population aged ≥85 years by the year 2044 (183). This report also found that the burden of cancer in Ireland is greater than the EU average, accounting for 26% of deaths in patients aged ≥65 years.

A report from the Irish Government Department of Health noted that the average length of stay per patient rose from 5.7 days in 2016 to 6.4 days in 2022, however the COVID-19 pandemic was a factor that contributed to this (184). This report also states that "*Population ageing has been shown to have a demonstrable impact on resource utilisation and capacity in the acute care system*". The Department of Health analysis found that patients aged ≥65 years made up 15% of the population but were responsible for 58% of all inpatient bed days.

When you combine the increase in older adults currently, with the upward trend in ageing population against a backdrop of greater consumption of inpatient bed days, the macroeconomic impact of providing acute care for older adults is growing rapidly. The addition of Ireland's above-average cancer burden, paired with increasingly effective treatment strategies for cancer paints a picture of a future Ireland where geriatric oncology becomes a key driver of preventative healthcare, through CGA and optimisation of care for older adults.

3.7 Conclusion

Cancer is a disease associated with increased hospital length of stay, and interventions to reduce the incidence of unplanned hospitalisation in this patient population have potential to incur a positive health economic impact, at a greater level than general population interventions. In addition to this, it is deductible from these findings that polypharmacy may have a role in unplanned hospitalisation. This chapter provides evidence of the need to provide targeted interventions intended to reduce the risk of medication related harm in older adults being considered for SACT. Preventing potentially avoidable unplanned hospitalisation in older adults with cancer could have significant clinical and health economic benefits.

This chapter outlines the known association of polypharmacy and complications in frailer older adults with cancer and demonstrates the impact SACT has on polypharmacy status and subsequent unplanned hospitalisation due to SACT toxicity. This evidence provides justification for exploring in Chapters 4 and 6 the optimisation of SACT and supportive care medications. It also supports the exploration of

deprescribing opportunities for PIM use in this patient population to reduce toxicity-related unplanned hospitalisation.

Chapter 4 - Hospitalisation due to adverse drug events in older adults with cancer: A retrospective analysis

Peer-reviewed publications

Walsh DJ, Sahm LJ, O'Driscoll M, Bolger B, Ameen H, Hannan M, Goggin C, Horgan AM. Hospitalisation due to adverse drug events in older adults with cancer: A retrospective analysis. Journal of Geriatric Oncology, Volume 16, Issue 6, 102283. doi: https://doi.org/10.1016/j.jgo.2025.102283.

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Research Paper

Hospitalization due to adverse drug events in older adults with cancer, a retrospective analysis

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ABSTRACT

Introduction: Geriatric oncology is a rapidly evolving field of practice, where comprehensive geriatric assessments (CGA) and multidisciplinary team (MDT) input have the potential to improve patient outcomes. Polypharmacy and potential drug interactions (PDI) have been associated with an increased risk of adverse outcomes in older adults with cancer, receiving systemic anti-cancer therapy (SACT). Our aim was to assess the incidence of unplanned hospitalization in older adults with cancer attending medical oncology outpatient clinics and to determine whether an unplanned hospitalization was potentially due to an adverse drug event (ADE).

Materials and Methods: We identified patients who attended a medical oncology outpatient appointment from January 1st to March 31st, 2018. Medical records were examined to identify any unplanned hospital admissions between the clinic visit date and three and six months after initial clinic visit. Incidences of unplanned hospitalization were assessed to determine if an ADE potentially occurred.

Results: Data collected from 174 patients were analyzed. Over half (57 %) were female, median age was 75 years and 53 % had a favorable performance status. The most common malignancies were gastrointestinal (GI) at 31 % ($n = 54$), breast 29 % ($n = 51$), and genitourinary 22 % ($n = 37$). Seventy-two percent had advanced disease (Stage III/IV) and 61 % had systemic therapy (SACT and hormonal therapy). Polypharmacy (≥5 medications) was observed in 77 % of patients. The total number of admissions at six months was 99, with 55 % of these potentially due to an ADE. On multivariate analysis performance status ($p \leq 0.001$), monochemotherapy ($p = 0.012$), polychemotherapy ($p \leq 0.001$) and radiotherapy ($p = 0.048$), were independent predictors of unplanned hospitalization. Monochemotherapy ($p = 0.039$), and polychemotherapy ($p \leq 0.001$) were independent predictors of unplanned hospitalization due to ADE on multivariate analysis.

Discussion: We observed that older adults with cancer have a high risk of unplanned hospitalization due to ADE. Medication review as part of a CGA in newly diagnosed older adults with cancer by a clinical pharmacist is recommended. This may identify opportunities to avoid medications that could potentially lead to unplanned hospitalization.

Author Contributions:

Writing – original draft: DJW, MO'D, AMH, LJS

Writing – review & editing: DJW, LJS, MO'D, AMH, BB, HA, CG

Methodology: DJW, LJS, MO'D, AMH. Dr. Edel Burton (EB), Pharmacoepidemiologist in the School of Pharmacy, University College Cork was consulted in generating the data analysis strategy.

Data extraction: DJW, BB, HA

Data analysis: DJW, MO'D, AMH, LJS, EB

4.1 Abstract

Introduction

Geriatric oncology is a rapidly evolving field of practice, where CGA and MDT input have the potential to improve patient outcomes. Polypharmacy and PDI have been associated with an increased risk of adverse outcomes in older adults with cancer, receiving SACT.

Aim

Our aim was to assess the incidence of unplanned hospitalisation in older adults with cancer attending medical oncology outpatient clinics and to determine the prevalence of unplanned hospitalisation potentially due to an ADE.

Methods

We identified patients who attended a medical oncology outpatient appointment from January 1st to March 31st, 2018. Medical records were examined to identify any unplanned hospital admissions between the clinic visit date and three and six months after the initial clinic visit. Incidences of unplanned hospitalisation were assessed to determine if an ADE potentially occurred.

Results

Data collected from 174 patients were analysed. Over half (57%) were female, median age was 75 years and 53% had a favourable performance status. The most common malignancies were gastrointestinal (GI) at 31% (n=54), breast 29% (n=51), and genitourinary 22% (n=37). Seventy-two percent had advanced disease (Stage III/IV) and 61% had systemic therapy (SACT and hormonal therapy). Polypharmacy

(≥5 medications) was observed in 77% of patients. The total number of admissions at six months was 99, with 55% of these potentially due to an ADE. On multivariate analysis performance status OR 2.23 CI (1.41-3.69), monochemotherapy OR 3.62 CI (1.31-10.49), polychemotherapy OR 11.01 CI (3.63-37.14), and radiotherapy OR 6.22 CI (1.24-38.21), were independent predictors of unplanned hospitalisation. Polychemotherapy OR 9.05 CI (3.06-29.58) was the only independent predictor of unplanned hospitalisation due to ADE on multivariate analysis.

Conclusion

We observed that older adults with cancer have a high risk of unplanned hospitalisation due to ADE. Medication review as part of a CGA in newly diagnosed older adults with cancer by a clinical pharmacist is recommended. This may identify opportunities to avoid medications that could potentially lead to unplanned hospitalisation.

4.2 Introduction

Given the paucity of published literature highlighted in Chapter 2, and the need to assess the burden of unplanned hospitalisation in older adults with cancer identified in Chapter 3, this chapter aims to identify the incidence of unplanned hospitalisation in older adults with cancer, in the absence of a CGA, a structured medication review, or tailored frailty-related interventions.

This chapter is a single-centre retrospective study of the incidence of unplanned hospitalisation in older adults with cancer who attended a medical oncology clinic in UHW, making it the first paper to our knowledge, assessing unplanned hospitalisation due to all-cause ADE in ambulatory older adults with cancer.

Geriatric oncology is a rapidly evolving field of practice, where CGA and MDT input have the potential to improve patient outcomes (185). The optimisation of medicines in this patient cohort is an area where pharmacists may have the opportunity to reduce the incidence of unplanned hospitalisation due to ADE (115). The literature widely reports the incidence of hospitalisation due to SACT toxicity in both retrospective and prospective studies (39, 43, 125, 186). However, there are few studies with a focus on hospitalisation due to non-SACT medications in older adults with cancer. In an observational study conducted in Cork University Hospital (CUH) Ireland, Lavan and colleagues reported that more than a quarter of hospitalisations in older adults with cancer were potentially due to ADE, which included both SACT toxicity and non-SACT ADE (64). Nightingale *et al*. have also reported on the lack of data in this area, and highlighted it as a research priority for clinicians caring for older adults with cancer (187).

Polypharmacy and PDI have been associated with an increased risk of adverse outcomes in older adults with cancer, receiving SACT (9). These patients have the added complexity of potentially being offered both radiotherapy and/or surgery as part of their cancer journey (188). Each of these treatment options typically contains additional ancillary medications as part of the treatment protocol, which can add to pre-existing polypharmacy, PIM, and PDI. This in turn can lead to ADE, which may potentially result in unplanned hospitalisation (9). Pharmacist-led medication reviews have demonstrated a benefit in preventing ADE in older adults in an inpatient setting (189), and in identifying PIM and medication related issues in older adults with cancer (54, 115, 190), as well as reducing the prevalence of PIM in this cohort (191).

Many ADE that results in unplanned hospitalisation due to SACT toxicity, such as neutropenic sepsis associated with cytotoxic chemotherapy, are unavoidable (192). In contrast, ADE in non-SACT medications, in older adults have been shown to be potentially avoidable in approximately 50% of cases (193, 194).

4.3 Aim

Our aim was to assess the incidence of unplanned hospitalisation in older adults with cancer attending medical oncology outpatient clinics and to determine whether an unplanned hospitalisation was potentially due to an ADE.

4.4 Methods

4.4.1 Objectives

To conduct a retrospective analysis of older adults with cancer seen in a medical oncology outpatient setting and assess the incidence of hospitalisation due to ADE at the 6-month time point after the index clinic visit.

Secondary objectives included assessment of the incidence of hospitalisation in older adults with cancer associated with non-SACT medication and investigate any association between polypharmacy and hospitalisation.

4.4.2 Patient identification

Our institution is a tertiary cancer centre, with approximately 431 inpatient and 85-day care beds, catering for a population of approximately 500,000 people in the Southeast of Ireland at the time of conducting this research.

A report was generated using the iPMS software to identify all patients who had attended a medical oncology outpatient department (OPD) (new or review appointment) from January 1st to March 31st, 2018. The following exclusion criteria were applied: <70 years at the clinic visit date; patients who did not attend their OPD appointment; older adults with cancer not attending a medical oncology appointment were also excluded.

Ethical approval was obtained from the HSE Southeast Research Ethics Committee.

4.4.3 Data collection and extraction

The following patient data were collected from iPMS: age; gender; clinic visit date. A medical chart review was used to collect the cancer type, cancer stage and Eastern Cooperative Oncology Group performance status (ECOG) (195). A G8 score (44), was

calculated for the patient using medical notes in conjunction with clinic visit notes. Co-morbidities were identified using the patients' medical record, and the Charlson Comorbidity Index (196) was used to quantify the co-morbidity burden. Height and weight were obtained from the clinic visit notes and ideal body weight, and body surface area (BSA), using actual and ideal body weight, was calculated using the Dubois and Dubois method (197). Biochemistry results from the clinic visit were also examined and levels of alanine transaminase (ALT), aspartate aminotransferase (AST), bilirubin, and serum creatinine were obtained. Creatinine clearance was calculated using the Cockcroft and Gault equation (198). The patient's medication list was retrieved from the medical records. Non-polypharmacy was defined as <5 medications, polypharmacy was defined as ≥5 medications and hyperpolypharmacy was defined as ≥10 medications. The patient's treatment type was retrieved from either the medical notes, or the chemotherapy dispensing software from the pharmacy department. Patients were categorized into hormone/targeted therapy, monochemotherapy (one cytotoxic agent), polychemotherapy (>1 cytotoxic agent), radiotherapy (patients who received radiation alone as their treatment), surgery (patients who only received surgical intervention to treat their cancer), or supportive care/surveillance (patients who were not on active cancer therapy at the time of their clinic visit). iPMS and the medical records were examined to identify any unplanned hospital admissions between the clinic visit date and two time points, namely three and six months after initial clinic visit date. For patients who were admitted, two pharmacists examined whether an ADE was possibly associated with the admission by analysing the patient's medication list on admission. If an ADE was suspected, the summary of product characteristics (SPC) of the medication was used to see if the

ADE was listed. The likelihood of the ADE being avoidable was assessed using the method outlined by Hallas and colleagues, adapted for retrospective analysis (199). In the case of potential SACT toxicity, the Common Terminology Criteria for Adverse Events (CTCAE) v5.0 grading of the toxicity (200), and whether, as a result of the ADE, SACT dosing was subsequently altered or discontinued was also examined. Two pharmacists undertook the review of each patient's medical record independently and validated their findings. In the case of any disagreement a third pharmacist was the final arbiter.

4.4.4 Data analysis

The median age, mean, standard deviation, and range for continuous variables and the frequencies for categorical variables were calculated as part of a descriptive analysis.

A univariable logistic regression analysis was used to assess the impact of cancer site, gender, stage, comorbidities performance status, treatment type, and polypharmacy status (non-polypharmacy, polypharmacy and hyperpolypharmacy) on unplanned hospitalisation (dependent variable) and ADE (dependent variable) separately. Multivariable logistic regression analysis was then used to identify independent predictors of unplanned hospitalisation (dependent variable) and ADE (dependent variable) separately, using independent variables that were statistically significant in univariate analysis. A priori level of $p < 0.05$ was deemed statistically significant. R studio was used to conduct data analysis (201).

4.5 Results

Data collected from 174 patients who attended the medical oncology OPD were analysed. Patient demographics are summarized in Table 13. Over half (57%; n= 100) were female, median age was 75 years and 53% (n=92) had a favourable performance status (ECOG of 0-1). The most common malignancies were gastrointestinal (GI) at 31% (n=54), breast 29% (n=51) and genitourinary 22% (n=37). Seventy-two percent (n=126) had advanced disease (Stage III/IV) and 61% (n=107) had systemic therapy (SACT and hormonal therapy), with 18% (n=31) receiving polychemotherapy. Polypharmacy was observed in 77% (n=134) of patients with 37% (n=64) of these receiving hyperpolypharmacy.

Table 13: Patient demographics

n=174	n	%
Age (years)		
Mean	75.73	
Median (range)	75(70-94)	
Gender		
Male	74	43
Female	100	57
ECOG PS		
0	18	10
1	74	43
2	57	33
3	21	12
4	0	0
Unknown	4	2
Cancer Type		
GI	54	31
Breast	51	29
GU	37	22
Lung	23	13
Melanoma	4	2
CUP	4	2
Head and Neck	1	1
Cancer Stage		
I	6	4
II	42	24
III	37	21
IV	89	51
Treatment Regimen		
Hormone/Targeted therapy	46	26
Monochemotherapy	30	17
Polychemotherapy	31	18
XRT alone	10	6
Surgery alone	7	4
Surveillance	50	29
Medication Burden		
Mean number of medications (range)	12.16 (0 - 28)	
Non-polypharmacy	40	23
Polypharmacy	70	40
Hyperpolypharmacy	64	37

Key: GI – gastrointestinal; GU – genitourinary; CUP – cancer of unknown primary; XRT - radiotherapy

4.5.1 Hospitalisation

The incidence of unplanned hospitalisation at six months, as well as the prevalence of unplanned hospitalisation potentially due to ADE, and potentially avoidable ADE are outlined in Table 14. At the six-month time point, the total number of hospitalised

patients was 43% (n=75), with 56% (n=42) of all those hospitalisations potentially due to an ADE. Multiple unplanned hospitalisations were observed in 9% of patients (n=16).

Table 14: Unplanned hospitalisation and unplanned hospitalisation due to ADE

n=174	**6 months n(%)**
Unplanned hospitalisation	75 (43)
Multiple unplanned hospitalisation	16 (9)
Unplanned hospitalisation potentially due to ADE	42 (56)
Total admissions (n=99)	**n(%)**
Total number of admissions potentially due to ADE	54 (55)
Potentially avoidable admissions	18 (33)

Key: ADE – adverse drug events

The total number of admissions at six months was 99 admissions in 75 patients, with 55% (n=54) of these potentially due to an ADE (Table 14). Thirty-three percent (n=18) of these admissions were deemed to be potentially avoidable. The relationship between unplanned hospitalisation and the total number of medications a patient was taking is represented in Figure 15. Unplanned hospitalisation potentially due to ADE is shown in Figure 16, with the lower dashed line indicating the threshold for polypharmacy (5 medications), and the higher dashed line indicating the threshold for hyperpolypharmacy (10 medications).

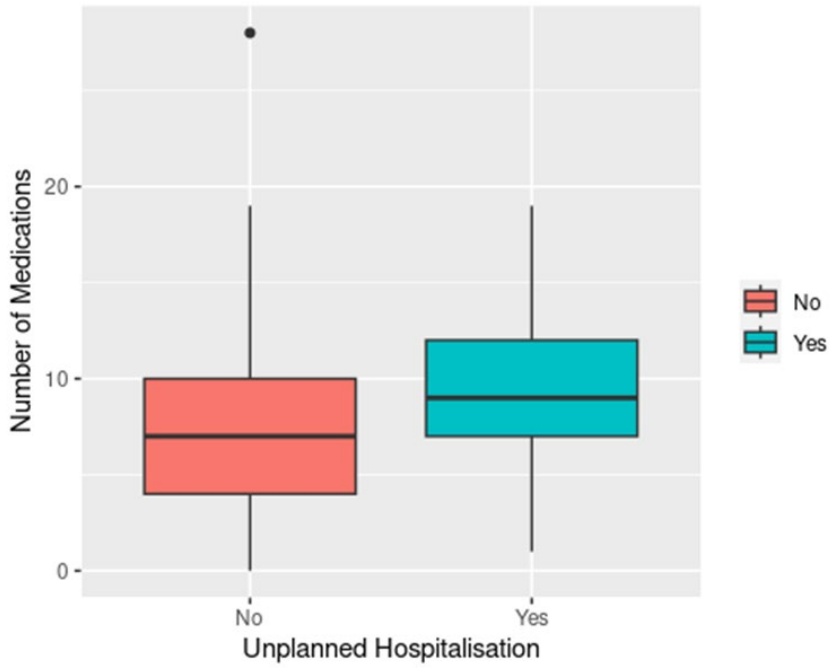


Figure 15: The relationship between unplanned hospitalisation and number of medications

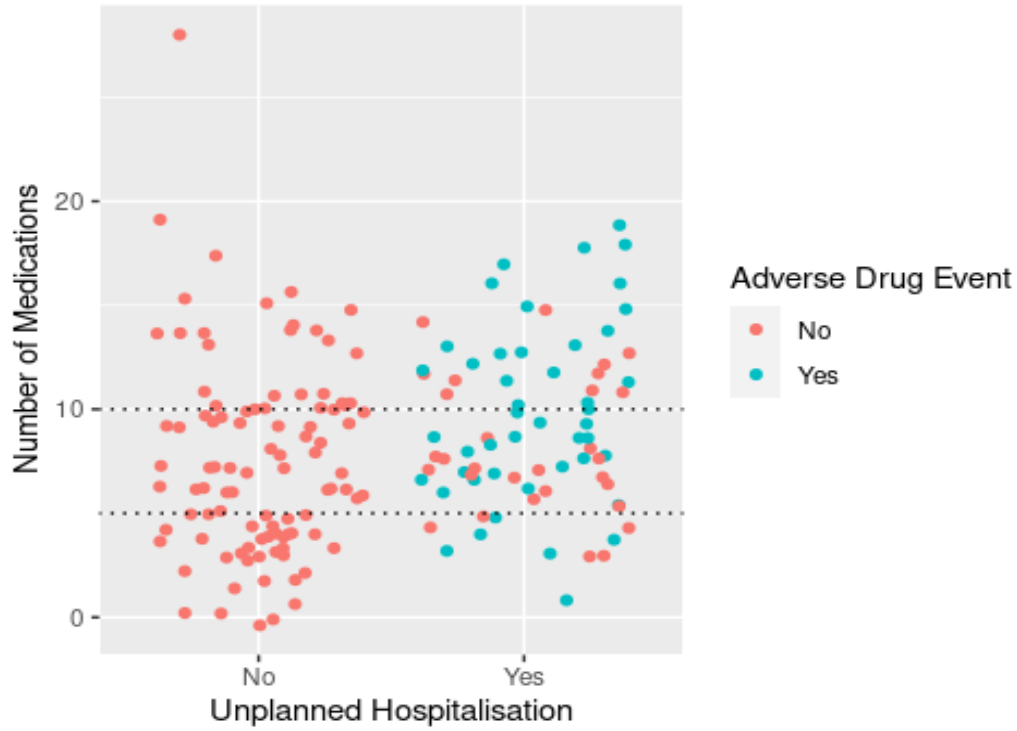


Figure 16: Unplanned hospitalisation due to ADE

4.5.2 SACT and non-SACT toxicity in hospitalised patients

Data for SACT and non-SACT toxicity are summarised in Table 15. SACT toxicity was deemed potentially responsible for 72% (n=39) of patient admissions due to ADE.

SACT was subsequently dose reduced in 28% of these patients (n=11) and discontinued in 41% (n=16) of these patients. Non-SACT toxicity was potentially responsible for 28% (n=15) of unplanned hospitalisations due to ADE.

Table 15: Data for SACT and non-SACT toxicity

Potential ADE n=54	**n**	**%**
SACT Toxicity	**39**	**72**
CTCAE Grade		
3	28	72
4	9	23
5	2	5
Subsequent dose reduction	11	28
Treatment discontinued	16	41
Non-SACT toxicity	**15**	**28**

Key: ADE – Adverse drug event; CTCAE – Common terminology criteria for adverse events; SACT – Systemic anticancer therapy

The most frequent non-SACT medications suspected of causing or contributing to an unplanned hospitalisation were proton pump inhibitors (PPIs) (n=3), NSAIDs (n=2), and antipsychotics (n=2). Medications implicated in potential non-SACT related admissions met either the STOPP or Beers criteria in 7/15 (47%) of admissions (151, 202).

4.5.3 Predictors of unplanned hospitalisation and adverse drug events

A diagnosis of lung cancer OR 2.83 CI (1.18 – 7.85), performance status OR 1.62 CI (1.27 – 2.07), monochemotherapy OR 1.29 CI (0.64 – 2.63), polychemotherapy 3.00 (1.41 – 7.13), and radiotherapy OR 2.33 CI (0.65 – 10.83) were found to be statistically significantly associated with an increased risk of unplanned hospitalisation on univariate analysis (Table 16). On multivariate analysis performance status OR 2.41 CI (1.47 – 4.12), monochemotherapy OR 4.77 CI (1.46 – 16.63), polychemotherapy OR 12.87 CI (3.34– 55.53), and radiotherapy OR 7.55 CI (1.09 – 63.37) were independent predictors of unplanned hospitalisation (Table 16).

Table 16: Univariate and multivariate analysis of unplanned hospitalisation

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	**P value**	**OR (95% CI)**	**P value**
Cancer Site				
Breast	0.34 (0.18 – 0.63)	**<0.001***	0.03 (0.01 – 0.10)	**<0.001***
Cancer of Unknown Primary	1.00 (0.12 – 8.33)	1.00		
Gastrointestinal	0.74 (0.43 – 1.27)	0.28		
Genitourinary	1.18 (0.62 – 2.27)	0.62		
Head and Neck	0.00 (NA – 165.35)	0.99		
Lung	2.83 (1.18 – 7.85)	**0.03***	0.12 (0.01 – 0.81)	**0.034***
Melanoma	0.33 (0.02 – 2.6)	0.34		
Stage	0.97 (0.88 – 1.06)	0.48		
ECOG performance status	1.62 (1.27 – 2.07)	**<0.001***	2.41 (1.47 – 4.12)	**<0.001***
CCI	2.14 (0.94 – 4.88)	0.07		
Treatment				
Monochemotherapy	1.29 (0.64 – 2.63)	**0.006***	4.77 (1.46 – 16.63)	**0.012***
Polychemotherapy	3.00 (1.41 – 7.13)	**<0.001***	12.87(3.34– 55.53)	**<0.001***
Radiotherapy	2.33 (0.65 – 10.83)	**0.01***	7.55 (1.09 – 63.37)	**0.048***
Surgery	0.17 (0.01 – 0.98)	0.56		
Surveillance/Supportive Care	0.45 (0.24 – 0.82)	0.47		
Polypharmacy Status				
Polypharmacy	0.97 (0.61 – 1.55)	**<0.001***	1.29 (0.41– 4.14)	0.06
Hyperpolypharmacy	1.00 (0.61 – 1.64)	**<0.001***	2.83 (0.96 – 8.94)	0.64

Key: ECOG PS - Eastern Cooperative Oncology Group; CCI – Charlson comorbidity index

Polychemotherapy OR 2.20 CI (1.07 – 4.86) was the only statistically significantly predictor of unplanned hospitalisation due to ADE on univariate analysis (Table 17). Monochemotherapy OR 3.67 CI (1.08 – 13.10), and polychemotherapy OR 20.30 CI (5.13 – 90.89) were independent predictors of unplanned hospitalisation due to ADE on multivariate analysis.

Table 17: Univariate and multivariate analysis of unplanned hospitalisation due to ADE

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Cancer Site				
Breast	0.21 (0.10 - 0.42)	**<0.001***	0.06 (0.06 – 0.41)	**0.008***
Cancer of Unknown Primary	1.00 (0.12 – 8.3)	1.00		
Gastrointestinal	0.32 (0.16 – 0.58)	**<0.001***	0.04 (0.002 – 0.54)	**0.019***
Genitourinary	0.68 (0.35 – 1.30)	0.25		
Head and Neck	0.00 (NA – 165.35)	0.99		
Lung	0.35 (0.13 – 0.85)	**0.03***	0.05 (0.002 – 0.08)	**0.04***
Melanoma	0.33 (0.02 – 2.60)	0.34		
Stage	0.76 (0.69 – 0.84)	**<0.001***	1.08 (0.60 – 1.96)	0.79
ECOG performance status	1.11 (0.83 - 1.48)	0.47		
CCI	1.18 (0.46 – 3.01)	0.73		
Treatment				
Monochemotherapy	0.52 (0.24 – 1.07)	**0.006***	3.67 (1.08 – 13.10)	**0.039***
Polychemotherapy	2.20 (1.07 – 4.86)	**<0.001***	20.30 (5.13 – 90.89)	**<0.001***
Radiotherapy	0.25 (0.04 – 0.99)	0.87		
Surgery	<0.001 (na – 64.97)	0.98		
Surveillance/Supportive Care	0.01 (0.01 – 0.18)	0.1		
Polypharmacy Status				
Polypharmacy	0.37 (0.21 – 0.61)	0.097		
Hyperpolypharmacy	0.52 (0.31 – 0.87)	**0.02***	1.38 (0.39 - 5.32)	0.62

Key: ECOG PS - Eastern Cooperative Oncology Group; CCI – Charlson comorbidity index

When cancer diagnosis is discounted as an independent variable, due to the broad range of diagnoses within the patient population, performance status, monochemotherapy, polychemotherapy, and radiotherapy were independent predictors of unplanned hospitalisation on univariate and multivariate analysis (Table 18).

Table 18: Unplanned hospitalisation without diagnosis as an independent variable

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	**P value**	**OR (95% CI)**	**P value**
Stage	0.97 (0.88 – 1.06)	0.48		
ECOG performance status	1.62 (1.27 – 2.07)	**<0.001***	2.23 (1.41 – 3.69)	**<0.001***
CCI	2.14 (0.94 – 4.88)	0.07		
Treatment				
Monochemotherapy	1.29 (0.64 – 2.63)	**0.006***	3.62 (1.31 – 10.49)	**0.01***
Polychemotherapy	3.00 (1.41 – 7.13)	**<0.001***	11.01 (3.63– 37.14)	**<0.001***
Radiotherapy	2.33 (0.65 – 10.83)	**0.01***	6.22 (1.24 – 38.21)	**0.03***
Surgery	0.17 (0.01 – 0.98)	0.56		
Surveillance/Supportive Care	0.45 (0.24 – 0.82)	0.47		
Polypharmacy Status				
Polypharmacy	0.97 (0.61 – 1.55)	**<0.001***	2.80 (1.02 – 8.32)	0.05
Hyperpolypharmacy	1.00 (0.61 – 1.64)	**<0.001***	1.62 (0.56– 4.96)	0.38

Key: ECOG PS - Eastern Cooperative Oncology Group; CCI – Charlson comorbidity index

When cancer diagnosis is discounted as an independent variable, polychemotherapy is the only independent predictor of unplanned hospitalisation due to ADE on univariate and multivariate analysis (Table 19).

Table 19: Unplanned hospitalisation due to ADE without diagnosis as an independent variable.

Variable	Univariate analysis		Multivariate analysis	
	OR (95% CI)	**P value**	**OR (95% CI)**	**P value**
Stage	0.76 (0.69 – 0.84)	**<0.001***	1.36 (0.85 – 2.23)	0.21
ECOG performance status	1.11 (0.83 - 1.48)	0.47		
CCI	1.18 (0.46 – 3.01)	0.73		
Treatment				
Monochemotherapy	0.52 (0.24 – 1.07)	**0.006***	2.16 (0.74 – 6.54)	0.16
Polychemotherapy	2.20 (1.07 – 4.86)	**<0.001***	9.05 (3.06 – 29.58)	**<0.001***
Radiotherapy	0.25 (0.04 – 0.99)	0.87		
Surgery	<0.001 (na – 64.97)	0.98		
Surveillance/Supportive Care	0.01 (0.01 – 0.18)	0.1		
Polypharmacy Status				
Polypharmacy	0.37 (0.21 – 0.61)	0.097		
Hyperpolypharmacy	0.52 (0.31 – 0.87)	**0.02***	1.56 (0.47 - 5.76)	0.48

Key: ECOG PS - Eastern Cooperative Oncology Group; CCI – Charlson comorbidity index

4.6 Discussion

To our knowledge, this is the first report of the incidence of unplanned hospitalisation due to any ADE in ambulatory older adults with cancer, including those on active surveillance, receiving supportive care, surgery, radiotherapy alone

and/or SACT. The prevalence of ADE in hospitalised older adults with cancer in an Irish setting has been previously reported (64), however, that study did not include an ambulatory patient cohort.

We have demonstrated that older adults with cancer have a high prevalence of polypharmacy, which is important given the association between polypharmacy and ADE in this patient cohort (47, 49, 203-205). Drug-drug interactions have also been identified as being highly prevalent and implicated in poorer outcomes in older adults with cancer (9, 206).

The independent predictors for unplanned hospitalisation we identified are unsurprising. Patients with poorer performance status, and patients receiving either monochemotherapy, polychemotherapy or radiation therapy were independently associated with an increased risk of hospitalisation.

The analysis in unplanned hospitalisation due to ADE, however, is interesting. Polychemotherapy was the only strong, independent predictor of ADE as opposed to polypharmacy status. This indicates that the nature of medication prescribed is a stronger predictor of unplanned hospitalisation due to ADE than the cumulative number of medications prescribed. SACT are deemed high-risk medication by classifications systems such as the **A**nti-infective, **P**otassium and other electrolytes, **I**nsulin, **N**arcotics, **C**hemotherapeutic agents, **H**eparin and anticoagulants (APINCH) acronym (176). Almost half unplanned hospitalisations due to ADE (47%) with a non-SACT medication, were PIM as per STOPP/START version 2 or the 2019 AGS Beers criteria (151, 202).

Our data analysis evaluates data prior to patients routinely receiving a CGA at our institution. The effective introduction of a medication review and optimisation of medication use, as part of a CGA, could prevent potentially avoidable ADE, hospitalisation due to ADE and drug-drug interactions. Potentially inappropriate medications would be identified and deprescribed where appropriate (153), using tools such as STOPP/START and Beers Criteria (151, 202). A clinical pharmacist with specialist knowledge of oncology is ideally placed to conduct these medication reviews. The SIOG NAH working group have recently published guidance on how to conduct these reviews (56).

It is recognized that the feasibility of offering a medication review, as part of a CGA, to all older adults with cancer may be challenging from a resource viewpoint (56). However, given that patients experiencing polypharmacy and drug-drug interactions are at an increased risk of adverse outcomes (49), and there is no single cut-off for polypharmacy in terms of predicting adverse outcomes with the definition of five or more medications being deemed as “reasonable” it may be tempting to propose a prioritisation strategy (166).

Where medication review as part of a CGA is being implemented and pharmacist resources are scarce, prioritising patients with hyperpolypharmacy, followed by polypharmacy and then non-polypharmacy is reasonable. However, based on our data, an alternative approach, that considers patients eligible for either monochemotherapy or polychemotherapy may be more clinically relevant, due to the increased risk for unplanned hospitalisation and unplanned hospitalisation due to ADE. The aim should unequivocally be to reach a level where all patients aged ≥70

years are offered a medication review. Our data show that a prioritisation strategy based on number of medications may in fact miss the higher-risk medications that may result in hospital-requiring-ADE, even in the context of a low number of medications, as patients still may experience an unplanned hospitalisation due to ADE in the absence of polypharmacy (Figure 16).

Our study has some limitations. It is a retrospective analysis with a relatively small sample size. A further limitation is the challenge, in a retrospective study, to accurately calculate the probability of an admission being caused by a suspected ADE, especially in relation to non-SACT medications, and to comprehensively evaluate the preventability of ADE. Ideally, this should be done prospectively (64). A limitation of retrospective studies is the inability to address confounding in the study design.

4.7 Conclusion

The data from this retrospective analysis shows that older adults with cancer receiving either monochemotherapy or polychemotherapy have a high risk of unplanned hospitalisation due to ADE. Medication review as part of a CGA in an outpatient setting for all older adults with cancer, or as part of an inpatient service for newly diagnosed older adults with cancer by a clinical pharmacist is recommended. This may identify opportunities to avoid medications that could potentially lead to unplanned hospitalisation.

This chapter demonstrates the significant impact SACT can have on an older adult with cancer, increasing the likelihood of an unplanned hospitalisation due to an ADE.

One of the key findings of this chapter is the presence of medications that meet either the STOPP or Beer's criteria in 47% of instances where a non-SACT medication

was implicated in an unplanned hospitalisation due to an ADE. This shows that these tools have a place in identifying PIM in this patient population, but a more comprehensive assessment is required to truly optimise pharmacotherapy. The need to design a medication review that is adaptive to the heterogeneous clinical circumstances of each patient is apparent, and the application of these tools alone is insufficient to prevent unplanned hospitalisation due to ADE in this patient population.

This chapter validates they hypothesis that older adults with cancer being considered for SACT are at a significant risk of ADE and supports the development of a clinical pharmacist intervention that is targeted at reducing the incidence and severity of ADE.

Chapter 5 – Development of a medication review assessment for ambulatory older adults with cancer

Peer-reviewed publications

Walsh DJ, O'Driscoll M, Sahm LJ, Meagher AM, Doblas P, McGowan E, Smith-Lehane G, Hannan M, Goggin C, Buckley C, Horgan AM. Ageing-related considerations for medication used in supportive care in cancer. J Geriatr Oncol. 2024 Jun;15(5):101760. doi: 10.1016/j.jgo.2024.101760. Epub 2024 Mar 30. PMID: 38556399.

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

Review Article

Ageing-related considerations for medication used in supportive care in cancer

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ABSTRACT

Both randomized controlled trials (RCTs) and retrospective studies have shown that a comprehensive geriatric assessment (CGA) prior to a patient commencing systemic anti-cancer therapy (SACT) results in improved quality of life outcomes and is associated with a decreased risk of grade 3–5 toxicity; however, data are lacking in relation to adverse drug events (ADE) associated with supportive care medications. Supportive care medications are prescribed as prophylactic agents in a SACT regimen, for management of treatment related toxicity and for symptoms caused by the disease itself. While necessary, the commencement of SACT and supportive medications may cause, or exacerbate, a significant drug burden in older patients, some of whom may have existing comorbidities. For many medications, older adults are underrepresented in pharmacokinetic and pharmacodynamic modelling studies. In this article we will review ageing-related changes in pharmacokinetics and pharmacodynamics, as well as how these changes may impact supportive care medications. Additional considerations for prescribing these medications in older adults with cancer, such as polypharmacy, potentially inappropriate medications, drug-drug interactions, and anticholinergic burden, as well as ageing-related considerations and recommendations for supportive care medications commonly used in older adults with cancer are also reviewed.

Manuscript author Contributions:

Writing – original draft: DJW, MO'D, LJS, AMH

Writing – review & editing: DJW, MO'D, LJS, AMH, AMM, PD, EMG, GSL, MH, CG, CB

Methodology: DJW, MO'D, LJS, AMH, MH, CG, CB

Data extraction: DJW, AMM, PD, EMG, GSL

Data analysis: DJW, MO'D, LJS, AMH, AMM, PD, EMG, GSL, MH, CG, CB

Further research presented in this chapter is being prepared for journal submission.

Thesis chapter author Contributions:

Writing – original draft: DJW, MO'D, AMH, LJS

Writing – review & editing: DJW, LJS, MO'D, AMH, BB, HA, CG

Methodology: DJW, LJS, MO'D, AMH. Dr. Edel Burton (EB), Pharmacoepidemiologist in the School of Pharmacy, University College Cork was consulted in generating the data analysis strategy. Dr. Sheena McHugh, implementation scientist was consulted on the development of the methodological strategy. Dr. Padraig Bambrick, consultant medical oncologist, and Dr. Caitríona Goggin, consultant medical oncologist, were involved in the adaptive iterative development.

Data extraction: DJW, BB, HA

Data analysis: DJW, MO'D, AMH, LJS, EB

5.1 Abstract

Introduction

To optimise medication management in older adults with cancer, an assessment composed of a structured medication review that can assess the unique needs of these patients is vital. This medication review should meet the definition of clinical pharmacy as outlined by the European Society of Clinical Pharmacy (ESCP) and should be aligned with the European Association of Hospital Pharmacy (EAHP) European statements on hospital pharmacy.

Aim

To describe the pragmatic adaptive iterative process in designing a comprehensive patient-centred medication review process in the GOAL clinic.

Methods

An adaptive, iterative approach to developing complex interventions based on the model for complex interventions described by Greenhalgh *et al*., was developed between July 2022 and October 2024. This was integrated into the framework identified by Skivington *et al*., using the ADAPT guidance was developed.

Conclusion

The adaptive, iterative methodology allows for a multi-tiered approach to medication reviews in older adults with cancer, creating a comprehensive review that is increasingly able to cater for patient heterogeneity.

5.2 Introduction

To optimise medication management in older adults with cancer, an assessment composed of a structured medication review that can assess the unique needs of these patients is vital. It is imperative that such an assessment is rooted in good clinical pharmacy practice and is built to accommodate the heterogeneity of the geriatric oncology population. The diversity within this population necessitates agility and adaptability to meet individual patient needs.

5.2.1 Clinical pharmacy in the geriatric oncology MDT

Clinical assessments by pharmacists should adhere to the principles of clinical pharmacy. The ESCP defines clinical pharmacy as a representation of both professional practice and a field of research (207). The core definition states that clinical pharmacy practice should:

i. Ensure optimal medication usage, to achieve person-centred and public health goals.
ii. Be practised solely by pharmacists.
iii. Be practised regardless of setting.
iv. Encompass pharmaceutical care but is not restricted to it.
v. Encompass cognitive, managerial and interpersonal skills related to all stages of the medicines use process, and as a field of research generates knowledge that informs clinical decision-making, health care organisations or policy design and implementation.

This definition clearly emphasises the relationship between clinical pharmacy practice, and clinical pharmacy research, and the mutualistic symbiotic relationship between the two, when they effectively complement each other (Figure 17).

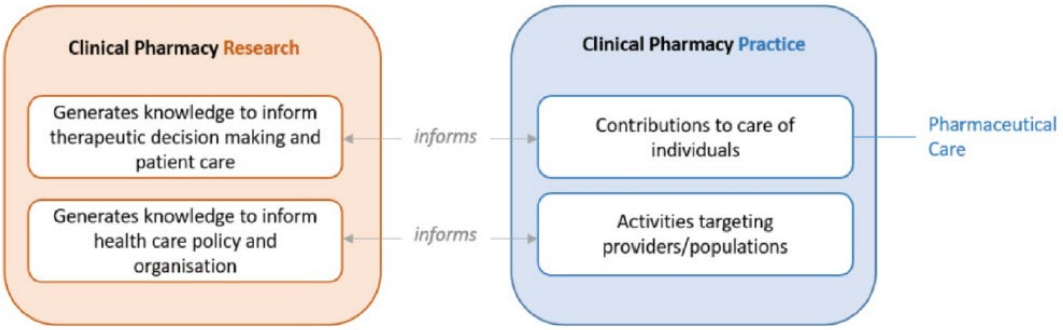


Figure 17: The relationship between clinical pharmacy research and practice, reproduced with permission from Dreischulte et al (208).

In the context of Irish hospital pharmacy, the Hospital Pharmacists Association of Ireland (HPAI) (https://hpai.ie/) endorse the EAHP European statements of hospital pharmacy (208). The statements express commonly agreed objectives which should be obtained by every European health system in the delivery of hospital pharmacy services. The statements have six sections. Section four pertains to clinical pharmacy services. There are two key statements in section four that provide justification for exploring clinical pharmacy interventions in an outpatient setting for older adults with cancer, namely statement 4.1 and statement 4.8:

Statement 4.1:

"Hospital pharmacists should be involved in all patient care settings to prospectively influence collaborative, multidisciplinary therapeutic decision-making; they should play a full part in decision making including advising, implementing and monitoring medication changes in full partnership with patients, carers and other health care professionals."

To date, the role of the pharmacist in the geriatric oncology outpatient setting has yet to be investigated. This setting allows for prospective influence over collaborative decision making, aiming to identify potential ADE, rather than responding to an ADE in a reactive manner in the inpatient setting.

Statement 4.8:

"Clinical pharmacy services should continuously evolve to optimise patients' outcomes."

In the inpatient setting, Herledan *et al*. showed a reduction in drug-related problems (DRP) in older adults with cancer who had a comprehensive medicines reconciliation and review (209). Evaluating the impact of pharmacist interventions in the outpatient setting, to prospectively reduce the incidence of DRP at admission is the natural evolution of clinical pharmacy practice in geriatric oncology, informed by clinical pharmacy research, using a prospective collaborative MDT approach.

5.2.2 Medication review processes

5.2.2.1 Definition of a medication review

The Pharmaceutical Care Network Europe (PCNE) have defined a medication review as *"a structured evaluation of a patient's medicines with the aim of optimising medicines use and improving health outcomes. This entails detecting drug related problems and recommending interventions."* (210).

This process involves assessing all prescribed, over-the-counter (OTC), and complementary medicines that a patient is taking to identify and resolve DRP.

The PCNE classifications of medication reviews depends on (i) the complexity of the patient case, and (ii) the number of sources used to conduct the medication review (Table 20). According to the European Directorate for the Quality of Medicines & HealthCare (EDQM), medication reviews are essential for ensuring the safe and effective use of medicines, particularly in complex cases such as those involving older adults with multiple comorbidities (211).

Table 20: The PCNE classification of medication review (210)

Classification	Process	Detail
Type 1: Simple review	Screening that can be conducted rapidly to determine if medicines are appropriate.	Based on the available medication history to the pharmacist. It reveals interactions, side-effects, unusual dosages and some adherence problems.
Type 2a: Intermediate review	Can be performed when the patient can contribute and is based mainly on the medication history.	It reveals interactions, manifest/actual side-effects, unusual dosages, medicine-food interactions, efficacy, problems with non-prescription medicines and, identifies the patient's experience(s) and preferences.
Type 2b: Intermediate review	Carried out when the patient is not available. If clinical and laboratory data are available, they can be combined with medication history and medical information to give a detailed review.	It is used to detect medicine interactions, some side-effects, unusual dosages, medicine-food interactions, effectiveness issues, indications without a medicine, medicines without an indication, potentially inappropriate medicines and some adherence problems.
Type 3: Advanced review	Used to assess complex cases. Carried out with the patient using the full medication history, including non-prescription medicines and herbal, complementary and other supplements and treatments together with clinical and laboratory data.	Can address adherence issues. It may also be used when the patient is not capable of full participation but has a dedicated expert carer.

The PCNE classification, and the EDQM guideline outline the advised medication review process, including the identification and prioritisation of patient groups in whom an advanced medication review (Type 3) may be beneficial. They are intended to assist pharmacists to conduct consistent and systematic medications reviews.

The potential benefits of a structured medication review, as outlined by the EDQM guidelines are:

- Enhanced patient understanding of medication use and management.
- Improved collaborative understanding between patients, prescribers and pharmacists about treatment goals.
- The creation of an opportunity to engage with and empower patients so that they have an active role in the pharmacological management of their condition(s).
- A reduction in PIM use and improved medication adherence.
- A reduction in ADE.
- Improved management of the patient's condition(s).
- A reduction in unplanned healthcare utilisation; including emergency department visits and unplanned hospitalisation.
- Improved overall health outcomes associated with optimal medicine use.

The EQDM criteria to identify patients who may benefit from an advanced medication review is outlined in Table 21. With respect to older adults with cancer, all these criteria can potentially be met (211).

Table 21: Conditions that may require an advanced medication review (211)

1. Goals of therapy not reached or maintained, including suboptimal response
2. Chronic condition associated with a high risk of unplanned hospitalisation
3. Significant changes to medicine regimen for a chronic condition, including newly prescribed medicines
4. High-risk medicines requiring close monitoring for adverse effects and/or efficacy
5. Three or more chronic medical conditions
6. Polypharmacy
7. Recent discharge from hospital or frequent unplanned hospital admissions
8. Vulnerable groups at risk of harm and/or with reduced chance of benefit from medicine use
9. Difficulty understanding and following medical advice and medicine regimens

Factors from Table 21 to be considered in a medication review:

1. Goals of therapy

The goals of therapy for older adults can change with a cancer diagnosis. For example, European Society of Cardiology (ESC) Cardio-oncology guidelines recommend the target systolic blood pressure for a cancer patient be adjusted based on prognosis (65). Therefore, a patient on chronic antihypertensive therapy, may have been meeting their therapeutic goals prior to diagnosis, and now the goals of therapy may have changed, resulting in a need to review the potential for over-prescribing antihypertensives, where they were previously appropriate. The de-escalation of antihypertensive therapy, through deprescribing, becomes an appropriate intervention, as prognosis declines.

Similarly, the Joint British Diabetes Societies (JBDS) guidelines on the outpatient management of glycaemic control in people with cancer recommend revised target blood glucose levels (212). The HSE have produced guidelines for patients with advanced cancer and a prognosis of ≥2 years which also has detailed recommendations for when to avoid or discontinue antihyperglycaemic medications, based upon (i) their prognosis, (ii) renal or (iii) hepatic function, (iv) disease site or

(v) metastatic locations (66). Therefore, patients with cancer should also have revised goals of antihyperglycaemic therapies, and their treatment adjusted accordingly, to avoid overtreatment and exposure to unnecessary ADE.

2. ***Chronic condition associated with a high risk of unplanned hospitalisation and***

5. ***Three or more chronic medical conditions***

It is estimated that two thirds of older adults with cancer have least two comorbidities, with approximately 25% having at least four comorbid conditions at diagnosis (213). Comorbid conditions increase (i) vulnerability, (ii) the risk of severe chemotherapy toxicity, and (iii) unplanned hospitalisation (214).

3. ***Significant changes to medicine regimen including newly prescribed medicines***

SACT treatment plans include new medications to treat the patient's cancer, prevent SACT ADE, and if required, new medications to control the symptoms associated with cancer (3, 134).

4. ***High-risk medicines requiring close monitoring for adverse effects and/or efficacy***

Older adults with cancer are often exposed to high-risk medications. The most common way to identify classes of high-risk medications is the APINCH acronym (176). Classes, examples of errors and ADE associated with them, and their potential use in older adults with cancer can be found in Table 22.

Table 22: APINCH medications and their potential use in older adults with cancer

High-risk medication groups	Examples of medication errors and adverse drug reactions	Example of indication in older adults with cancer
A: Anti-infective	Dosage and administration errors, therapeutic drug monitoring	Sepsis secondary to SACT (89)
P: Potassium and other electrolytes	Preparation and administration errors (e.g. intravenous infusions incorrectly prepared, concentrated solutions administered in place of diluted solutions)	Depletion secondary to nausea and vomiting (83)
I: Insulin	Dosage and administration errors (e.g. incorrect use of non-insulin syringes, misunderstanding of doses expressed in U or UI for units)	Type 3c diabetes secondary to pancreatic cancer (66)
N: Narcotics (Opioids)	Prescribing, dosage and administration errors	Cancer-related pain (86)
C: Chemotherapeutic agents	Dosage and monitoring errors (e.g. toxicity due to overdosing)	Cancer treatment
H: Heparin and anticoagulants	Dosage and monitoring errors (e.g. risk of inefficacy due to underdosing, risk of bleeding due to overdosing)	Cancer-associated thrombosis (85)

6. Polypharmacy

The incidence of polypharmacy in older adults with cancer can be up to 80% (165), with 77% of patients having polypharmacy in the retrospective study conducted in Chapter 4 (215). In a secondary analysis from the GAP70+ study, polypharmacy was significantly associated with a greater incidence of grade ≥2 toxicities and grade ≥3 toxicities (59). Polypharmacy (defined as concurrent use of ≥8 medications) was also found to be associated with a decline in activities of daily living, key indicators of functional capacity and independence (216).

7. Recent discharge from hospital or frequent unplanned hospital admissions

There are several possible reasons for an unplanned hospital admission in an older adult with cancer. Herledan *et al.,* noted the following reasons for hospital admission (209):

- Cancer treatment administration;
- Deterioration of general condition;
- Fever or infectious disease;
- Exploratory examination;
- Dyspnoea or COPD exacerbation;
- Pain management;
- Fall;
- Bowel obstruction;
- Renal failure;
- Other causes.

A systematic review in 2017 found that significant predictors of readmission in cancer patients in the US included (i) concurrent comorbidities, (ii) older age, (iii) advanced disease, and (iv) index length of hospital stay (217). Higher rates of readmission were also observed in patients with bladder, pancreatic, ovarian, or liver cancer.

8. Vulnerable groups at risk of harm and/or with reduced chance of benefit from medicine use

The potential risk of harm from SACT in older adults with cancer has been demonstrated in the literature, with 71.2% of patients in the control arm, and 50.1% of patients in the intervention arm of the GAP70+ study experiencing a grade 3-5 SACT toxicity (39), i.e. a toxicity that lead to an unplanned hospitalisation. Older adults still garner the same magnitude of benefit as younger patients from SACT, however, necessitating a need to optimise care around SACT delivery where possible.

In relation to supportive care medications, the NCCN Older Adult Oncology guideline includes a list of medications commonly used for supportive care that are of concern for older adults (90). Hshieh *et al.* examined the association of this list of medications, as well as polypharmacy (defined in this paper as ≥8 medications), with frailty and found that with each additional medication on this list, the odds of being frail, or pre-frail, increased by 65% (218).

9. Difficulty understanding and following medical advice and medicine regimens

It can be difficult for cancer patients to absorb the significant amount of information presented to them during their initial clinic visits. Conversations in relation to

diagnosis and prognosis take place alongside education on SACT and supportive care treatments. In a population survey assessing the needs of cancer patients and caregivers (n=800), 98% of patients identified the need for more information about their cancer treatment (219). In the same survey, 63% of patients and caregivers stated that they needed help in dealing with symptoms, indicating a potential lack of understanding or ability to follow supportive care regimens.

5.2.2.2 Young SIOG recommendations for patients who need a medication review

The recommended criteria for a targeted medication review for older adults with cancer, by Young SIOG, can be seen in Chapter 1, Figure 8 (56). This guideline recommends a medication review for all older adults on ≥5 medications who are starting chemotherapy. It also recommends the following criteria to trigger a follow up medication review:

- A change in renal or hepatic function;
- Unplanned hospitalisation;
- At transitions of care;
- When additional medications are added to polypharmacy.

In order to create a medication review that (i) complies with the principles of patient centred care outlined in the ESCP definition of clinical pharmacy (207), (ii) follows the key EAHP statements (208), and (iii) meets the principles outlined in the EDQM guidelines on medication review (211), the inclusion criteria outlined by Young SIOG are restrictive and will result in patients who may still benefit from a medication review not being included.

The findings from Chapter 4 (Figure 15), highlighted the need to develop an intervention for all older adults with cancer. Supporting this, are the findings by Herledan *et al.*, that 70.9% of older adults had at least one drug-related problem identified on hospital admission (209). Therefore, an intervention aimed at all older adults with cancer, irrespective of baseline number of medications and treatment intent at the outset is justified.

5.2.3 Identifying the need for complex intervention

5.2.3.1 Complex interventions

Complexity in healthcare systems is defined as "*a dynamic and constantly emerging set of processes and objects that not only interact with each other, but come to be defined by those interactions"* (220). Therefore, when developing an assessment for a diverse patient population it is important to have adaptable interventions that can be adjusted as needed (221). Complex interventions commonly occur in healthcare settings, and research related to complex interventions is backed up by an adaptive iterative approach to each phase of intervention development (222). To develop a complex intervention in older adults with cancer, it is important to conduct research that is characterised by well-developed theoretical constructs, adaptable methodology, pragmatic adaptation to emerging evidence bases, and contributes to generative learning and theoretical transferability (221).

Older adults with cancer are a unique, heterogeneous population. Ther propensity for the existence of multiple comorbidities, in addition to the variability in their treatment modalities and treatment intent affects cancer outcomes (223). It is

therefore reasonable to respect this heterogeneity and it's potential to affect the outcome of interventions based on a medication review.

The identification of the Young SIOG guideline as a foundation for an assessment, and the recognition of the need to adapt this for this population, using the core principles of medication review outlined by the PCNE and EDQM is in line with the ADAPT guidance (224). This outlines a framework for taking a pre-existing intervention and adapting it for the needs of the research being conducted. Adaptation is defined as the *"intentional modification(s) of evidence informed intervention"* which can include both planned, and responsive adaptations (224).

Context is a critical concept when adapting a complex intervention. Context in the field of implementation science has been described as *"a set of characteristics and circumstances that consist of active and unique factors, within which the implementation is embedded*" (225). Therefore, context does not act as a benign environment, but rather a direct influencer of interventions. While the evaluation of the role of a clinical pharmacist in an outpatient geriatric oncology clinic is not implementation science, this definition of context in research of complex interventions is relevant. The intervention must adapt to the context of the patient, and the nature of their cancer. Cancer is indeed active and unique to each patient, and therefore, an approach that consists of an individualised adaptive analysis of medications within that heterogeneity is logical.

5.2.4 Pragmatic clinical research

The need to use an adaptive iterative approach to develop a complex intervention that is based on patient-specific context aligns with the theory of pragmatic clinical research (226).

Pragmatic research evaluates clinical interventions differently to conventional efficacy research. In linear research models, where context and conditions are controlled, a clinical intervention is assessed in ideal circumstances, as opposed to pragmatic methodologies, that examine the impact of clinical interventions in the clinical care setting appropriate for the intervention (226).

Pragmatic research in the context of cancer care is not a novel concept. Designing interventions that have a direct applicability to clinical practice is highly desirable, particularly in patient populations that are traditionally under-represented in standard efficacy studies, such as older adults with cancer. Indeed, Stewart *et al.* describe a "*hybrid pragmatic clinical trial*" as one that merges rigorous scientific methodologies with pragmatic characteristics to enhance the applicability of the trial design in the clinical setting (227).

The key differences between trials with explanatory features compared to pragmatic features are described in Table 23, which has been adapted from Sankar *et al.* (228).

Table 23: Explanatory versus pragmatic research in geriatric oncology

Study features	Explanatory research	Pragmatic research	Pragmatic research relevance to geriatric oncology
Setting	Well-resourced ideal setting	Everyday clinical practice	Outpatient geriatric oncology clinic
Participants	Highly selective inclusion/exclusion criteria	Minimal selection criteria	All patients with frailty and cancer included
Intervention	Strong adherence enforced, stringent application	Flexible, allows for modifications as would be the case in everyday practice	Adaptive to patient goals of care and complex comorbidities
Outcomes	Often surrogates (eg, objective response rate, progression-free survival)	Relevant to participants and health care providers (health-related quality of life)	Aim to reduce unplanned hospitalisation and unplanned hospitalisation due to ADE
Relevance to practice	Indirect – setting and participants not always reflective of real-world practice	Direct – conducted in real-world clinical practice setting	Assesses pharmacist interventions and multidisciplinary team impact

Sethuraman's description of clinical pragmatism strengthens the case for this approach in the context of geriatric oncology, where evidence based medicine, patient sense of coherence and pragmatic ethical decision-making leads to optimal patient care (229).

Clinical pragmatism combines clinical practice guidelines, protocols and clinical decision-making tools as a starting point. Incorporating the clinician's expertise and experience, while considering the patient's goals of care to optimally utilise those tools provides true evidence-based medicine, as outlined in Figure 18.

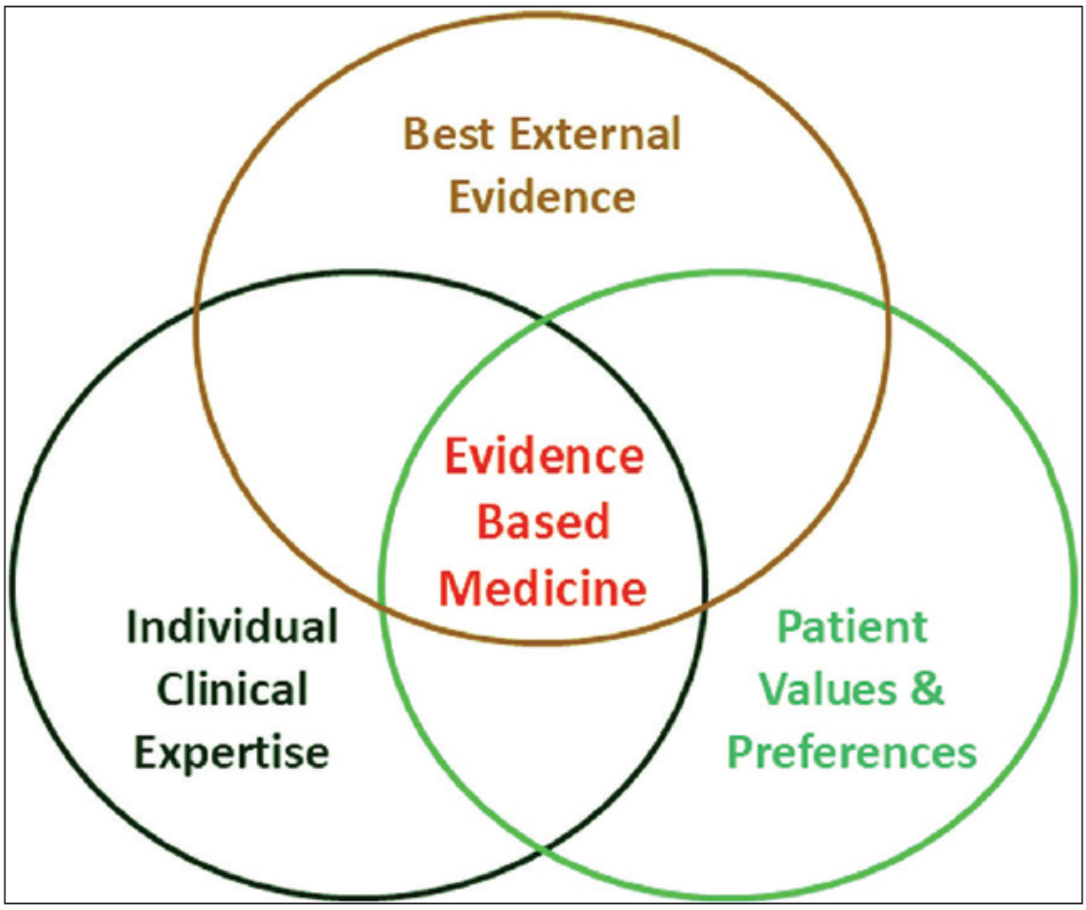


Figure 18: Evidence based medicine in clinical pragmatism (reproduced with permission from Sethuraman (230))

A patient's sense of coherence is their perception of comprehension, meaningfulness and manageability with respect to their own life. For an older adult with cancer to feel positive about their care, they must:

i. Comprehend their disease and prognosis;

ii. Understand their options for managing their disease;

iii. Be enabled with coping strategies to address their healthcare needs.

From the perspective of developing a medication review for this patient population, a pharmacist must therefore:

i. Understand the patient's comprehension of their disease and prognosis in a holistic manner;

ii. Find an evidence-based and pragmatic care plan;

iii. Agree to the care plan with the patient and/or their carers.

This is a core principle of clinical pragmatism, made necessary by the complexity of healthcare for the older adult with cancer. Clinical pragmatism enables evidence based medicine to be incorporated into a patient's sense of coherence, therefore leading to a intervention that is less confined by rigid principles and is adaptively built around the care needs of the patient (229).

While the Young SIOG guideline inclusion criteria may be restrictive, and therefore more emblematic of an efficacy intervention than a pragmatic one, it forms a strong basis for meeting the needs of an advanced medication review, as per the EDQM guidelines (56, 211). Therefore, this guideline forms the baseline to design an intervention around. and pragmatically adapt for, a heterogenous patient population.

5.3 Aim

To describe the pragmatic adaptive iterative process in designing a comprehensive patient-centred medication review process in the GOAL clinic.

5.4 Methods

5.4.1 Development phase

The initial development of the medication review intervention was structured around the clinic operations and based on the Young SIOG guidance for medication review, as well as the CGA toolkit produced by the British Geriatrics Society (19, 56, 230).

Clinic operations

The clinic operations in July 2022 consisted of an afternoon clinic where a patient underwent a CGA by an Advanced Nurse Practitioner (ANP), followed by a medical oncologist review, and was then educated on their treatment decision by a clinical nurse specialist. Integrating the clinical pharmacist into the clinic was a challenge therefore due to a) a lack of physical space and infrastructure in the clinic, and b) a short window of time to complete a comprehensive advanced medication review (Figure 19).

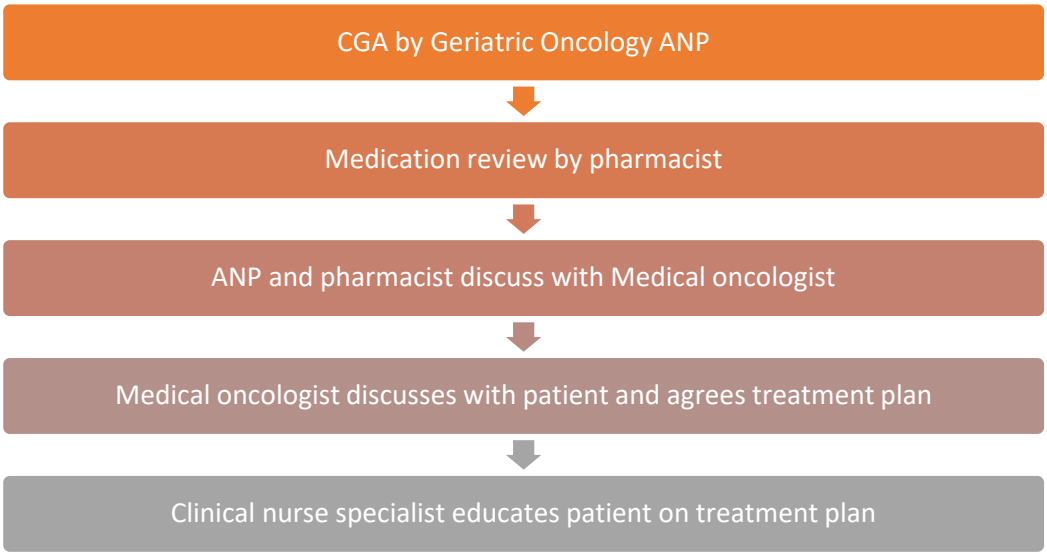


Figure 19: Baseline clinic operations July 2022

The list of resources used to inform interventions during the development phase can be seen in Table 24.

Table 24: Baseline medication review intervention resources

Domain	Resource
General	Medication-specific SPC
	BNF (231)
SACT	NCCP Protocols
Supportive care	NCCP Protocols
Drug interactions	Stockley's drug interaction checker (232)
	Cancer-drug interactions (233)
PIM	STOPP version 2 (151)
	BNF (231)
	NEWT Guidelines (234)
	MSKCC About Herbs
Prescribed medications	START version 2 (151)
ACB	ACB Calculator (177)
	CRIDECO Anticholinergic Load Scale (117)

Key: SACT – Systemic Anticancer Therapy; SPC – Summary of Product Characteristics; BNF – British National Formulary; NCCP – National Cancer Control Programme; PIM – Potentially Inappropriate Medication; STOPP – Screening Tool of Older Person's Prescriptions; MSK – Memorial Sloan Kettering Cancer Centre; ACB – Anticholinergic Burden; CRIDECO – CRIbado de DEterioro COgnitivo para promover ciudades neuroprotegidas

This resulted in the medication review comprising (i) medicine reconciliation, (ii) drug interaction check, (iii) screening for PIM and (iv) a calculation of ACB. Patient notes, outpatient letters, and the patient's referral documentation to medical oncology were available to the pharmacist, to compile a medication history prior to the clinic visit.

Tools to be used:

Completion of the medicine reconciliation involved a screening of recent outpatient letters, discharge prescriptions and the patient's dispensing record from their community pharmacy in the 6 months prior, via the Primary Care Reimbursement System (PCRS). This was then reconciled with the patient and/or their carer during the in-person medication review.

Drug interactions were assessed using Stockley's Drug Interaction Checker (232), accessed via Medicines Complete, through a HSE library subscription. Cancer drug

interactions (Radboud UMC and University of Liverpool) was also used for patients commencing SACT as a cross reference (233), and their NCCP protocol checked for clinically relevant drug-interactions.

To assess for PIM, current medications were matched to an indication via the patient's medical history. All medication and dose appropriateness were then assessed based on the patient's biochemistry, including renal and hepatic function. Finally, STOPP/START v2 was used to screen for PIM (151). Anticholinergic Burden was initially assessed using the ACB calculator (177).

The baseline review designed for implementation in clinic is visualised in Figure 20. After this assessment, any interventions that were recommended were discussed with the medical oncologist and ANP in clinic and an outpatient clinic letter with a report sent to the patient's GP (Appendix 5).

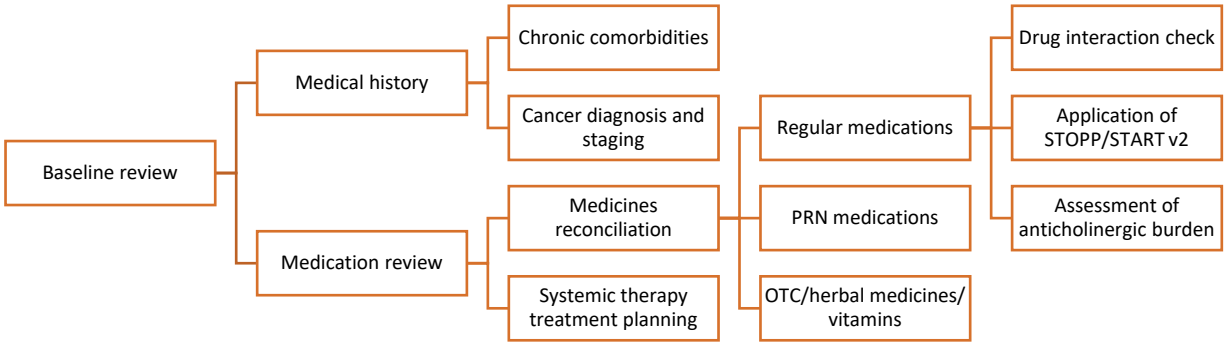


Figure 20: Baseline medication review process

The baseline medication review was introduced to the GOAL clinic, and the intervention was iteratively adapted in line with the ADAPT framework (Figure 21).

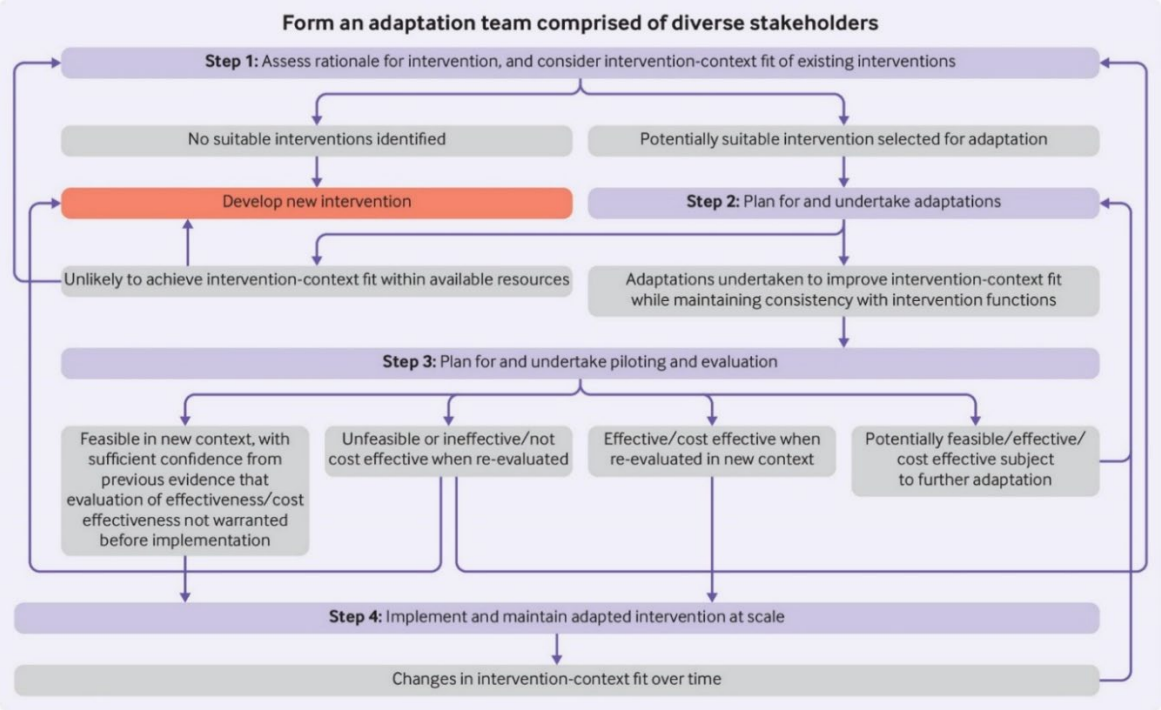


Figure 21: The ADAPT framework, reproduced with permission from Moore et al. (225)

5.4.2 Early introduction phase

The hallmarks for pragmatic clinical trials that were adapted for patients attending the GOAL clinic are shown in Figure 22.

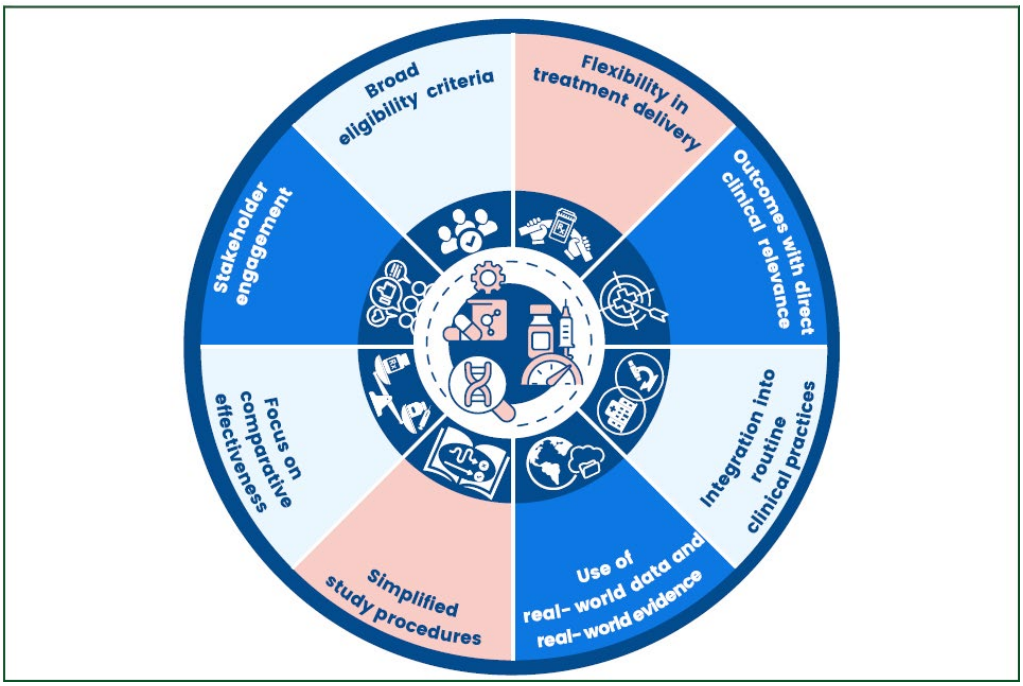


Figure 22: Hallmarks of pragmatic clinical trials in hybrid designs. Reproduced with permission from Stewart et al (228).

Hallmarks of pragmatic clinical trials:

Adapting these hallmarks for an intervention for older adults with cancer in the GOAL clinic was be done by:

Broadening eligibility criteria

Including all patients for a medication review, even in the absence of polypharmacy, and patients who may not be suitable for SACT.

Flexibility in intervention delivery

Adapting the interventions by referring to clinical practice tools and guidelines specific to the context of the patient, at an individual level, integrating flexibility into the intervention delivery.

Outcomes with direct clinical relevance

A potential reduction in (i) unplanned hospitalisation and (ii) unplanned hospitalisation due to ADE.

Integration into routine clinical practice

Designing an intervention that is tested and adapted within the real-world clinical setting ensures feasibility for integration into routine clinical practice, in geriatric oncology.

Use of real-world data and real-world evidence

Conducting the research in the real-world setting ensures the evidence generated informs real-world clinical practice, in line with the ESCP definition of clinical pharmacy (207).

Simplified study procedures

Patients received a medication review as part of their visit to the GOAL clinic. They were offered the opportunity to consent to taking part in the study, their care received was not affected by participation status.

Focus on comparative effectiveness

Chapter 4 enabled a comparison of patients before the GOAL MDT was active.

Stakeholder engagement

Each patient and/or carer took an active part in the medication review process through a clinic visit. The MDT members were consulted on each patient via presentation at an MDT meeting, with the methods of medication review discussed for each patient.

The initial adaptation team consisted of the pharmacist, and the other GOAL MDT members, namely a consultant medical oncologist, ANP and clinical nurse specialist. Section 5.4.1 outlined the first round of undertaking of the ADAPT framework.

The intervention outcomes were discussed directly with the medical oncologist and ANP. Amendments to SACT and supportive care were made by the medical oncologist and ANP (registered non-medical prescriber). Interventions related to chronic medications were either implemented by the medical oncologist, if they felt it was within their clinical remit, or a report was sent to the patient's GP and/or other services directing their therapy. The structure and layout of the report can be found in Appendix 5.

Feedback was received from consultant medical oncologists, GPs and hospital pharmacists in the early intervention phase. This predominantly related to the volume of information contained withing the report. This resulted in the move from dissemination of the intervention outcomes via a comprehensive report to a more concise outpatient letter. The outpatient letter template can be found in Appendix 6.

GPs reported that this letter offered improved clarity over who was responsible for what intervention. Medical oncology colleagues felt this letter suited the patient follow up more, as it mirrored the format for documenting treatment decision making in relation to SACT. When the outpatient letter template was discussed with hospital pharmacist colleagues, they felt the outpatient letter gave greater clarify to the medication related problems identified for the patient and made the medicines reconciliation easier to find in the event of an admission. Indeed, this letter was a time-stamped source for medicines reconciliation in the event of an unplanned hospitalisation.

In August 2022, a Geriatric Oncology Fellow and a registered dietitian joined the MDT, and the adaptation team. This increased the capacity of the clinic, allowing for additional patients to be seen, but did not allow for the expansion of the medication review as the same constraints remained.

5.4.3 Continuous evaluation of service

From the baseline evaluation, the service was continually adapted iteratively. When a clinical scenario specific to a patient was encountered, clinical practice guidelines were consulted. If a pharmacological intervention was recommended, it was

reviewed in conjunction with the patient-specific factors such as concomitant medications, renal and hepatic function, contraindications, comorbidities and patient goals of care. This dynamic process is outlined in Figure 23.

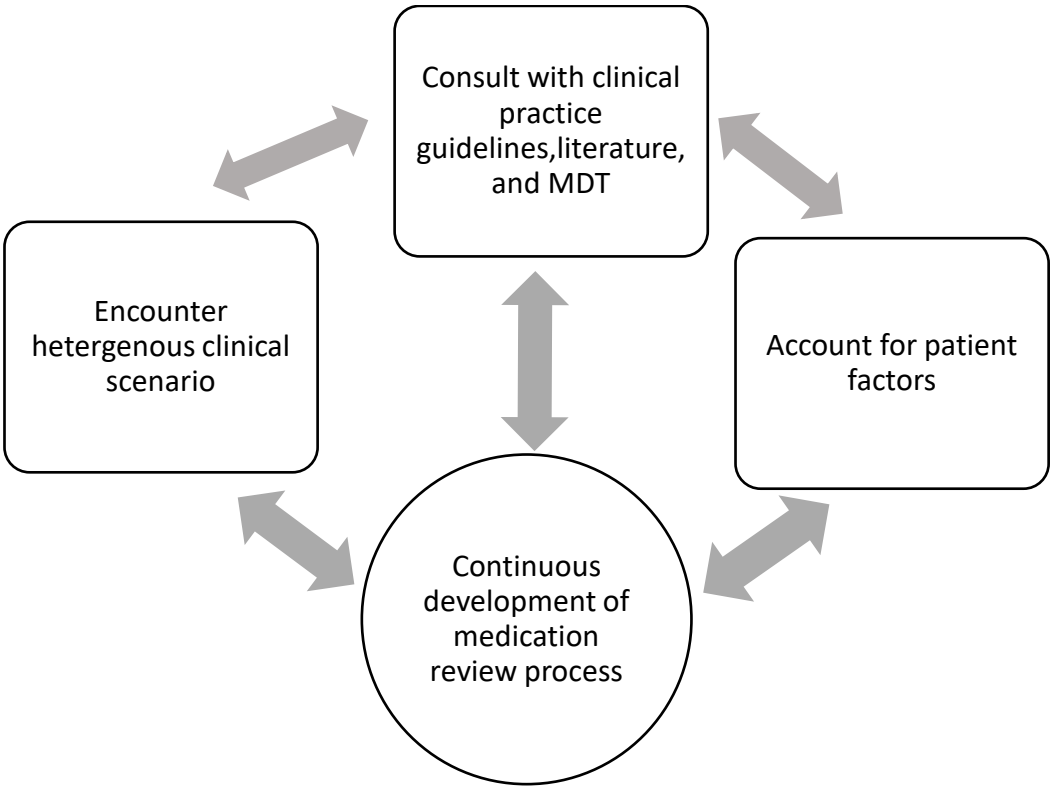


Figure 23: Continuous evolution of medication review process

Additionally, feedback from stakeholders, including GPs, consultants from other specialties and community pharmacists, influenced how the interventions were disseminated. As this process continued, the medication review intervention grew in its complexity, clinical specificity, and became increasingly pragmatic, incorporating new resources cumulatively over time to develop a bank of resources that could be used when a clinical scenario presented. This process was nonetheless limited by the clinic operations until the clinic was moved to a different location in April 2023, with additional clinical space. This provided the adaptation team with an opportunity to

review overall clinic operations, and to assess how the medication review might evolve.

5.4.4 Two-day model of care

The operational changes to the clinic, in April 2023, led to the MDT deciding to adopt a two-day model of care. This move made increasing sense as the MDT would now be joined by a consultant geriatrician and an occupational therapist. The new two-day model is outlined in Figure 24.

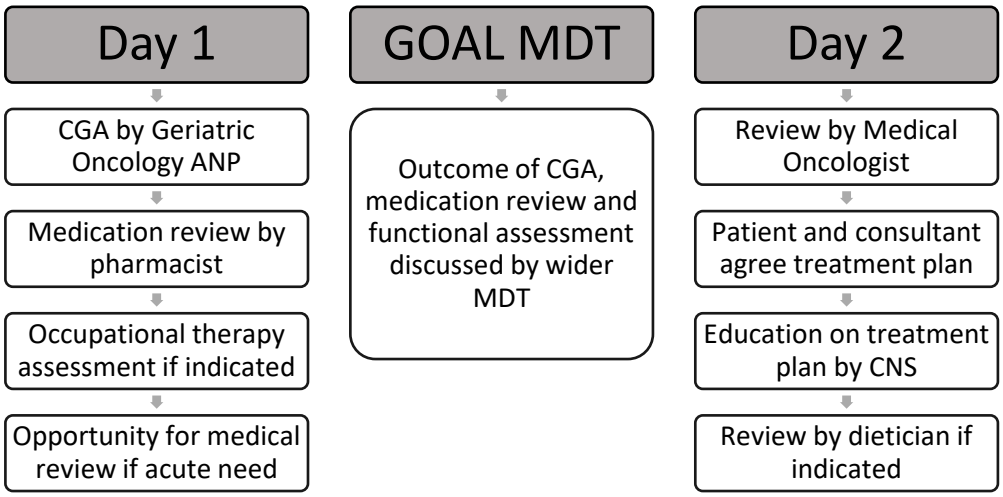


Figure 24:Two-day model of care in the GOAL clinic

The new two-day model was introduced in June 2023. A second medical oncologist joined the MDT in October 2023. The move to a two-day model facilitated dedicated pharmacist space in the clinic, meant increased time for the face-to-face medication review and allowed for a comprehensive medication review in preparation for the MDT. This increased in time allowed for the introduction of an assessment of medication adherence, patient swallow status, and FRIDs. The increased time in face-to-face consultation also enabled greater discussions in relation to cancer symptoms, improving the capacity to assess for palliative-focused interventions.

The primary focus of pharmacists is dependent on the clinical context of the patient. In this setting, a pharmacist assesses medication through the prism of geriatrics, oncology and palliative care, incorporating the principles of one, or more of these disciplines when determining the appropriate tools and guidelines to inform the medication review process. This process is outlined in Figure 25.

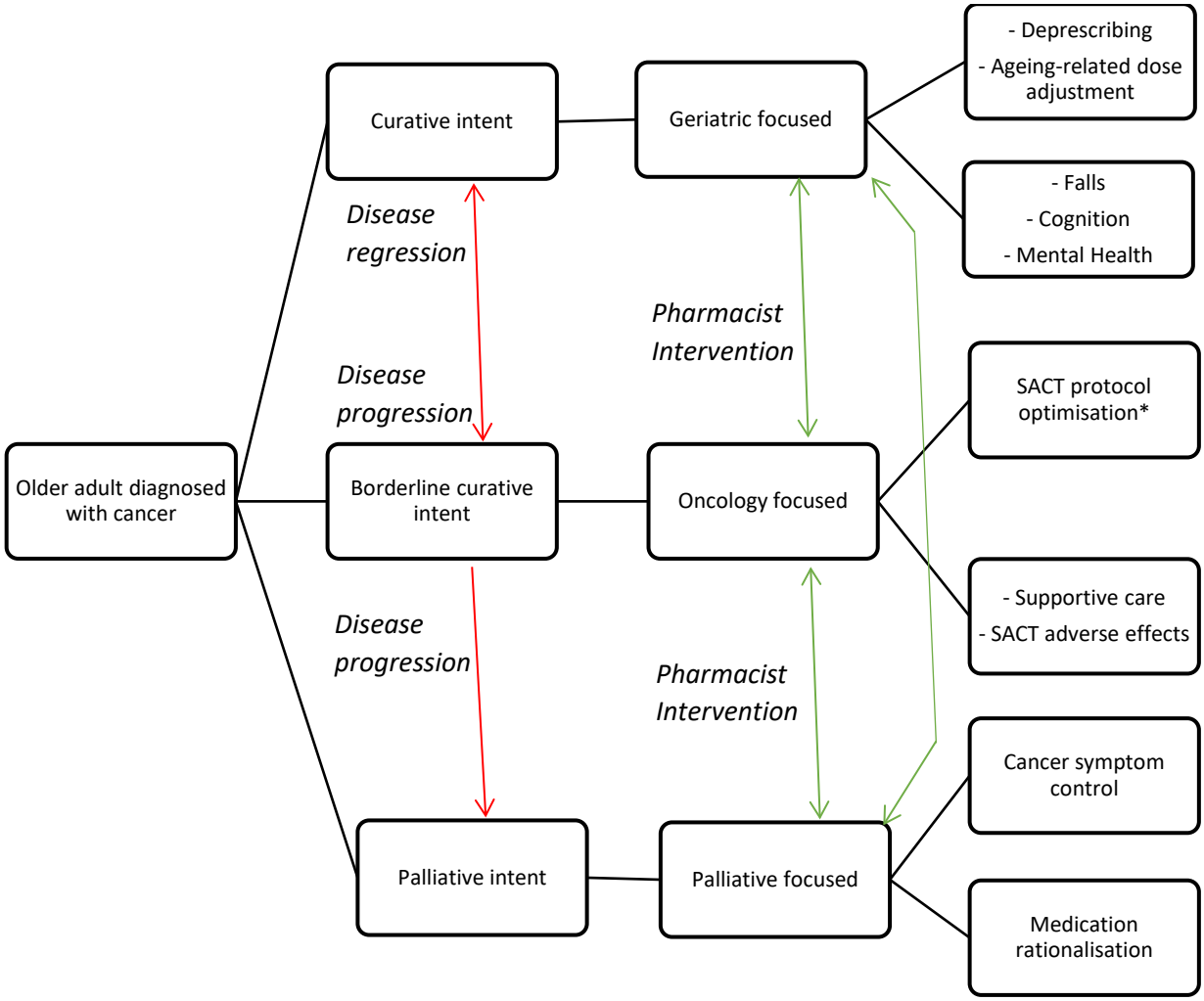


Figure 25: The dynamics of a medication review in Geriatric Oncology

Curative intent

For patients with curative disease, the pharmacist focused on the geriatric components of care, optimising the patient's medication management of their

chronic diseases to prolong life independent of cancer. The pharmacist would also have an oncology focus, assessing SACT, supportive care medications and medications used in the treatment of SACT related ADE. These patients have been undergoing neoadjuvant therapy prior to surgery, adjuvant therapy postoperatively, or using SACT as a primary mode of cancer cure.

Borderline curative intent

In the borderline curative setting, the pharmacist focused on oncologic care to begin with, as these patients require SACT to be efficacious at tumour regression to facilitate curative surgical and/or radiotherapeutic intervention. Therefore, optimising SACT is the focus, until the patient is either a curative candidate, or progresses to palliative intent.

Palliative intent

Patients with incurable cancer are treated with palliative intent, and this may or may not involve SACT. Therefore, the primary focus is on cancer symptom control for quality of life and medication rationalisation matched to frailty and estimated prognosis.

This is a dynamic process, where two similar patients form a geriatric perspective may be curative, borderline or palliative depending on their site of primary tumour, the presence of metastatic disease, and most importantly, the treatment goals of the patient. Therefore, there are scenarios where a pharmacist may conduct a medication review in this setting using just one, two or at times all three principles of geriatric, oncology and palliative care clinical practice.

This agility ensures a pragmatic clinical approach to a medication review, that accounts for evidence-based practice, and the patient's needs (207, 208, 210, 211).

5.4.5 Changing GOAL clinic structure and adapting medication review

Upon moving to a two-day model, a more in-depth patient medication management was feasible. The list of resources used to inform interventions after transitioning to a two-day model can be seen in Table 25.

Table 25: Resources used in the medication review intervention in the two-day clinic model

Domain	Resource		
General	Medication-specific SPC	GOAL MDT consensus expert opinion	BNF (231)
SACT	NCCP Protocols	British Columbia Cancer Association drug monographs	ESC Cardio-oncology guidelines (65)
	Administration of oral systemic anticancer therapy (SACT) via enteral feeding tubes and other methods Guidance on the use of oral SACT for patients unable to swallow (235)	Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. (70)	International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (236)
Supportive care	NCCP Protocols	ASCO supportive care guidelines	UHW antiemetic guidelines
	ESMO supportive care guidelines	EviQ supportive care guidelines	GOAL MDT consensus expert opinion
	NCCN Supportive Care guidelines	British Columbia Cancer Association drug monographs	Palliative Care Formulary (237)
	ESC Cardio-oncology guidelines (65)	Haematology consult	UK CAT guidelines (238)
	Canadian CAT guidelines (239)	ESMO CAT guidelines (85)	NICE guidelines Type 2 Diabetes (240)
	Role of direct oral anticoagulants in the treatment of cancer-associated venous thromboembolism: guidance from the Scientific and Standardization Committee of the ISTH (241)	Management of cancer-associated thrombosis in patients with thrombocytopenia: guidance from the Scientific and Standardization Committee of the ISTH (242)	Symptomatic Treatment of Cough Among Adult Patients With Lung Cancer CHEST Guideline and Expert Panel Report (243)
	Literature on steroid-sparing antiemetic regimens (179-181)	HSE Diabetes care towards end-of-life clinical care recommendations (66)	
	Diabetes UK End Of Life Guidance For Diabetes Care (244)	JBDS 15 Inpatient Care of the Frail Older Adult with Diabetes (245)	JBDS 17 The management of glycaemic control in people with cancer (212)
Drug interactions	Stockley's drug interaction checker (232)	Credible meds (246)	BNF (231)
	Cancer-drug interactions (233)	MedSafetyScan (247)	Martindale ADR Checker (248)
	Memorial Sloan-Kettering Cancer Centre (MSKCC) About Herbs (249)		ESC Cardio-oncology guidelines (65)
PIM	STOPP version 2 (151)	STOPP version 3 (7)	2023 AGS Beer's Criteria (8)
	BNF (231)	ThinkCascades (113)	NEWT guidelines (234)

Domain	Resource		
	MSKCC About Herbs (249)	STOPPFrail version 2 (88)	STOPPFall (105)
	Drug Administration via Enteral Feeding Tubes (250)	National Health Service (NHS) Scotland Polypharmacy Guidance (118)	Scottish Palliative Care Guidelines (251)
	Renal Drug Database (252)	National Prescribing Service Guidelines for switching between specific antidepressants (253)	Palliative Care Formulary (237)
	European Society for Clinical Nutrition and Metabolism guidelines on nutrition in cancer patients (254)	ESC guidelines for the management of elevated blood pressure and hypertension (255)	Orthostatic Hypotension in Adults With Hypertension: A Scientific Statement From the American Heart Association (256)
	ESC guidelines for the management of atrial fibrillation (257)	National Cancer Institute Guidelines on taking medications after total gastrectomy (258)	
Potentially omitted medications	START version 2 (151)	Palliative Care Formulary (237)	Our Lady's Hospice and Care Services Palliative Meds Info (259)
	Scottish Palliative Care Guidelines (251)	Global Initiative for Chronic Obstructive Lung Disease guidelines (260)	
	National Osteoporosis Guideline Group Osteoporosis Guidelines (261)	NHS Scotland Polypharmacy Guidance (118)	START version 3 (7)
	Cancer Anorexia-Cachexia Syndrome updated guidelines (81, 262)		NCCN Palliative Care Guidelines (263)
ACB	ACB Calculator (177)	CRIDECO Anticholinergic Load Scale (117)	

Key: SACT – Systemic Anticancer Therapy; SPC – Summary of Product Characteristics; GOAL – Geriatric Oncology Assessment and Liaison; MDT – Multidisciplinary Team; BNF – British National Formulary; NCCP – National Cancer Control Programme; ESC – European Society of Cardiology; ESMO – European Society of Medical Oncology; ASCO – American Society of Clinical Oncology; UHW – University Hospital Waterford; CAT – Cancer Associated Thrombosis; UK – United Kingdom; ISTH – International Society on Thrombosis and Haemostasis; HSE – Health Service Executive; JBDS – Joint British Diabetes Society; ADR – Adverse Drug Reaction; AGS – American Geriatrics Society; PIM – Potentially Inappropriate Medication; STOPP – Screening Tool of Older Person's Prescriptions; MSK – Memorial Sloan Kettering; START - Screening Tool to Alert doctors to Right Treatment; NHS – National Health Service; NCCN – National Comprehensive Cancer Network ACB – Anticholinergic Burden; CRIDECO – CRIbado de DEterioro COgnitivo para promover ciudades neuroprotegidas

The adaptive iterative process led to a more complex and advanced intervention from the baseline medication review from July 2023 until October 2024 (Figure 26).

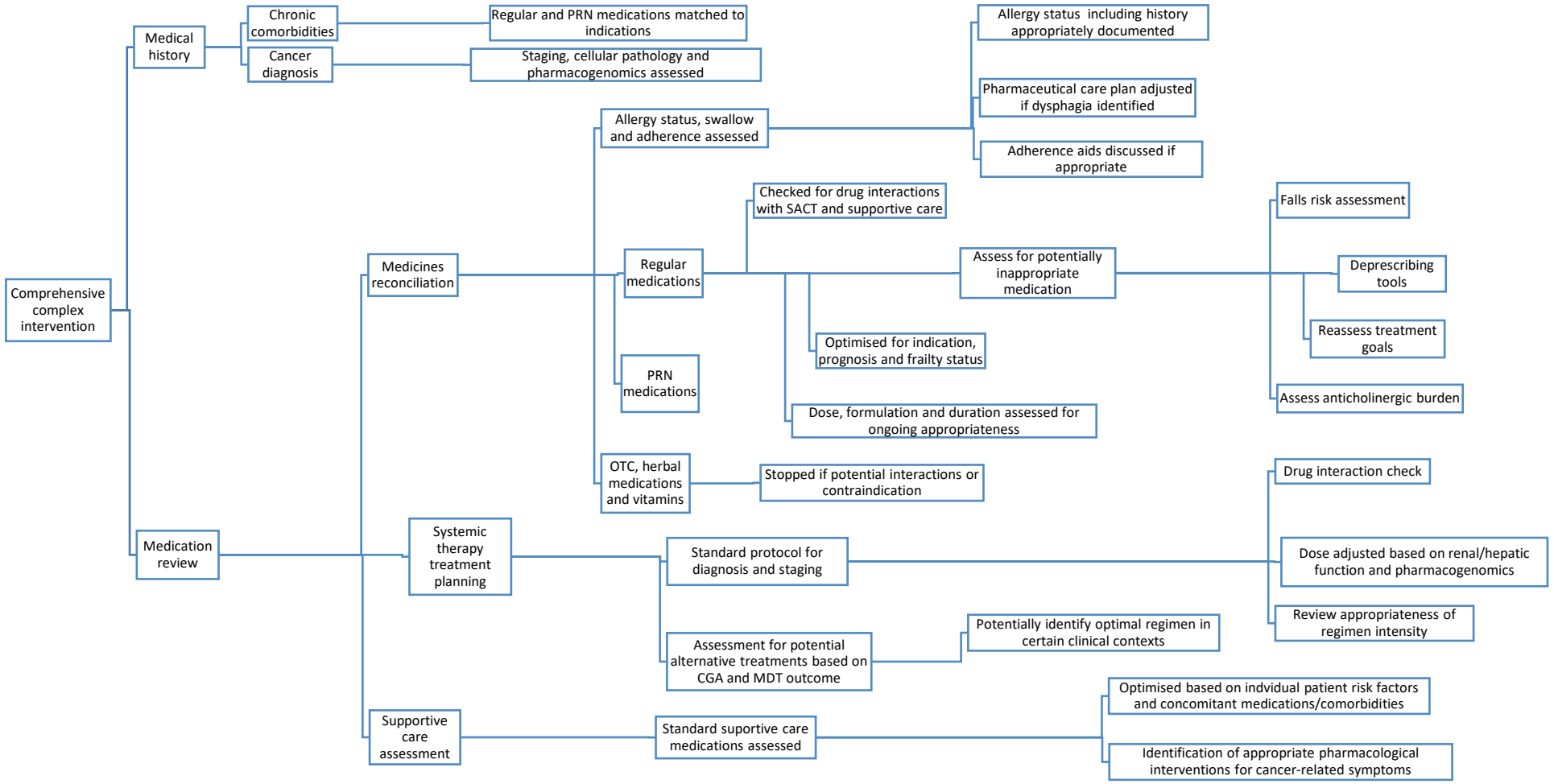


Figure 26: Iteratively adapted medication review developed from Figure 20 Key: PRN – Pro re nata; OTC – over-the-counter; SACT – Systemic anticancer therapy

5.5 Discussion

The baseline intervention was successful as a scoping exercise to test the capacity for a pharmacist to integrate into the MDT. Using previous guidance as a starting point created the foundation required to iteratively adapt this intervention (56, 230).

This approach has successfully led to the real-time continuous implementation of the cycle used by the ESCP to define the interlinked relationship between clinical pharmacy practice and clinical pharmacy research (207). By using clinical pharmacy research at an individual level, a continuous cumulative accrual of knowledge is generated to inform clinical decision-making in the MDT/clinic setting.

This approach meets the key EAHP guidance by placing a pharmacist in a setting where they are proactively involved in therapeutic decision making, in addition to engaging in a process of continuous improvement and evolution (208).

Whilst the baseline review met the majority of PCNE, EDQM and Young SIOG criteria for an advanced medication review (56, 210, 211), there were some limitations due to the clinic context at the time.

The pivot to a two-day model, with unrestricted time allocated for an advanced medication review allowed for a progressively complex intervention that was more patient centred, in the clinic. The pragmatic methodology allowed for the development of an intervention appropriate to the changing context within which the medication review was being conducted. The inclusion of a weekly MDT in addition to the medication review allowed for a widening of clinical practice guideline and resource utilisation.

The use of the ADAPT guidance in an iterative case-by-case model enabled each MDT member to have input into the resources and methods used to optimise medications in each individual way in a manner that aligned appropriately with pragmatic clinical practice (224), incorporating elements of evidence-based medicine with patient sense of coherence.

The pragmatic clinical practice approach in dealing with the complexity of the interventions required also allowed for a fluid medication review process as per Figure 26. This enabled the medication review intervention to adapt to the patient's needs and goals of care, rather than trying to fit them into a rigidly structured intervention. Recommendations were not implemented through the austere application of a clinical practice guideline, but instead discussed in a MDT setting, that accounted for patient sense of coherence, treatment burden and pharmacological appropriateness.

Future perspectives

This intervention has been developed for newly diagnosed patients, or patients who have progressive disease, being referred to the GOAL clinic. These patients are mostly ambulatory and being considered for SACT. This intervention could be adapted and streamlined to facilitate a relatively rapid follow up medication review in an outpatient clinic setting for review patients who are undergoing SACT, with a greater emphasis on assessing SACT tolerability, toxicity, and adherence to supportive care.

Additionally, this intervention would need to be adapted for the inpatient setting, where patients are acutely unwell, prioritising the acute cause of admission, and assessing for potentially medication-related factors that led to the admission.

Patients who are electively admitted for diagnostics, or for SACT could receive an intervention based on this model, provided their admission what a short-term admission for procedural activities only, such as central-venous access device insertion, SACT administration and diagnostic tests.

The perioperative care of older adults with cancer would benefit from a medication review intervention similar to the intervention developed, however greater emphasis would need to be placed on the principles of perioperative medication management, anaesthesia and adaptations to standard of care being individualised may involve a more complex MDT discussion, including surgeons and anaesthetists. This intervention may be less feasible in clinical practice in this setting.

Limitations

A limitation of this intervention is that it was conducted in a healthcare setting with paper-based healthcare records. This occasionally impacted the capacity to be comprehensive in generating a medication and medical history. Patients attending private consultants in different healthcare regions may have diagnoses that were not documented in the public healthcare patient record. Outpatient correspondence from institutions outside of UHW were not always accessible at the time of medication review, occasionally leading to a lack of clarity regarding staging and treatment intent. This information, however, was subsequently available through the MDT and medical oncologist visit. The paper-based healthcare record also introduces a time-bias in some instances. The dictation or typing of a letter to relevant stakeholders is printed and posted, which introduces variables outside of the intervention control, and is contingent on physicians receiving the letters, reading them and acting upon their recommendations.

5.6 Conclusion

Medication reviews by pharmacists play a crucial role in optimising medication use and improving health outcomes for older adults with cancer. Adhering to established standards and processes ensures that these reviews are conducted effectively and efficiently.

The adaptive, iterative methodology allows for a multi-tiered approach to medication reviews in older adults with cancer, creating a comprehensive review that is increasingly able to cater for patient heterogeneity. The capacity for this approach to better identify medication-related problems and to have a clinically meaningful impact on patients' needs to be determined using prospective observational studies.

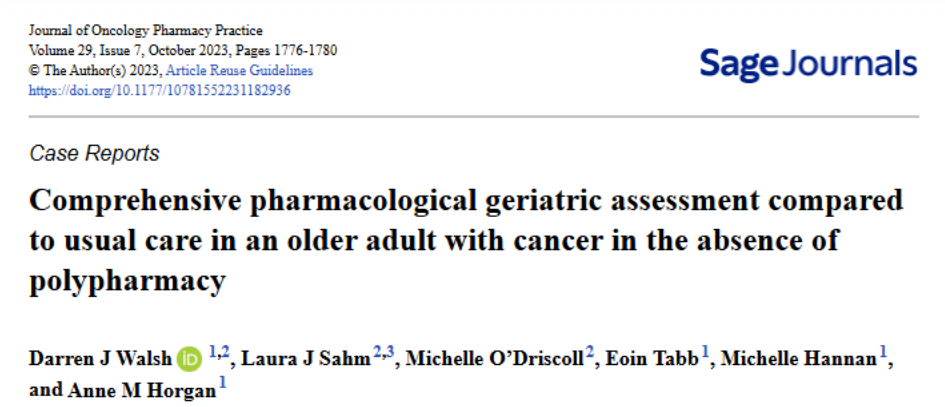
The move to a two-day model that incorporated an expanded MDT between the CGA and the medical oncologist review allowed for a greater alignment with the EAHP hospital pharmacy statements on clinical practice (208). This ensured proactive collaborative therapeutic decision making, embedding the pharmacist into the decision-making process.

This intervention generated a theoretical improvement in medication management that should lead to a reduction in unplanned hospitalisation due to ADE. This approach provides the setting for the work conducted in the GOAL clinic by the pharmacist and the integration of that work into the MDT, through its development. The outcomes of this intervention are explored in Chapter 6.

Chapter 6 – Medication optimisation in a geriatric oncology outpatient clinic: A prospective interventional study

Peer-reviewed publications

Walsh DJ, Sahm LJ, O'Driscoll M, Tabb E, Hannan M, Horgan AM. Comprehensive pharmacological geriatric assessment compared to usual care in an older adult with cancer in the absence of polypharmacy. *Journal of Oncology Pharmacy Practice*. 2023;29(7):1776-1780. doi:10.1177/10781552231182936



Journal of Oncology Pharmacy Practice
Volume 29, Issue 7, October 2023, Pages 1776-1780
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Sage Journals

Case Reports

Comprehensive pharmacological geriatric assessment compared to usual care in an older adult with cancer in the absence of polypharmacy

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Author Contributions:

Writing – original draft: DJW, MO'D, AMH, LJS

Writing – review & editing: DJW, LJS, MO'D, AMH, BB, HA, CG

Methodology: DJW, LJS, MO'D, AMH. Dr. Edel Burton (EB), Pharmacoepidemiologist in the School of Pharmacy, University College Cork was consulted in generating the data analysis strategy. Dr. Sheena McHugh, implementation scientist was consulted on the development of the methodological strategy.

Data extraction: DJW, BB, HA

Data analysis: DJW, MO'D, AMH, LJS, EB

Further research presented in this chapter is being prepared for journal submission.

6.1 Abstract

Introduction

The impact of pharmacist interventions has yet to be explored in detail in the outpatient geriatric oncology clinic. The literature demonstrates that medication-related problems are frequently found in older adults with cancer, and structured medication reviews have the capacity to improve medication adherence, identification of PIM and patient confidence in medication management.

Aim

To determine the impact of a pharmacist as part of the MDT on unplanned hospitalisation and unplanned hospitalisation due to ADE.

Methods

A prospective interventional study was undertaken. Patients who attended the GOAL clinic in UHW between July 2022 and October 2024 and aged ≥70 years were eligible for inclusion. Ethical approval was obtained by the HSE South East Research Ethics Committee. During the patient consultation, patients were asked to consent to their data being utilised for the study.

During the clinic visit patients undertook medicines reconciliation and a comprehensive medication review was conducted, to identify medication-related problems. These were communicated to the relevant stakeholders, and implementation of recommendations recorded.

Medical records were examined to identify any unplanned hospital admissions between the clinic visit date and six months after the initial clinic visit. Incidences of unplanned hospitalisation were assessed to determine if an ADE potentially occurred. Predictors of unplanned hospitalisation and unplanned hospitalisation due

to ADE were identified. The outcomes were then compared to the findings in Chapter 4.

Results

Medication related problems were identified in 86% of patients. Interventions were either fully or partially implemented in 89% of patients. Unplanned hospitalisation occurred in 39% of patients within 6 months of index clinic visit. Unplanned hospitalisation due to ADE occurred in 10% of patients.

Performance status OR 11.89 95% CI (3.39-52.52), Polychemotherapy OR 14.98 95% CI (1.89-337.51), and PIM OR 5.80 95% CI (1.49-30.78) were all independent predictors of unplanned hospitalisation due to ADE. Inter-rater reliability demonstrated moderate agreement for the probability and preventability of ADE in these patients.

The findings, when compared to the findings in Chapter 4, were associated with a 65% decreased risk in unplanned hospitalisation due to ADE in older adults with cancer who receive a structured medication review by a pharmacist.

Conclusion

Pharmacist integration into a geriatric oncology outpatient clinic and MDT leads to a reduction in unplanned hospitalisation due to ADE. Pharmacists can play a key role in identifying medication related problems at baseline and recommending interventions to address these problems.

6.2 Introduction

Chapter 6 presents the outcomes of the implementation of the medication review intervention outlined in Chapter 5. It examines the identification of medication-related problems in patients who had a medication review, the implementation of those outcomes in patients who attended the GOAL clinic and underwent this intervention and describes the incidence of unplanned hospitalisation and unplanned hospitalisation due to ADE in these patients. Predictors of these outcomes are explored, and the outcomes of this chapter are compared to the outcomes in the retrospective study reported in Chapter 4.

In the inpatient setting, Herledan and colleagues in Lyon Sud Hospital in France identified medication-related problems in 70.9% of patients on admission and 47.7% on discharge (209). After pharmacist intervention and recommendations this reduced to 34.3% on admission and 16% on discharge ($p<0.001\%$ for both). This study demonstrated the clinical and economic benefit of pharmacist interventions in the inpatient setting. Polypharmacy was present in over 80% of patients on admission, and medication-related problems identified included omitted medications, overdosage, underdosage, PIM, drug interactions, inappropriate administration, and non-formulary drug usage (209). These findings in the inpatient setting, demonstrate the potential for pharmacist input in older adults with cancer. Medication review in the outpatient setting, should therefore, be the ideal place to address medication-related problems to prevent avoidable unplanned hospitalisation.

The impact of pharmacist interventions has yet to be explored in detail in the outpatient setting. Research from the Senior Adult Oncology Programme in the Royal

Marsden NHS Trust showed that a structured pharmacist medication review can be successfully integrated into a CGA (264). This study also assessed patient satisfaction with their clinic visit. It found that higher medication adherence rates, improved identification of inappropriate medications, and enhanced patient confidence in managing their conditions occurred after a structured medication review conducted by a pharmacist in an outpatient geriatric oncology clinic (264).

Ramsdale *et al.* in a secondary analysis of 718 patients enrolled in the GAP70+ study identified polypharmacy in 61.3%, hyperpolypharmacy in 14.5% and PIM in 67.1% of older adults with cancer prior to starting SACT (265). Mohamed *et al*. in a separate secondary analysis of the same data found that polypharmacy was associated with an increase in treatment related toxicities (59).

The lack of literature outlined in Chapter 2 in relation to ADE in older adults with cancer creates a knowledge gap that requires addressing. The potential health economic benefits described in Chapter 3, can have synergistic benefits to health services when combined with the potential clinical benefits found in the retrospective study conducted in Chapter 4. Older adults with cancer experienced unplanned hospitalisation due to ADE, irrespective of polypharmacy status at baseline, and polychemotherapy was the only independent predictor of unplanned hospitalisation due to ADE. The incidence of unplanned hospitalisation due to ADE was 24% of patients and the prevalence of ADE among unplanned hospitalisations was 55%.

Optimising medications through the pragmatic patient-centred approach outlined in Chapter 5 may reduce treatment burden for patients, and the incidence of unplanned

hospitalisation due to ADE. The EDQM guidelines have 8 clear goals of a structure medication review which, along with their relevance to older adults with cancer is described in Chapter 5 (211). The methodology employed in designing and implementing a medication review intervention for patients who attend the GOAL clinic is also described in Chapter 5. Chapter 6 explores the outcomes of these interventions, as well as their clinical and statistical significance.

6.3 Aims

The aim of this chapter is to determine the impact of a pharmacist as part of the MDT on unplanned hospitalisation and unplanned hospitalisation due to ADE.

Objectives:

- To measure the incidence of unplanned hospitalisation in older adults with cancer who have had a medication review by a pharmacist as part of a CGA.
- To determine the prevalence of unplanned hospitalisation due to ADE in those patients.

6.4 Methods

A prospective interventional study was undertaken. Patients who attended the GOAL clinic in UHW between July 2022 and October 2024 and were aged ≥70 years were eligible for inclusion. Eligible patients, and a carer or family member in attendance, were given a patient information leaflet on the study, and a consent form prior to their appointment commencing. Patients received a medication review by a pharmacist and once the medication review was completed they were asked if they understood the consent form and the patient information leaflet. Eligible patients then provided written informed consent for study inclusion as per standard protocol. Patients who had an unplanned hospitalisation between the clinic visit and the MDT discussion were excluded to remove time bias from the unplanned hospitalisation analysis. Ethical approval was obtained for this study by the HSE South East Research Ethics Committee in February 2022, with protocol amendments approved in August 2023 and September 2025 (Appendix 7).

6.4.1 Data collection and analysis

During the patient consultation, patients were asked to consent to their data being utilised for the study (Figure 27). Patients who consented had their personal identifiable data saved to a password encrypted spreadsheet. All other data were saved in a separate password encrypted spreadsheet, and the primary investigator was the only one with the key. Patients who did not consent had a structured medication review; however, their data were not collected for research purposes.

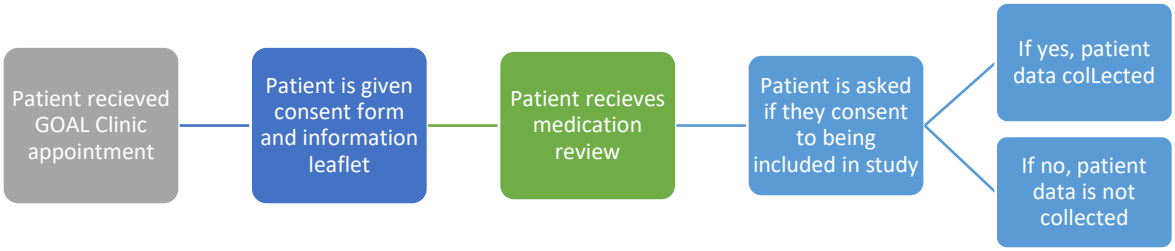


Figure 27: Patient consent process

Participant demographics, cancer diagnosis and stage, past medical history and the patient's medication record from community pharmacy, were collated in advance of the patient consultation. Relevant laboratory reports including urea and electrolytes, liver function tests, iron studies, histopathology, and pharmacogenomics were also reviewed prior to patient consultation. A medicines reconciliation was performed with each participant during the consultation. They were asked the following general questions first:

1. Do you have any allergies to any medications?
2. Do you ever have any difficulty swallowing your oral medications?*
3. Do you ever forget to take, or miss, a dose of your regular medications?*

4. Do you use anything to help you to take your regular medications, such as a blister pack or pill box?*
5. Do you take any over the counter medicines, herbal medicines, vitamins, supplements or natural remedies?

*Only asked and recorded from the introduction of the two-day model of care

Patients who reported allergies were asked detailed questions about the nature of an allergy, and where reported allergies did not align with true allergy, they were de-labelled as allergic, and the de-labelling documented in the notes.

Patients who reported difficulty swallowing oral medications were asked which medications caused them trouble, and individual plans were made to circumvent this swallowing difficulty.

Patients were classified as fully adherent if they reported never missing a dose of their medication, partially adherent if they reported occasionally or non-intentionally missing doses of their medication and non-adherent if they actively did not take some, or all, of their medication as prescribed.

Their medication list was then reconciled and compared to their past medical history. SACT options and the supportive care medications that usually accompany the standard protocol for that SACT were discussed. Possible deviations from the standard protocol, and potential medication-related problems with their SACT, supportive care medications and regular medications were discussed, and education provided for some cancer- and SACT-specific toxicities.

A drug interaction check, assessment for PIM, POM and ACB calculation then took place. Once completed, the findings of the overall assessment were discussed at the GOAL MDT, and outcomes were communicated to relevant stakeholders, which may have included the patient's GP, community pharmacy, and other specialists caring for the patient.

Communication was predominantly made through the medical dictation and clinical correspondence app TPro (266). Potential medication related problems were clearly communicated to the GP, with recommended changes to optimise medication usage for chronic conditions. Where a potential medication related issue affected a medication managed by another specialty, they were cc'd on the letter. The patient's medical oncologist was notified of potential optimal amendments to the standard of care for the patient, given their complex comorbidities, e.g., using a steroid sparing antiemetic regimen for a diabetic patient. Issues such as potential non-adherence with oral medication were explored and communicated to the consultant, when OAM was being considered. Changes and specialist counselling points, particularly regarding OTC medication use were communicated to the community pharmacist. A copy of the letter was stored in the patient's medical notes. Recommendations were referenced with rationale for suggested change outlined.

Implementation of recommendations was determined using the following methodology:

1. **SACT:** Implementation of recommendations related to SACT were determined by reviewing the SACT prescription verified for cycle 1.

2. **Supportive care:** Implementation of recommendations related to supportive care were determined by discussing with a prescribing member of the MDT, or by checking a combination of the verified SACT prescription for cycle 1 or the PCRS dispensing data for the patient.
3. **Regular medication:** Implementation of recommendations for regular medication was determined by checking PCRS dispensing data, subsequent clinic visit letters, and where relevant, admission medicines reconciliation.
4. **Monitoring:** Recommendations related to monitoring was determined by using a combination of laboratory data, medical notes and nursing notes.

Implementation was determined as full when all recommendations were implemented. Implementation was determined as partial when at least one recommendation was implemented, and at least one recommendation was not implemented. Implementation was recorded as "none" when none of the recommendations could be seen to have been actioned.

Participant medical charts were followed up at 6 months. Participants who were determined to potentially have had an unplanned hospitalisation due to ADE had the details of their admission and suspected ADE anonymously compiled into ADE summary sheets (Appendix 8). Basic demographic data (age and gender), and clinical background, including diagnosis and relevant medical history were included. Details in relation to the medication(s) implicated in the ADE were provided, as well as a list of concomitant medications. A description of the ADE, including information on the severity, management and outcome of the event were also given, as well as laboratory data if relevant. Finally, additional notes, including other possible causes,

if the ADE was previously reported using the Martindale ADR Checker (248), and any additional preventable factors were included.

An expert panel of assessors was used to conduct inter-rater reliability testing on the probability and preventability of each ADE. The panel consisted of a consultant medical oncologist experienced in geriatric oncology, a consultant geriatrician experienced in geriatric oncology, an advanced specialist geriatric oncology pharmacist, a Chief 2 clinical oncology pharmacist, and a generalist staff grade hospital pharmacist.

The probability of an unplanned hospitalisation suspected to be caused by or contributed to by a medication was assessed using the Naranjo scale (Table 26) (267).

Table 26: The Naranjo Scale for assessing ADE probability (267)

Question	Yes	No	Do Not Know
1. Are there previous conclusive reports on this reaction?	1	0	0
2. Did the adverse event appear after the suspected drug was administered?	2	-1	0
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	1	0	0
4. Did the adverse event reappear when the drug was readministered?	2	-1	0
5. Are there alternative causes that could on their own have caused the reaction?	-1	2	0
6. Did the reaction reappear when a placebo was given?	-1	1	0
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?	1	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	1	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	1	0	0
10. Was the adverse event confirmed by any objective evidence?	1	0	0

A score of 0 means an ADE is doubtful. A score of 1-4 means an ADE is possible, a score of 5-8 means an ADE is probable and a score of ≥9 means an ADE is considered definite (268).

Preventability was assessed using the Liverpool Adverse Drug Reaction Avoidability Assessment Tool (Figure 28) (269) .

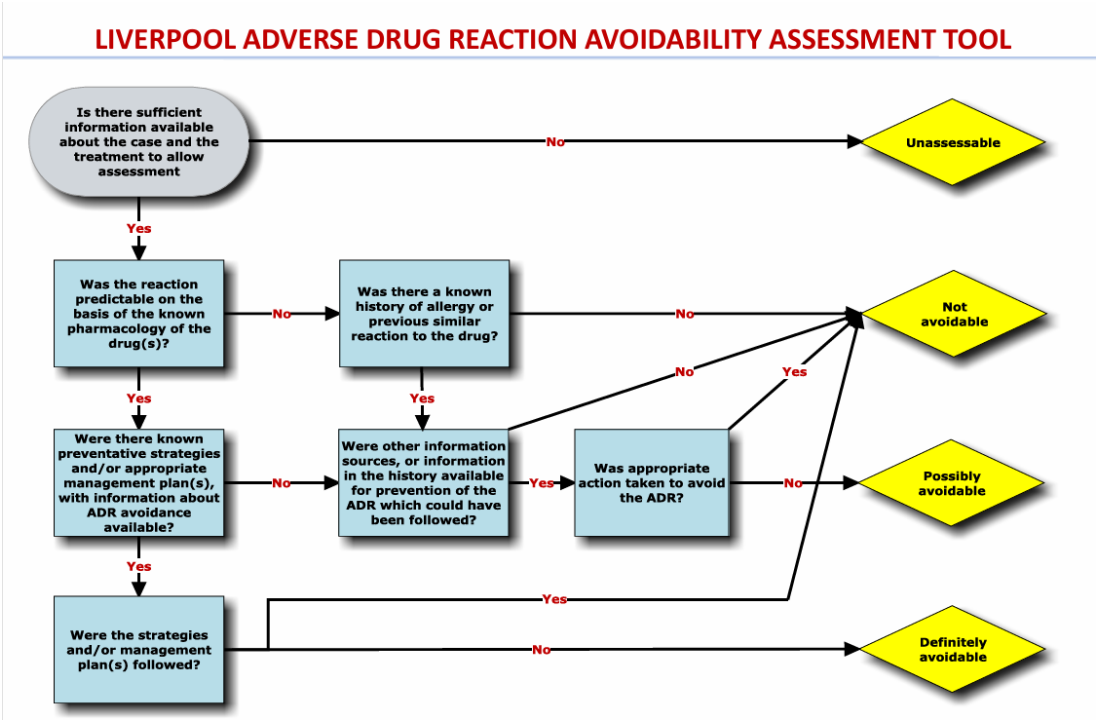


Figure 28: Liverpool Adverse Drug Reaction Avoidability Assessment Tool, reproduced with permission from Bracken et al. (270)

These forms were completed on a HSE encrypted OneDrive file, with each participant having a folder with a copy of each draft summary for individual participants. Once completed the primary researcher collated the data from each rater.

Finally, the incidence of unplanned hospitalisation, and unplanned hospitalisation due to ADE in the retrospective study in Chapter 4 was compared to the incidence of unplanned hospitalisation, and unplanned hospitalisation due to ADE in this study.

6.4.2 Statistical analysis

Descriptive statistics

Descriptive statistics were used for sociodemographic data and the incidence of unplanned hospitalisation, unplanned hospitalisation due to ADE, drug related problems (drug interactions, PIM, POM and ACB), and the rate of implementation of pharmacist's recommendations. A Shapiro-Wilk normality test was applied to cumulative ACB scores. A Wilcoxon signed-rank test was conducted to compare cumulative ACB prior to intervention, to cumulative ACB if medications were fully optimised post-intervention. A density curve using a boxplot superimposed on a violin plot was generated to visualise the difference between groups in ACB. Intraclass correlation coefficient 2 (ICC2) for continuous variables was calculated for rater assessment on the Naranjo scale. Fleiss' Kappa for categorical ratings was calculated for rater assessment of the Liverpool Adverse Drug Reaction Avoidability Assessment Tool.

Regression analyses

The OR and their 95% CI for the relationship between independent variables and dependent variables (unplanned hospitalisation, and unplanned hospitalisation due to ADE) were analysed using logistic regression in four models, comparing patients who had an unplanned hospitalisation, or an unplanned hospitalisation due to ADE to those who had not. The first was a univariable logistic regression; the second was a multivariable logistic regression adjusted for demographics (age and gender); the third was adjusted for clinical parameters (ECOG performance status, stage and

treatment type); and the fourth was adjusted for medication related problems (polypharmacy, DDI, PIM, POM, and ACB).

Differences in demographic details between the retrospective findings from Chapter 4 and the prospective findings in Chapter 6 were identified using either Welch's t-test for continuous variables or Chi-squared test (X^2) using a 2x2 contingency table for categorical variables to assess comparability. To quantify the strength of this association, an odds ratio (OR) was calculated. Statistical significance was determined as $p<0.05$.

6.5 Results

A total of 254 patients were invited to take part in the study. Four patients (2%) did not consent. Ten patients (4%) were excluded as they were admitted, either directly from clinic or within 72 hours of clinic attendance. This gave an attrition rate of 6% of patients. A total of 240 patients were included in the final data analysis.

6.5.1 Patient characteristics

The demographic details of included patients can be found in Table 27.

Table 27: Patient demographics

n = 240	**n (%)**
Age (years)	
Mean (Standard Deviation)	78 (±5.25)
Median (range)	77.5 (70-93)
Gender	
Male	135 (56)
Female	105 (44)
Diagnosis	
Gastrointestinal	128 (53)
Hepatopancreatobiliary	29 (12)
Lung	25 (10)
Genitourinary	24 (10)
Breast	11 (4)
Gynaecological	9 (4)
Melanoma	5 (2)
Neuroendocrine	5 (2)
Head and Neck	3 (1)
Cancer of Unknown Primary	1 (1)
Stage	
I/II	36 (15)
III/IV	200 (83)
Unknown	4 (2)
ECOG performance status	
0/1	160 (67)
≥2	78 (32)
Not documented	2 (1)
Number of medications at baseline	
Mean (range)	9.2 (0-24)
Baseline polypharmacy status	
Hyperpolypharmacy (≥10 medicines)	104 (43)
Polypharmacy (5-9 medicines)	86 (36)

n = 240	n (%)
Non-polypharmacy (<5 medicines)	50 (21)
Treatment intent	
Curative	79 (33)
Palliative	155 (65)
Undetermined	6 (2)
Treatment Plan	
SACT	
Monochemotherapy	72 (30)
Polychemotherapy	59 (25)
Hormone therapy	24 (10)
Concurrent chemoradiation	10 (4)
Other treatment modalities	
Radiotherapy alone	11 (5)
Surgery alone	2 (1)
Not for treatment	
Surveillance	30 (13)
Best supportive care	26 (11)
Pending further investigations	6 (2)

Key: ECOG – Eastern Cooperative Oncology Group; SACT – Systemic anticancer therapy

Allergy status

Allergy status was documented for all patients. In total 29 patients (12%) had a confirmed allergy with a history of a hypersensitivity reaction. There were 41 total allergies documented in those 29 patients. A history of allergy to multiple agents was present in six patients (3%). Stated allergies that upon investigation were intolerances were corrected on the patient record. A list of patient allergies is outlined in Table 28. Patients who had allergy status documented or declared an allergy that on consultation described an intolerance were not listed and the nature of their reaction clarified on their medical record.

Table 28: Medications for which patients had a documented history of hypersensitivity/allergy

Medications patients reported allergies/hypersensitivity to			
Medication	**Incidence**	**Medication**	**Incidence**
Penicillin	11	Amitriptyline	1
Opioids	8	Alginic acid	1
NSAID	4	CT contrast	1
Benzodiazepines	2	Iron	1
Cephalosporins	2	Metronidazole	1
Corticosteroids	2	Nifedipine	1
Co-Trimoxazole	2	Pregabalin	1
Macrolides	2	Sulphur-containing medications	1

Key: NSAID-Non-steroidal anti-inflammatory drugs; CT – Computed tomography

Swallow status

Self-reported ability to swallow solid oral medications was documented in 96 patients (40%). Swallow did not affect medication administration in 84 patients (88%). Swallow partially affected medication administration in 10 patients (10%), requiring either changes to drug formulation or route of administration. Two patients (2%) were completely dysphagic and could not administer any oral dosage forms.

Patient-reported adherence

Patient-reported adherence was assessed in 99 patients (41%). Complete adherence was reported in 63 (63%) patients. Partial adherence was reported in 32 (32%) patients. Four patients (4%) reported being non-adherent.

The use of adherence-aids was also documented for these patients. Fifty-one patients (51%) did not use any form of adherence aid and solely relied on their own routine and memory to take their medications. Self-sorted pill boxes were used by 20 patients (20%). Blister packs were used by 18 patients (18%). Nine patients (9%) relied on a carer or a spouse to assist them in taking their medications. One patient

(1%) used their morning, and evening cup of tea as an adherence aid, dispersing their oral medications in a cup of tea.

6.5.2 Identification of medication related problems

A total of 206 patients (86%) of patients had at least (i) one drug interaction, (ii) one PIM, (iii) one POM or (iv) one medication with anticholinergic properties at baseline (Table 29).

Table 29: Classification of medication-related problems

Medication-related problem	Drug Interaction	Potentially inappropriate medication	Potentially omitted medication	Severe Anticholinergic Burden (≥3)
Yes n (%)	140 (58)	132 (55)	111 (46)	83 (35)
No n (%)	100 (42)	108 (45)	129 (54)	157 (65)

Note: Numbers for each parameter add up to 240 as each patient was assessed. The figure of 206 patients accounts for those who had at least one medication-related problem, some patients had more than one category of medication-related problem.

Drug interactions

In total, 140 (58%) patients had at least one DDI that required an intervention based on MDT discussion. There was a total of 456 drug interactions identified, requiring an intervention. The details of the pharmacist recommended interventions can be found in Table 30.

Table 30: Recommendations base on drug interactions deemed clinically significant

Recommendation	n = 456 (%)
Monitor electrolytes	206 (45)
Stop regular medication	82 (18)
Monitor for symptoms	61 (13)
Change regular medication	46 (10)
Electrocardiogram	15 (3)
Monitor blood glucose levels	12 (3)
Monitor blood pressure	11 (2)
Change dose of regular medication	11 (2)
Other	12 (3)

The groups of medications implicated in clinically relevant drug interactions can be found in Table 31. A full breakdown of these groups into classes and individual medications can be found in Appendix 9. SACT were implicated in DDI on 89 occasions. Supportive care medications were implicated in DDI on 169 occasions. Regular or PRN medications were implicated in DDI on 654 occasions.

Table 31: Medications that flagged with potentially clinically significant interactions requiring intervention

Medication (n=912)	**n (%)**
SACT (n=89)	
Cytotoxic chemotherapy/Targeted therapy	59 (6)
Hormone therapy	30 (3)
Supportive care (n= 169)	
Prophylaxis	147 (16)
Symptom control	22 (2)
Regular/PRN medications (n= 654)	
Cardiac medications	237 (26)
Psychotropic medications	95 (10)
Gastrointestinal	77 (8)
Analgesics	62 (7)
Respiratory	55 (6)
Endocrine	43 (5)
Other	30 (3)
Central Nervous system	19 (2)
Genitourinary	14 (2)
Musculoskeletal	12 (1)
Antimicrobials	10 (1)

Key: SACT – Systemic Anticancer Therapy; PRN – Pro re nata

Potentially inappropriate medication

Potentially inappropriate medications were identified in 132 patients (55%). There were a total of 276 potentially inappropriate medications identified. The ten most frequently identified PIM can be found in Table 32. A comprehensive list of PIM identified can be found in Appendix 10.

Table 32: Potentially inappropriate medications

Potentially inappropriate medications	
Medication (n=276)	**n (%)**
Antiplatelet	20 (7)
PPI/ H2 antagonist	18 (7)
Statin/Ezetimibe	13 (5)
NSAID	12 (4)
Diuretic	12 (4)
Z-drugs	12 (4)
Formulation-specific issue	11 (4)
Opioid	11 (4)
SSRI	11 (4)
Metformin	10 (4)

Key: PPI – Proton Pump Inhibitor; H2 antagonist – Histamine-2 receptor antagonist; NSAID – Non-steroidal Anti-inflammatory Drugs; SSRI – Selective Serotonin Reuptake Inhibitor

Potentially omitted medication

There were a total of 111 patients (46%) who had a potentially omitted medication (POM). In total there were 167 potentially omitted medications identified. The ten most frequently identified POM can be found in Table 33. A comprehensive list of PIM identified can be found in Appendix 11.

Table 33: Potentially omitted medication

Potentially omitted medication	
Medication (n=167)	**n (%)**
PPI/H2 antagonist	38 (23)
Laxatives	12 (7)
Anticoagulant	10 (6)
Denosumab	10 (6)
Opioids	9 (5)
Intravenous Iron	8 (5)
Silodosin	8 (5)
ONS	8 (5)
Formulation change	7 (4)
Antidepressant	6 (4)
DPP4i	6 (4)

Key: PPI – Proton Pump Inhibitor; H2 antagonist – Histamine-2 receptor antagonist; ONS – Oral Nutritional Supplement; DPP4i - Dipeptidyl peptidase 4 inhibitor

Anticholinergic burden

There was a total of 399 medications with anticholinergic properties prescribed at baseline in 175 patients. Anticholinergic burden at baseline can be seen in Figure 29.

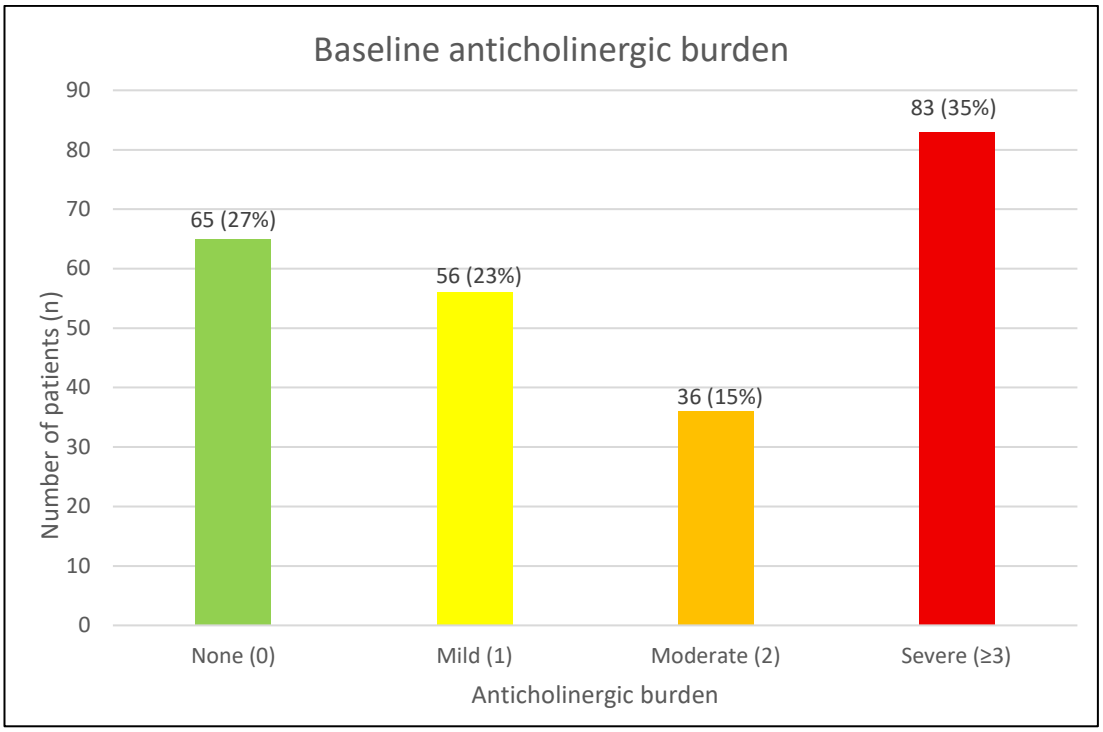


Figure 29: Baseline anticholinergic burden

The mean anticholinergic burden at baseline was 2.3 (0-13). If fully optimised, the mean anticholinergic burden was 1.7 (0-10), a statistically significant decrease V = 2278, p <0.001 (Figure 30).

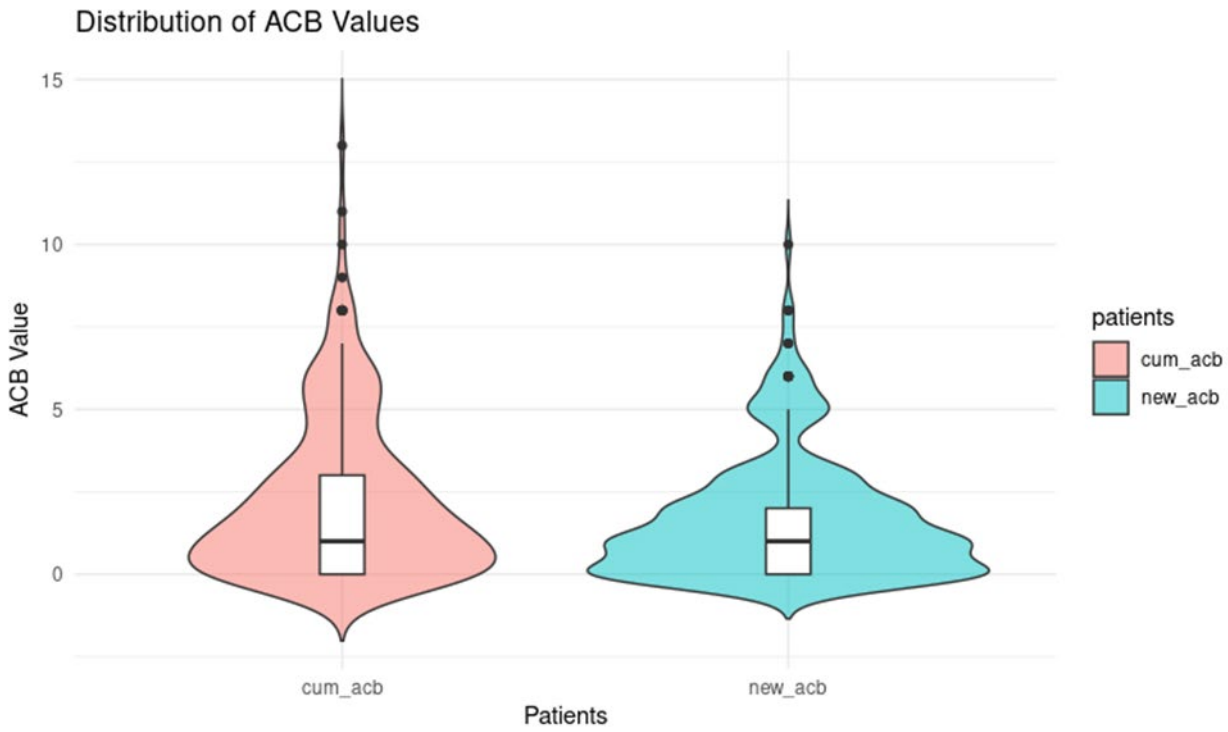


Figure 30: Violin plot of cumulative ACB pre-intervention and if fully optimised. cum_acb = pre-intervention, new_acb = fully optimised.

The ten most frequent medications at baseline that had at least an ACB of 1 at the time of clinic visit can be found in Table 34. A comprehensive list of medications prescribed at baseline for patients with an ACB of at least 1 can be found in Appendix 12.

Table 34: Medication with anticholinergic properties

Medications with anticholinergic properties	
Medication (n= 399)	**n (%)**
Dexamethasone	69 (17)
Loperamide	28 (7)
Codeine	20 (5)
Metoclopramide	19 (5)
Metformin	18 (5)
Furosemide	13 (3)
Alprazolam	12 (3)
Tramadol	11 (3)
Lansoprazole	10 (3)
Mirtazapine	10 (3)
Morphine sulphate	10 (3)

6.5.3 Implementation of recommendations

The frequency rate of implementation of pharmacist's recommendations can be seen in Table 35. Of 192 patients with an intervention requiring implementation, 89% (171) had their recommendation fully, or partially, implemented.

Table 35: Implementation of recommendations

Implementation of medication-related recommendations from GOAL MDT	
Implementation	**Total (n=240) n(%)**
Full	108 (45)
Partial	63 (26)
None	21 (9)
No recommendations	48 (20)

6.5.4 Unplanned hospitalisation and unplanned hospitalisation due to ADE

A total of 93 patients (39%) had an unplanned hospitalisation. Of these, 24 (10%) were potentially due to an ADE. The remaining 69 (29%) patients who were admitted, did not have an ADE. The 93 patients had a total of 126 unplanned hospital admissions between them. Of the 126 admission events, 24 (19%) were due to ADE (Figure 31).

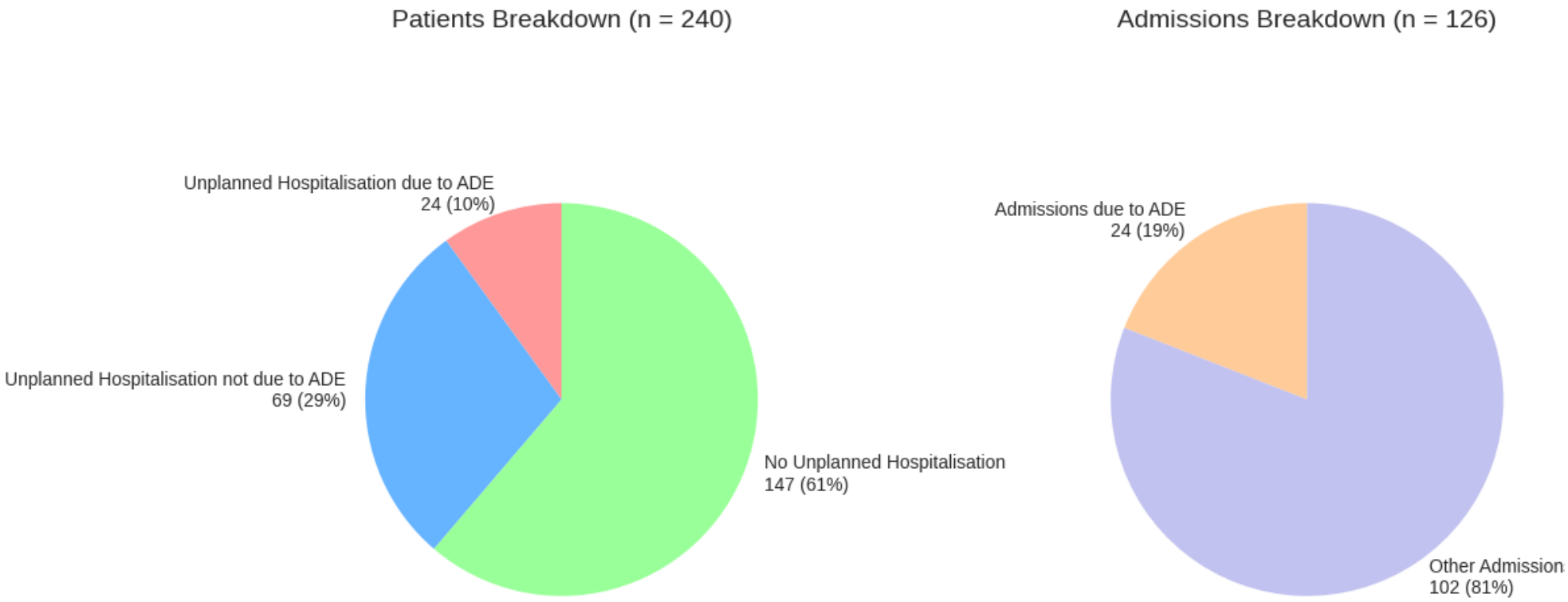


Figure 31: Unplanned hospitalisation and unplanned hospitalisation due to adverse drug events. Key: ADE -Adverse drug event

The medication(s) potentially associated with ADE and the cause of admission are detailed in Table 36.

Table 36: Medications potentially associated with ADE and cause of admission

Medication	Cause of Admission
Amitriptyline	Tachycardia
Buprenorphine	Constipation
Carboplatin and Etoposide	Systemic toxicity - Pneumonia - Diarrhoea - Dehydration
Dapagliflozin	UTI, dehydration and confusion
Fluorouracil	Hypokalaemia
Fluorouracil	Diarrhoea
Fluorouracil	Sepsis of unknown source
Fluoxetine	Symptomatic hyponatraemia
Furosemide and Hydrochlorothiazide	Hypovolaemic hyponatraemia
Ibuprofen	Fluid overload
Ibuprofen	AKI
Irinotecan	Diarrhoea
Irinotecan	Neutropenic sepsis
Naproxen	Bleeding secondary too primary tumour
Oxaliplatin	CINV
Oxaliplatin and Fluorouracil	Lower Respiratory Tract Infection
Oxaliplatin	Nausea and fatigue
Oxaliplatin, Irinotecan and Fluorouracil	Nausea abdominal pain and general malaise
Pembrolizumab	Immune checkpoint inhibitor-related colitis
Sertraline	Bleeding secondary too primary tumour
Sunitinib	Diarrhoea
Tramadol	Recurrent falls
Vinorelbine	Vinorelbine toxicity - Constipation - Fatigue
Zopiclone	Fall secondary to pathologic fracture

Key: UTI – Urinary Tract Infection; AKI – Acute Kidney Injury;

Predictors of unplanned hospitalisation

Predictors of unplanned hospitalisation can be seen in Table 37. In univariate regression analysis, cancer stage OR 3.70 95% CI (1.57-10.20), ECOG performance status OR 2.37 95% CI (1.36-4.14), best supportive care OR 2.62 95% CI (1.02-6.92),

presence of DDI OR 2.23 95% CI (1.30-3.89), POM OR 1.76 95% CI (1.04-3.01), and severe ACB OR 2.38 95% CI (1.20-4.89), were predictors of unplanned hospitalisation. Using the multi-model approach only cancer stage OR 3.43 95% CI (1.38-9.84) and ECOG performance status OR 2.21 95% CI (1.13-4.36) were independent predictors of unplanned hospitalisation.

Table 37: Independent predictors of unplanned hospitalisation

Variable	Model 1 OR (95% CI), p-value	Model 2 OR (95% CI), p-value	Model 3 OR (95% CI), p-value	Model 4 OR (95% CI), p-value
Age	0.99 (0.94-1.04), 0.66	0.99 (0.94-1.04), 0.69		
Gender	0.79 (0.47-1.33), 0.38	0.79 (0.47-1.34), 0.39		
Stage	3.70 (1.57-10.20), **0.01***		3.71 (1.54-10.43), **0.01***	3.43 (1.38-9.84), **0.01***
ECOG	2.37 (1.36-4.14), **0.002***		2.46 (1.33-4.61), **0.004***	2.21 (1.13-4.36), **0.02***
Treatment				
BSC	2.62 (1.02-6.92), **0.048***		1.47 (0.53-4.15), 0.46	1.40 (0.48-4.10), 0.54
Monochemotherapy	1.22 (0.57-2.70), 0.61		1.05 (0.47-2.39), 0.91	0.86 (0.36-2.05), 0.72
Polychemotherapy	1.79 (0.80-4.15), 0.16		1.91 (0.81-4.67), 0.14	1.31 (0.50-3.47). 0.59
Polypharmacy				
Polypharmacy	1.32 (0.64-2.80), 0.46			0.71 (0.29-1.70), 0.44
Hyperpolypharmacy	1.67 (0.83-3.44), 0.16			0.54 (0.20-1.41), 0.21
DRP				
DDI	2.23 (1.30-3.89), **0.004***			1.89 (0.90-4.08), 0.10
PIM	1.76 (1.04-3.01), **0.04***			1.13 (0.59-2.17), 0.71
POM	1.64 (0.97-2.78), 0.06			1.16 (0.61-2.22), 0.65
ACB				
Mild	1.83 (0.85-3.99), 0.13			1.13 (0.45 -2.8), 0.79
Moderate	2.26 (0.96-5.38), 0.06			1.37 (0.48-3.87), 0.55
Severe	2.38 (1.20-4.89), **0.02***			1.29 (0.51-3.29), 0.59

Key: ECOG – Eastern Co-operative Oncology Group; BSC – Best Supportive Care; DRP – Drug-related problem; DDI – Drug-drug interaction; PIM – Potentially Inappropriate Medication; POM – Potentially Omitted Medication; ACB – Anticholinergic burden; OR – Odds ratio

*** = statistically significant**

Predictors of unplanned hospitalisation due to ADE

Predictors of unplanned hospitalisation due to ADE can be seen in Table 38. Univariate regression analysis found that ECOG performance status OR 4.33 95% CI (1.85-10.73), polychemotherapy OR 9.69 95% CI (1.8-180.14), PIM OR 7.00 95% CI (2.34 -30.19), and severe ACB OR 14.12 95% CI (2.74-258.95) were predictors of unplanned hospitalisation due to ADE. Using the multi-model approach ECOG performance status OR 11.89 95% CI (3.39-52.52), Polychemotherapy OR 14.98 95% CI (1.89-337.51), and PIM OR 5.80 95% CI (1.49-30.78) were all independent predictors of unplanned hospitalisation due to ADE.

Table 38: Predictors of unplanned hospitalisation due to adverse drug events

Variable	Model 1 OR (95% CI), p-value	Model 2 OR (95% CI), p-value	Model 3 OR (95% CI), p-value	Model 4 OR (95% CI), p-value
Age	0.99 (0.92-1.07), 0.86	0.99 (0.92-1.07) 0.86		
Gender	0.99 (0.43-2.32), 0.98	0.99 (0.43-2.34), 0.99		
Stage	4.55 (0.91-82.69), 0.14		4.77 (0.84-91.88), 0.15	4.67 (0.78-91.37), 0.16
ECOG	4.33 (1.85-10.73), **<0.001***		10.74 (3.59-38.55), <**0.001***	11.89 (3.39-52.52), <**0.001***
Treatment				
BSC	4.34 (0.53-90.23), 0.21		1.44 (0.13-32.81), 0.78	1.22 (0.09-29.9), 0.88
Monochemotherapy	4.11 (0.74-76.99), 0.19		3.63 (0.6-69.98), 0.24	3.06 (0.43-62.9), 0.33
Polychemotherapy	9.69 (1.80-180.14), **0.03***		22.63 (3.47-462.91), **0.01***	14.98 (1.89-337.51), **0.03***
Polypharmacy				
Polypharmacy	4.03 (1.04-26.61), 0.08			1.98 (0.36-15.57), 0.46
Hyperpolypharmacy	2.90 (0.74-19.21), 0.18			0.49 (0.06-4.64), 0.50
DRP				
DDI	2.46 (1 .00-6.97), 0.07			0.56 (0.13-2.38), 0.42
PIM	7.00 (2.34 -30.19), **0.002***			5.80 (1.49-30.78), **0.02***
POM	2.25 (0.97-5.52), 0.07			0.55 (0.17-1.73), 0.30
ACB				
Mild	6.27 (0.97-122.24), 0.10			2.77 (0.32-61.56), 0.41
Moderate	8.00 (1.13-159.98), 0.07			7.03 (0.67-172.25), 0.14
Severe	14.12 (2.74-258.95), **0.01***			7.10 (0.89-157.08), 0.11

Key: ECOG – Eastern Co-operative Oncology Group; BSC – Best Supportive Care; DRP – Drug-related problem; DDI – Drug-drug interaction; PIM – Potentially Inappropriate Medication; POM – Potentially Omitted Medication; ACB – Anticholinergic burden; OR – Odds ratio

*** = statistically significant**

6.5.5 Probability and preventability of ADE

Probability

The results each rater gave are outlined in Table 39. Rater 1 was an advanced specialist geriatric oncology pharmacist, rater 2 a generalist hospital pharmacist, rater 3 a Chief 2 oncology pharmacist, rater 4 a consultant medical oncologist, and rater 5 a consultant geriatrician.

Table 39:Naranjo scale ratings for ADE

Patient	Rater 1	Rater 2	Rater 3	Rater 4	Rater 5	Mean	Category
1	9	7	8	4	7	7	Probable
2	3	3	4	2	3	3	Possible
3	3	0	3	6	3	3	Possible
4	8	8	6	6	6	6.8	Probable
5	8	5	5	7	6	6.2	Probable
6	6	5	4	7	2	4.8	Probable
7	4	5	4	4	2	4.2	Possible
8	1	1	1	2	4	1.8	Possible
9	8	8	7	7	6	7.2	Probable
10	3	3	3	2	3	2.8	Possible
11	8	8	7	6	5	6.8	Probable
12	3	3	3	3	2	2.8	Possible
13	5	5	4	4	4	4.4	Possible
14	8	8	6	7	7	7.2	Probable
15	4	5	7	2	7	5	Probable
16	8	7	6	5	5	6.2	Probable
17	7	10	4	8	6	7	Probable
18	5	5	4	7	3	4.8	Probable
19	8	8	7	7	7	7.4	Probable
20	7	7	7	5	7	6.6	Probable
21	3	2	3	2	3	2.6	Possible
22	8	8	5	7	6	6.8	Probable
23	3	4	3	6	3	3.8	Possible
24	8	7	7	7	6	7	Probable

Using the average score amongst raters, 15 patients (63%) had a probable ADE, and nine patients (37%) possible ADE. None of the suspected ADE were categorised as definite or doubtful.

The ICC was 0.65 (95% CI: 0.48–0.80), indicating moderate absolute agreement between the raters, using the two-way random effect models and "single random" unit, $p < 0.0001$.

Preventability

All cases were deemed assessable by all raters. There was moderate agreement between the raters, kappa = 0.413, $p < 0.0001$. Consensus (at least 3 raters agreeing) was reached in 23 (96%) of cases. Fourteen cases (58%) were deemed not avoidable. Five cases (21%) were deemed definitely avoidable, and four cases (17%) were deemed possibly avoidable. Four cases (17%) were deemed either potentially avoidable or definitely avoidable. One case had a varied outcome.

Table 40: Liverpool Adverse Drug Reaction Assessment rater results for ADE

Patient	Rater 1	Rater 2	Rater 3	Rater 4	Rater 5
1	Definitely avoidable	Not avoidable	Possibly avoidable	Not avoidable	Not avoidable
2	Not avoidable	Not avoidable	Possibly avoidable	Not avoidable	Possibly avoidable
3	Definitely avoidable	Definitely avoidable	Definitely avoidable	Possibly avoidable	Possibly avoidable
4	Not avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable
5	Not avoidable	Not avoidable	Possibly avoidable	Not avoidable	Not avoidable
6	Possibly avoidable	Definitely avoidable	Possibly avoidable	Not avoidable	Possibly avoidable
7	Not avoidable	Definitely avoidable	Definitely avoidable	Possibly avoidable	Not avoidable
8	Not avoidable	Not avoidable	Possibly avoidable	Possibly avoidable	Not avoidable
9	Not avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable
10	Possibly avoidable	Possibly avoidable	Definitely avoidable	Possibly avoidable	Possibly avoidable
11	Not avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable
12	Definitely avoidable	Definitely avoidable	Possibly avoidable	Possibly avoidable	Possibly avoidable
13	Definitely avoidable	Definitely avoidable	Definitely avoidable	Definitely avoidable	Possibly avoidable
14	Possibly avoidable	Definitely avoidable	Definitely avoidable	Possibly avoidable	Possibly avoidable
15	Not avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable
16	Not avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable
17	Definitely avoidable	Definitely avoidable	Definitely avoidable	Not avoidable	Definitely avoidable
18	Possibly avoidable	Definitely avoidable	Definitely avoidable	Definitely avoidable	Possibly avoidable
19	Definitely avoidable	Definitely avoidable	Possibly avoidable	Definitely avoidable	Possibly avoidable
20	Possibly avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable
21	Not avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable
22	Not avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable
23	Not avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable
24	Not avoidable	Not avoidable	Not avoidable	Not avoidable	Not avoidable

Of the five definitely avoidable ADE, two cases were due to NSAID induced AKI, two cases were due to adverse effects associated with PIM identified in the GOAL clinic, in whom the recommendation to amend therapy was not taken, and one case was due to CINV in a patient who misinterpreted their antiemetic regimen and therefore undertreated themselves.

6.5.6 Comparison with retrospective study

The retrospective study, (Chapter 4), analysed 174 patients of whom, 42 (24%) had an unplanned hospitalisation due to ADE. Of 240 participants in the prospective study, 24 (10%) of these had an unplanned hospitalisation due to ADE. The difference in unplanned hospitalisation due to ADE between the groups was statistically significant X^2 (1, n = 414) = 15.046, $p < 0.001$. Patients in the prospective cohort demonstrated a significantly lower odds ratio of ADE-related hospitalisation compared to those in the retrospective cohort (OR 0.35; 95% CI, 0.20–0.60). This comparison is outlined in Table 41.

Table 41: Comparison between retrospective and prospective groups

Comparison between retrospective and prospective groups			
Variable	**Retrospective study (n=174)**	**Prospective study (n=240)**	**p-value**
Age			
Median (range)	75 (70-94)	77.5 (70-93)	**<0.001***
Gender		`	
Male	74	135	
Female	100	105	**0.006****
ECOG			
0-1	92	160	
≥2	68	78	**0.0484***
Stage			
1 or 2	48	36	
3 or 4	126	200	**0.0022****
Polychemotherapy			
Yes	31	59	
No	143	181	0.09**
Total number of medications			
Median (range)	12 (0-28)	11 (0-26)	**<0.001***
Polypharmacy Status			
Non-polypharmacy	40	50	
Polypharmacy	70	86	
Hyperpolypharmacy	64	104	0.40***
Unplanned hospitalisation			
Yes	75	93	
No	99	147	0.37**
Unplanned hospitalisation due to ADE			
Yes	42	24	
No	132	216	**<0.001****

* Welch's t-test for independent samples with unequal variances

** Chi-squared test using 2x2 contingency table

*** Chi-squared test using 2x3 contingency table

6.6 Discussion

To our knowledge this study is the first to examine the impact of a structured medication review by a pharmacist on unplanned hospitalisation due to ADE in older adults with cancer. The results support the integration of a pharmacist into the geriatric oncology MDT and demonstrates the potential role for pharmacists in the outpatient oncology clinic.

Medication related problems that required either an intervention or additional monitoring were identified in over three quarters of patients. Polypharmacy, or hyperpolypharmacy was prevalent in over three quarters of patients. Over half of patients had at least one clinically significant DDI. Over half of patients had at least one PIM at baseline. Just under half of patients had at least one POM. Almost three quarters of patients were on at least one medication with anticholinergic properties and over a third of patients had exposure to severe ACB at baseline. Other medication related issues were also identified and documented in the GOAL clinic, such as clarification of allergy status, identification of swallowing difficulties and/or dysphagia, and identifying potential concerns regarding medication adherence.

The outpatient clinic is a clinical setting where pharmacists in the Republic of Ireland are underused. Research from Northern Ireland and the USA has demonstrated the beneficial impact of pharmacists in an outpatient follow up clinic in cardiology and general medical patients respectively on hospital readmission rates (270, 271). A systematic review published in 2017 found that *"outpatient oncology practices may benefit from integrating pharmacists into care models in order to more effectively, efficiently, and holistically address the needs of patients with cancer"* (272). Our study adds to these findings, demonstrating a 65% reduced risk of unplanned hospitalisation due to ADE in ambulatory older adults with cancer compared to patients who did not receive a CGA.

The success of the medication review, followed by the MDT discussion and outcome dissemination via TPro was evident, with 89% of patients having recommendations being fully or partially implemented. Implementation in this study was much higher

than in studies such as the SENATOR RCT (273), which was a pragmatic, multi-national, parallel arm prospective randomized open-label, blinded endpoint controlled trial aiming to optimise medications in hospitalized older patients with multi-morbidity and polypharmacy. In SENATOR implementation of recommendations was approximately 15%. In the Optimising Therapy to Prevent Avoidable Hospital Admissions in Multimorbid Older Adults (OPERAM) cluster RCT (274), which aimed to prevent unplanned hospitalisation due to ADE within 12 months of discharge having had medication optimisation as an inpatient, implementation was 62% at two months post-discharge. SENATOR assessed adding software guided medication optimisation in patients under the care of specialists other than geriatricians. OPERAM was more successful at implementation as the patient's medications were reviewed and optimised during admission, and further potential interventions were sent to the patient's GP in a discharge summary. This study is closer aligned to OPERAM, however it took place in ambulatory older adults with cancer.

Making recommendations that informs decision making at the MDT level is an excellent example of clinical pharmacy practice aligning with the EAHP Hospital Pharmacy Statements to be proactively involved in therapeutic decision making (208). Expert consensus on all the ADE identified determined each case was either probable or possible ADE, with consensus on 50% of the ADE being definitively not avoidable.

Just over half of the ADE identified in this study were related to SACT medications. In the retrospective study SACT was responsible for 72% of unplanned hospitalisation

due to ADE. This reduction in SACT toxicity in patients who received a CGA in the prospective study, compared to those who didn't in the retrospective study, supports previous evidence from GAP70+ that highlight the benefits of a CGA prior to older adults with cancer commencing SACT (39). This also demonstrated the benefit of a structured medication review in all older adults with cancer, including those without polypharmacy, or in whom SACT has been deemed potentially too toxic or is not a consideration for the patient. Non-SACT medications can still contribute to unplanned hospitalisation in older adults with cancer, and optimising them, as well as SACT is an important component of the medication review process and the MDT function.

The predictors of unplanned hospitalisation due to ADE in this study are unsurprising, yet interesting. Performance status, PIM and polychemotherapy were found to be independent predictors of unplanned hospitalisation due to ADE. PIM are associated with a 47% increased risk of rehospitalisation in older adults according to a recently published meta-analysis (275). Polychemotherapy emerged as an independent predictor of unplanned hospitalisation in the retrospective study reported in Chapter 4 (215).

Cancer stage and performance status were also independent predictors of unplanned hospitalisation, however none of the medication-related independent variables were deemed independent predictors of unplanned hospitalisation. This may be an indicator that where PIM and ACB is optimised, and SACT treatment plans are adjusted for patients, ADE can potentially be minimised further.

Comparison with retrospective study

Comparison of the findings of the retrospective (Chapter 4) and prospective study is challenging. There were statistically significant differences between the two groups in relation to age, gender, performance status, cancer stage and total number of medications (Table 41).

Patients in the prospective study all screened positive on validated G8 screening tool, indicating they would potentially gain a benefit from a CGA due to pre-existing deficiencies in geriatric domains. Patients in the retrospective study were heterogenous, with both frail and fit patients, possibly explaining differences between the group, as a cohort of the patients in the prospective study would have been considered too fit or not frail enough to warrant a referral to the GOAL clinic.

Whilst the prospective study had a higher prevalence of patients with locally advanced and metastatic cancer and were older, no significant difference between the groups in terms of receiving polychemotherapy was found. This was the only independent predictor of unplanned hospitalisation due to ADE found in both studies. The increased average advanced stage and age in the prospective arm may have been surmised to have led to poorer outcomes in this group, and seen in this light, the 65% reduction in unplanned hospitalisation due to ADE in the prospective study was clinically likely more significant.

The clinical and statistical significance of the 65% reduction in unplanned hospitalisation due to ADE in the absence of a statistically significant reduction in overall unplanned hospitalisation offers interesting insight into the complex nature of caring for older adults with cancer. Despite the majority of ADE experienced by

patients in this study being unavoidable, preventing avoidable ADE through medication optimisation reduces mortality and length of stay associated with hospital admission. Suspected ADE are a significant predictor of increased length of stay and mortality in the hospitalised patient (276), and data from the Adverse drug reactions in an ageing PopulaTion study in Beaumont Hospital, Dublin published in 2022 found 70% of ADR on admission are preventable (277). Our figures, combined with our expert assessment of probability and avoidability, coupled with our relatively high implementation rate suggests that this intervention was effective in preventing avoidable unplanned hospitalisation due to ADE in patients who attended the GOAL clinic.

Limitations

These results are limited by a statistically significant difference in age, gender, performance status and cancer stage between the groups. This study was a single site study, and replication of this research across multiple sites to validate these findings are encouraged.

Future research into the utilisation of electronic health records, and patient/carer education would provide valuable insight into the potential for further improvements on the findings of this study.

6.7 Conclusion

Pharmacist integration into a geriatric oncology outpatient clinic and MDT leads to a reduction in unplanned hospitalisation due to ADE. Pharmacists can play a key role in identifying medication related problems at baseline and recommending interventions to address these problems. Placing a pharmacist in an outpatient

geriatric oncology clinic is an example of clinical pharmacy practice in line with the EAHP hospital pharmacy statements, and future policy at a national level should recommend pharmacist involvement in geriatric oncology MDT activities and prospective therapeutic decision making. The addition of non-medical prescribing privileges, and electronic health records could potentially lead to even further improvement in patient outcomes. Future research, when these developments occur, would be a welcome addition to the literature.

Chapter 7 – Discussion and conclusion

7.1 Discussion

This thesis examined the potential impact of a pharmacist on unplanned hospitalisation due to ADE in older adults with cancer. In this concluding chapter, a summary of the key findings will be discussed, before interpretation of these findings in the context of (i) ageing demographics (ii) workforce planning for geriatric oncology in national service plans, and (iii) potential implications for clinical practice and public healthcare policy. This will lead into a discussion on the strengths and weaknesses of the thesis, culminating in recommendations for future research in this field.

7.2 Summary of Findings

The preliminary work of this thesis began with an overview of the main concepts in this research area. This was followed in Chapter 2 with a systematic review of the literature, detailing the primary research on unplanned hospitalisation due to ADE in older adults with cancer, for all medications. Despite the paucity of studies, there were reported incidences for the inpatient setting, which ranged from 19% - 26% (64, 147, 215). Thus, a gap in the literature was identified i.e. the incidence of unplanned hospitalisation due to ADE from all medications in this population. Chapter 3 identified the potential scale of the problem with SACT toxicity in a local population and assessed the likely macroeconomic impact of unplanned hospitalisation in this patient group. It was determined that cancer patients have almost twice the average length of stay after an unplanned hospitalisation compared to the general population, and that the addition of SACT and supportive care altering polypharmacy status may be associated with increased toxicity. Chapter 4 was a retrospective

analysis of unplanned hospitalisation due to ADE. Key results indicated that for 174 patients who attended a UHW Medical Oncology outpatient clinic, 24% had an unplanned hospitalisation due to ADE, and this accounted for 55% of all unplanned hospitalisation visits. Chapter 5 described the methodology for the design of a structured, pragmatic and clinically relevant medication review intervention. This was conducted using an adaptive, iterative methodology tailored to the needs of older adults with cancer, within this setting. Chapter 6 assessed the outcomes for patients who received a structured medication review. It identified medication-related problems including DDI, PIM, POM and excessive ACB. Following this, recommendations were made regarding the optimisation of SACT and supportive cancer care through patient and carer consultation and MDT discussion. A minimum of one medication-related problem was identified in 86% of 240 patients assessed. The prevalence of clinically relevant DDI was 58%, PIM was 55%, POM was 48% and excessive ACB was 35%. Full or partial implementation of recommendations occurred in 89% of patients. Unplanned hospitalisation occurred in 39% of patients, with unplanned hospitalisation due to ADE occurring in 10% of patients. Unplanned hospitalisation due to ADE accounted for 19% of all hospitalisations. Performance status, polychemotherapy, PIM and ACB >3 were all independent predictors of unplanned hospitalisation due to ADE. A comparison of the retrospective group in Chapter 4 with the prospective group in Chapter 6 showed a 65% risk reduction in unplanned hospitalisation due to ADE.

7.3 Interpretation and implications of findings

7.3.1 Selecting patients for medication review

The findings from Chapter 4 demonstrated the potential benefit of providing all older adults with cancer attending geriatric oncology services with a structured medication review. Current guidelines from SIOG recommend older patients on ≥5 medications should be considered for a medication review (56), however this analysis shows that older adults with cancer experience unplanned hospitalisation due to ADE even in the absence of polypharmacy (Figure 16). This is supported by the multivariable logistic regression analyses conducted in both Chapter 4 and Chapter 6, where neither polypharmacy nor hyperpolypharmacy were independent predictors of unplanned hospitalisation due to ADE. These findings should inform future updates of these gold standard clinical practice guidelines to consider all patients receiving polychemotherapy as a priority for a medication review, even in the absence of polypharmacy. SIOG guidelines do recommend extending medication reviews to all patients where resources allow. Chapter 4 and Chapter 6 both support this recommendation; however, our results would indicate that patients being considered for polychemotherapy would be a better filter in limited resourced services than polypharmacy.

Guidelines focusing on the deprescribing of PIM, and optimising ACB in older adults with cancer are needed. Such guidelines should include the voice of the patient and be based upon the principles of shared decision making, to ensure that all stakeholders are involved.

To date, the literature has demonstrated that PIM identified using standard geriatric tools such as the STOPP criteria (7), and the AGS Beers Criteria (8) are prevalent in older adults with cancer. In an observational study in an Irish hospital, assessing 186 older adults with cancer, 73.1% of patients were taking at least one medication that met the STOPP criteria (278). Of the patients in this study that died within six months of enrolment, 81.8% of patients were taking a medication that met the OncPal criteria (279), a tool designed to identify PIM in palliative patients with a prognosis of ≤6 months.

A tool to identify PIM specific to geriatric oncology has been produced, based on the NCCN Older Adult Oncology guideline (90), called the geriatric oncology potentially inappropriate medication (GO-PIMS) scale (280). This scale has been studied in patients with haematological malignancies and was found to be associated with a cumulative increased risk of frailty (218).

Limitations of tools like STOPP and the AGS Beers criteria are related to their consensus validation not being specific to cancer patients, whereas GO-PIMs predominantly focuses on medication classes used in cancer supportive care. Therefore, the blanket application of such tools would have limited clinical effect, and the pragmatic adaptive iterative approach outlined in Chapter 5 outlines a method for conducting structured medication reviews in older adults with cancer that would apply these tools in a clinically appropriate context.

7.3.2 Impact for practice

Locally

The results of Chapter 4 and Chapter 6 have resulted in the reaffirmation of the commitment made by UHW to support clinical pharmacist activities in geriatric oncology. The clinical and statistical significance of the results from Chapter 6, informed by the evidence in Chapter 1 have been the foundation of a successful business case for a geriatric oncology pharmacist, which has been approved locally and will be funded by the NCCP, in line with the National Cancer Strategy 2017-2026 (42).

With the revised hospital pharmacist career structure in acute public hospitals coming into effect in 2025 (281), introducing a recognition of advanced specialist practice, this research has provided the pharmacy department in UHW with an example of effective advanced clinical practice in hospital pharmacy. Using the International Pharmaceutical Federation (FIP) global advanced development framework (282), the clinical activities outlined in Chapters 5 and 6 of this thesis are examples of pharmacy practice at the level of "Advanced Stage 2", defined as a practitioner who is an expert in their area of practice, and "Advanced Stage 3", defined as a pharmacist who is recognised as a leader in an area of expertise (nationally and internationally) (282).

As this thesis explored clinical activities that overlap between oncology, geriatrics and palliative care, it provided clear insight into advanced practice encompassing a broad scope (generalist), and a narrow scope (specialist) (282). This can be used as a framework locally to help design accreditation processes for other pharmacists.

Nationally

The most important component of this thesis is the methodology chapter (Chapter 5). This clearly outlined a methodology for delivering specialist clinical pharmacists structured medication reviews based on the EDQM framework and the EAHP hospital pharmacy statements(208, 211). To date, pharmacists have not been involved in oncology outpatient clinics in Ireland. The NCCP have allocated resources to prioritise geriatric oncology as part of the implementation of the National Cancer Strategy 2017-2026 (42). This includes the provision of four pharmacist posts across the country. This model of medication review still needs to be validated in the inpatient setting, to confirm the results observed by Herledan *et al.* in the French healthcare setting (209).

This thesis has demonstrated implementation rates of interventions that have been superior to the OPERAM and SENATOR RCT (273, 274). OPERAM was a multi-centre RCT conducted in four European sites, including one site in Cork, Ireland. SENATOR was conducted in six European sites, including one site in Cork, Ireland. Therefore, it is reasonable to compare the implementation rate found in the study reported in Chapter 6 to studies conducted within the context of Irish healthcare. A key component of implementation was the embedding of the pharmacist into the MDT, allowing for prospective influence over therapeutic decision making in relation to SACT, supportive care, and where the MDT felt it clinically appropriate, regular medications. This shows the synergistic benefit of collaborative pharmacist MDT participation with medical oncologists and consultant geriatricians.

The communication of the recommendations to primary care, in a format that provided a justification and a reference for that intervention, may also have influenced the encouraging implementation rate.

The Irish National Adverse Event Study-2 (INAES-2) assessed all adverse events reported for 2009 and 2015 and compared the results (283). ADE accounted for 19.1% of all events in 2009, compared to 25.3% in 2015 (p=0.13). In 2009, 18.3% of ADE were deemed preventable, this decreased to 15.6% in 2015 (p=0.6). This longitudinal study identified NSAID induced AKI as an ADE that was "Virtually certain evidence of preventability", an ADE which was observed in both the retrospective study in Chapter 4, and the prospective study in Chapter 6. This demonstrates a continuous need to review medication appropriateness, and the propensity for known ADE to occur. These ADE, occurring in the context of Irish healthcare, place a significant healthcare burden on the Irish healthcare system.

Internationally

The outcomes of the studies conducted in Chapter's 4 and 6 demonstrated the need to revise clinical practice internationally. SIOG guidelines inclusion of polypharmacy as an indicator of medication review appears to be less clinically meaningful than other indications (56). Where resources are limited, identifying patients who are commencing polychemotherapy is a better predictor of unplanned hospitalisation, and therefore may result in better allocation of resources, however, the need to consider a structured prospective medication review in all older adults with cancer appears to be justified.

The finding of PIM and polychemotherapy as independent predictors of unplanned hospitalisation due to ADE has significant implications for clinical practice. Currently there are no guidelines targeted at deprescribing PIM or reducing ACB specific to older adults with cancer. The transferability of tools aimed at deprescribing PIM or reducing ACB in older adults with cancer has also not been validated, therefore the pragmatic, adaptive iterative methodology outlined in Chapter 5 represents a more patient-centric approach to optimising these medications.

The impact of polychemotherapy on unplanned hospitalisation, and unplanned hospitalisation due to ADE reaffirms the needs for assessments in older adults with cancer that facilitates the use of toxicity calculators, such as the CARG tool (68), to help guide upfront dose reductions, or de-escalations of SACT.

7.3.3 Implications for policy

Locally

UHW revised the Clinical Pharmacy Services policy in 2025 to optimise clinical pharmacist activity in the context of limited resources. The methodology outlined in Chapter 5 was influential in determining the redesign of the service. Using the EDQM standards to define levels of clinical pharmacist activities, and being guided by the EAHP Hospital Pharmacy Statements, the policy is now aligned with international best practice (208, 211). This policy also follows a pragmatic, prognosis-based approach to specific interventions, such as electrocardiograph monitoring for QT prolonging medications, informed by the methodology employed in this thesis.

In relation to geriatric oncology, the role of the pharmacist is now firmly embedded into the GOAL MDT. The UHW geriatric oncology model of care has now evolved to include pharmacist input in the clinic and in the MDT setting.

Nationally

In 2025 the NCCP established the NCCP Geriatric Oncology Steering Committee (https://www.hse.ie/eng/services/list/5/cancer/about/structure/). This will oversee the development of a national model of care, and the next phase of geriatric oncology as part of the National Cancer Strategy (42).

With the introduction of a revised hospital pharmacy career structure and the recognition of advanced specialist pharmacist roles (281), this thesis highlights several of the competencies that should be included in accreditation processes for pharmacists working in oncology or haematology, in managing medications for older adults with cancer. The introduction of a medication optimisation educational module for older adults with cancer would be a valuable addition to the hospital pharmacist didactic portfolio.

This thesis supports the introduction of pharmacist prescribing in the acute hospital setting, particularly in specialist outpatient roles. The final report of the Expert Taskforce to Support the Expansion of the Role of Pharmacy by the Department of Health in Ireland proposes a timeline for the introduction of legislation to allow for pharmacist prescribing (284). The findings of this thesis emphasise the need for legislation to allow for pharmacist prescribing and deprescribing to take place within scope of practice, and demonstrates the capacity for pharmacists to identify opportunities to prescribe and deprescribe at a high level, with clinically meaningful

outcomes. Legislative changes that introduce pharmacist prescribing in Irish healthcare, must also support pharmacist-led deprescribing, to minimise preventable ADE, which may be reflected in further iterations of the longitudinal INAES studies, into the future.

Internationally

The implications for policy internationally begin with the findings that polychemotherapy, rather than polypharmacy, is a predictor of unplanned hospitalisation due to ADE. This finding should be considered in the next update of the Young SIOG guidelines for reviewing medications in older adults with cancer, with discussion around amending the inclusion criteria to include polychemotherapy, as opposed to polypharmacy, where resources are limited (56).

The identification of PIM as a predictor of unplanned hospitalisation due to ADE in Chapter 6 is a key finding. At present there are no guidelines for deprescribing aimed at older adults with cancer. Current practice is to use tools like STOPP/START, the AGS Beer's criteria, OncPal and others, however these tools are not validated for use in older adults with cancer, may not align with the patient prognosis (7, 8, 279). A deprescribing guideline, with recommendations matched to the patient context, such as patients being treated with curative intent, as opposed to non-curative intent is required to ensure these general deprescribing tools are appropriately incorporated. At present, the BOPA Geriatric Oncology Specialist Advisory Group are working on developing such a guideline. This is aimed at helping pharmacists determine if a deprescribing intervention is appropriate based on their prognosis, as well as their clinical context, signposting pharmacists to appropriate clinical practice

guidelines for identifying PIM in different clinical scenarios. An example of this would be using the HSE clinical practice guidelines on diabetes care towards end of life when reviewing medications in a diabetic palliative patient with a prognosis of <2 years, and giving that more weight than a generic deprescribing tool (66).

Working with pharmacists colleagues in SIOG, a protocol for a scoping review evaluating the educational needs of pharmacy professionals caring for older adults with cancer has been developed, due to the sparsity of educational material (158). This publication will be a key driver for postgraduate educational policy change amongst pharmacy professionals internationally, and the findings of this thesis help validate the need for pharmacists to be trained in optimising medications for older adults with cancer.

7.4 Strengths and limitations

A key strength of this study is in the pragmatic clinical approach which resulted in clinically significant interventions. This can be seen through the high level of acceptance of interventions, compared to other medication optimisation studies such as the SENATOR and OPERAM trials (273, 274), particularly in interventions specific to the GOAL MDT. The individualised patient-centric approach to the medication reviews also helped patients make shared decision making in relation to optimising medications including deprescribing.

There are some limitations associated with this thesis. The lack of a control arm was a significant consideration when designing this thesis outline. The creation of a pseudo-control arm using a retrospective analysis in Chapter 4 may be suboptimal from a statistical analysis perspective, however it was a practical necessity to

determine the impact of introducing a pharmacist on the GOAL clinic and MDT. The data at baseline for both groups demonstrated statistically significant differences in terms of age, gender, performance status, cancer stage, and total number of medications. The differences tended to favour a better outcome for those in the retrospective study due to younger age, and lower stage cancer at baseline. Patients in the prospective study had more advanced cancer, therefore increasing the likelihood of cancer-related complications and admissions and SACT toxicity.

A limitation of the studies reported in Chapter 4 and Chapter 6 is that they were conducted in a single centre, and the applicability of the results should be validated in a multi-centre study. The study reported in Chapter 6 details medication reviews conducted by a single pharmacist, which is also a limitation.

7.5 Recommendations for future research

This thesis has provided quantitative evidence of the benefit of pharmacist involvement in the geriatric oncology clinic and MDT. This represents an excellent starting point for the development of the geriatric oncology advanced specialist pharmacist role in geriatric oncology in Ireland. Further research could involve the following areas:

1. **Multi-centre validation of this research**

Primarily, reproducing research in this intervention across multiple sites in Ireland should be a research priority. Validation of these results in a multi-centre study would strengthen the findings considerably.

2. **Review clinic and oncology day ward**

This research was conducted exclusively in patients attending a GOAL clinic outpatient appointment prior to commencement of SACT. Future research should focus on the continuous assessment of patients who commence treatment, as they progress through their treatment cycles to allow for earlier interventions when SACT toxicity occurs, with the goal of keeping the grade of toxicity ≤2. Additional research should also on follow up medication reviews in older adults with cancer, who do not commence SACT due to the risk of toxicity, and to provide expert medication management advice on the use of supportive care medications in these patients. Research should also focus on the potential role of the pharmacist for patients established on SACT.

3. **Inpatient setting**

Future research should also focus on the impact of structured medication review for older adults with cancer in the inpatient setting. The impact of a structured geriatric oncology medication review on the detection of medication-related problems in Irish hospitals on admission, throughout admission and on discharge should also be a primary focus, assessing functionality, mortality, and length of stay as key outcome measures.

4. **Geriatric oncology pharmacists as non-medical prescribers**

The potential impact of geriatric oncology pharmacists as non-medical prescribers, after the full implementation of the final report of the Expert Taskforce to Support the Expansion of the Role of Pharmacy (284), should be a priority area for research. Additionally, the potential impact this may have on community and primary care teams should be examined.

5. Qualitative research

Finally, there is a dearth of qualitative research on the role of the pharmacist in geriatric oncology. Research into the barriers and facilitators of medication reviews in older adults with cancer, the experiences of stakeholders in pharmacist involvement in the clinic and MDT, as well as the expectations of stakeholders for pharmacist involvement would all add value to optimising pharmacist input into the geriatric oncology MDT.

By addressing the research priorities outlined above, pharmacist involvement in the targeted care of older adults with cancer, providing comprehensive medication management across the cancer care continuum will become the norm.

Addendum:

The initial search strategy in Chapter 2 identified two studied that met the inclusion criteria, De Glas *et al.* and Lavan *et al.* (64, 147). The updated literature search prior to manuscript submission to Research in Social and Administrative Pharmacy identified the retrospective study reported in Chapter 4 as having met the inclusion criteria (285). The addition of this study to the thesis chapter is outlined below.

Chapter 2 reflects the search of the literature prior to the completion of the work in Chapter 4. The final published paper reflects the updated search of the literature done prior to publication. This addendum reflects the published paper, with a PRISMA flow chart updated based on a final literature search conducted prior to thesis submission.

Results

An updated search strategy was conducted on 25.10.2025, and is outlined in Figure 32.

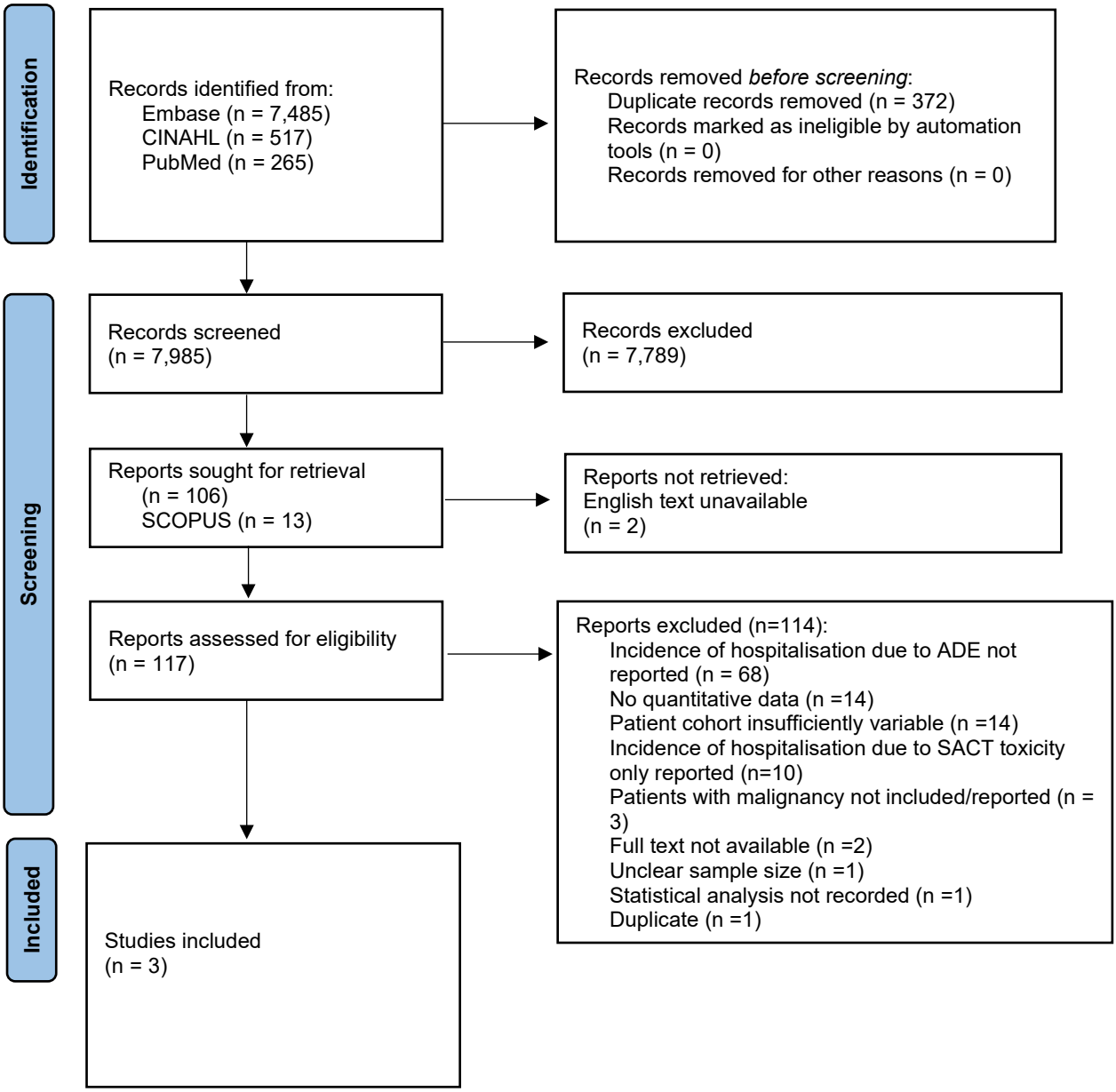


Figure 32: Updated PRISMA flow chart outlining the identification, screening, and subsequent inclusion of relevant papers.

This retrospective study reported 24% of patients who attended a medical oncology outpatient clinic had an unplanned hospitalisation due to ADE within 6 months of the index clinic visit (Table 42) (215).

Table 42: ADE in older adults with cancer, Walsh et al. (215)

Title	Author	Study type	Tumour Type	Total Number in Group (n)	Hospitalisation due to ADE (%)	Findings	Conclusions
Hospitalisation due to adverse drug events in older adults with cancer: A retrospective analysis (215)	Walsh *et al.* 2025	• Retrospective single-centre study • Older adults were defined as ≥70 years	All carcinoma	174	24	• Unplanned hospitalisation rate was 43% (n = 75), with 56% (n = 42) associated with an ADE. • Thirty-three percent of admissions were deemed to be potentially avoidable.	• Medication review as part of a CGA by a clinical pharmacist is recommended. • This may identify opportunities to avoid medications that could potentially lead to unplanned hospitalisation.

The MMAT assessment is shown in Table 43. Bias was found to be low, with sound methodological approaches for the study type, with some uncertainty about outcomes, due to no discernible comparator.

Table 43: MMAT assessment for Walsh et al. (215)

Walsh *et al.* (215)					
Category of study designs	**Methodological quality criteria**	**Responses**			
		Yes	**No**	**Can't tell**	**Comment**
Screening questions	S1. Are there clear research questions?	X			
	2. Do the collected data allow to address the research questions?	X			
Quantitative non-randomized	3.1. Are the participants representative of the target population?	X			
	3.2. Are measurements appropriate regarding both the outcome and intervention (or exposure)?	X			

	3.3. Are there complete outcome data?	X			
	3.4. Are the confounders accounted for in the design and analysis?	X			
	3.5. During the study period, is the intervention administered (or exposure occurred) as intended?			X	

The GRADE assessment is shown in Table 44. Certainty of evidence was determined to be low.

Table 44: GRADE assessment for Walsh et al. (215)

Study	**GRADE Assessment**							
	Baseline Certainty	**Risk of Bias**	**Imprecision**	**Inconsistency**	**Indirectness**	**Publication Bias**	**Reason for Ranking Up**	**GRADE Rating**
Walsh *et al.* (215)	Low – retrospective study	N/A	N/A	N/A	N/A	N/A	N/A	Low

Appendices

Appendix 1: PRISMA checklist for systematic review

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods – Inclusion criteria
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods – search strategy
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods – Study selection and data extraction

Section and Topic	Item #	Checklist item	Location where item is reported
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods – Study selection and data extraction
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods – data synthesis
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods – data synthesis
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods – assessment of methodological quality
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Methods – data synthesis
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Methods – data synthesis
	13b	Describe any methods required to prepare the data for presentation or	Methods – data synthesis

Section and Topic	Item #	Checklist item	Location where item is reported
		synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Methods – data synthesis
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Methods – assessment of methodological quality
	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Methods – assessment of methodological quality
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Results
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Results

Section and Topic	Item #	Checklist item	Location where item is reported
Study characteristics	17	Cite each included study and present its characteristics.	Results – study designs
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Results – Quality Appraisal
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Results
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Results – quality appraisal
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A – not conducting meta-analysis
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Results – quality appraisal
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Results – quality appraisal
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion – summary of evidence

Section and Topic	Item #	Checklist item	Location where item is reported
	23b	Discuss any limitations of the evidence included in the review.	Discussion – summary of evidence
	23c	Discuss any limitations of the review processes used.	Discussion – limitations and strengths
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion – Implications for practice and future research
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Methods
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Methods
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Can be found in PROSPERO record
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Declaration of sources of funding
Competing interests	26	Declare any competing interests of review authors.	Declarations of conflict of Interest
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Availability of data, code and other materials

Appendix 2: Systematic review search strategy

Embase Search Strategy:

No.	Query
#26	((geriatr*:ab,ti OR elderly:ab,ti OR aged:ab,ti OR geront*:ab,ti OR 'older adult':ab,ti OR senior*:ab,ti) OR ('geriatric'/exp OR 'geriatric assessment'/exp OR 'aged'/exp OR 'geriatrics'/exp)) AND ((cancer:ab,ti OR oncolog*:ab,ti OR malignan*:ab,ti OR neoplasm*:ab,ti OR tumo*:ab,ti OR carcinoma:ab,ti) OR ('malignant neoplasm'/exp OR 'carcinoma'/exp OR 'neoplasm'/exp)) AND ((hospitali?ation:ab,ti OR admission*:ab,ti OR readmission*:ab,ti OR 'hospital admission*':ab,ti) OR ('hospital admission'/exp OR 'hospital readmission'/exp OR 'hospitalisation'/exp)) AND (('adverse drug event':ab,ti OR 'side effect':ab,ti OR 'adverse drug reaction':ab,ti) OR ('adverse event'/exp OR 'side effect'/exp OR 'adverse drug reaction'/exp))
#25	('adverse drug event':ab,ti OR 'side effect':ab,ti OR 'adverse drug reaction':ab,ti) OR ('adverse event'/exp OR 'side effect'/exp OR 'adverse drug reaction'/exp)
#24	'adverse event'/exp OR 'side effect'/exp OR 'adverse drug reaction'/exp
#23	'adverse drug event':ab,ti OR 'side effect':ab,ti OR 'adverse drug reaction':ab,ti
#22	'adverse drug reaction'/exp
#21	'side effect'/exp
#20	'adverse event'/exp
#19	(hospitali?ation:ab,ti OR admission*:ab,ti OR readmission*:ab,ti OR 'hospital admission*':ab,ti) OR ('hospital admission'/exp OR 'hospital readmission'/exp OR 'hospitalisation'/exp)
#18	'hospital admission'/exp OR 'hospital readmission'/exp OR 'hospitalisation'/exp
#17	hospitali?ation:ab,ti OR admission*:ab,ti OR readmission*:ab,ti OR 'hospital admission*':ab,ti
#16	'hospitalisation'/exp
#15	'hospital readmission'/exp
#14	'hospital admission'/exp
#13	(cancer:ab,ti OR oncolog*:ab,ti OR malignan*:ab,ti OR neoplasm*:ab,ti OR tumo*:ab,ti OR carcinoma:ab,ti) OR ('malignant neoplasm'/exp OR 'carcinoma'/exp OR 'neoplasm'/exp)
#12	'malignant neoplasm'/exp OR 'carcinoma'/exp OR 'neoplasm'/exp
#11	cancer:ab,ti OR oncolog*:ab,ti OR malignan*:ab,ti OR neoplasm*:ab,ti OR tumo*:ab,ti OR carcinoma:ab,ti
#10	'neoplasm'/exp
#9	'carcinoma'/exp
#8	'malignant neoplasm'/exp
#7	(geriatr*:ab,ti OR elderly:ab,ti OR aged:ab,ti OR geront*:ab,ti OR 'older adult':ab,ti OR senior*:ab,ti) OR ('geriatric'/exp OR 'geriatric assessment'/exp OR 'aged'/exp OR 'geriatrics'/exp)
#6	'geriatric'/exp OR 'geriatric assessment'/exp OR 'aged'/exp OR 'geriatrics'/exp
#5	'geriatrics'/exp
#4	'aged'/exp
#3	geriatr*:ab,ti OR elderly:ab,ti OR aged:ab,ti OR geront*:ab,ti OR 'older adult':ab,ti OR senior*:ab,ti
#2	'geriatric assessment'/exp
#1	'geriatric'/exp

PubMed Search Strategy:

Search number	Query	Search Details
23	(((((((((geriatr*[Title/Abstract]) OR (elderly[Title/Abstract])) OR (aged[Title/Abstract])) OR (geront*[Title/Abstract])) OR (older adult*[Title/Abstract])) OR (senior*[Title/Abstract])) OR ((((("Geriatrics"[Mesh]) OR ("Geriatric Assessment"[Mesh])) OR ("Aged"[Mesh])) OR ("Aged, 80 and over"[Mesh]))) AND (((((((cancer[Title/Abstract]) OR (oncolog*[Title/Abstract])) OR (malignan*[Title/Abstract])) OR (neoplas*[Title/Abstract])) OR (tumo*[Title/Abstract])) OR (carcinoma*[Title/Abstract])) OR ((("Neoplasms"[Mesh]) OR ("Carcinoma"[Mesh])) OR ("Medical Oncology"[Mesh])))) AND (((((hospitali?ation[Title/Abstract]) OR (admission[Title/Abstract])) OR (readmission[Title/Abstract])) OR (hospital admission[Title/Abstract])) OR ((("Hospitalisation"[Mesh]) OR ("Patient Admission"[Mesh])) OR ("Patient Readmission"[Mesh]))))) AND (("Drug-Related Side Effects and Adverse Reactions"[Mesh]) OR (((adverse drug event*[Title/Abstract]) OR (adverse drug reaction*[Title/Abstract])) OR (side effect*[Title/Abstract]))))	("geriatr*"[Title/Abstract] OR "elderly"[Title/Abstract] OR "Aged"[Title/Abstract] OR "geront*"[Title/Abstract] OR "older adult*"[Title/Abstract] OR "senior*"[Title/Abstract] OR ("Geriatrics"[MeSH Terms] OR "Geriatric Assessment"[MeSH Terms] OR "Aged"[MeSH Terms] OR "aged, 80 and over"[MeSH Terms])) AND ("cancer"[Title/Abstract] OR "oncolog*"[Title/Abstract] OR "malignan*"[Title/Abstract] OR "neoplas*"[Title/Abstract] OR "tumo*"[Title/Abstract] OR "carcinoma*"[Title/Abstract] OR ("Neoplasms"[MeSH Terms] OR "Carcinoma"[MeSH Terms] OR "Medical Oncology"[MeSH Terms])) AND (("hospitali"[All Fields] AND "ation"[Title/Abstract]) OR "admission"[Title/Abstract] OR "readmission"[Title/Abstract] OR "hospital admission"[Title/Abstract] OR ("Hospitalisation"[MeSH Terms] OR "Patient Admission"[MeSH Terms] OR "Patient Readmission"[MeSH Terms])) AND ("Drug-Related Side Effects and Adverse Reactions"[MeSH Terms] OR ("adverse drug event*"[Title/Abstract] OR "adverse drug reaction*"[Title/Abstract] OR "side effect*"[Title/Abstract]))
22	("Drug-Related Side Effects and Adverse Reactions"[Mesh]) OR (((adverse drug event*[Title/Abstract]) OR (adverse drug reaction*[Title/Abstract])) OR (side effect*[Title/Abstract]))	"Drug-Related Side Effects and Adverse Reactions"[MeSH Terms] OR "adverse drug event*"[Title/Abstract] OR "adverse drug reaction*"[Title/Abstract] OR "side effect*"[Title/Abstract]
21	((adverse drug event*[Title/Abstract]) OR (adverse drug reaction*[Title/Abstract])) OR (side effect*[Title/Abstract])	"adverse drug event*"[Title/Abstract] OR "adverse drug reaction*"[Title/Abstract] OR "side effect*"[Title/Abstract]

20	"Drug-Related Side Effects and Adverse Reactions"[Mesh]	"Drug-Related Side Effects and Adverse Reactions"[MeSH Terms]
19	((((hospitali?ation[Title/Abstract]) OR (admission[Title/Abstract])) OR (readmission[Title/Abstract])) OR (hospital admission[Title/Abstract])) OR ((("Hospitalisation"[Mesh]) OR ("Patient Admission"[Mesh])) OR ("Patient Readmission"[Mesh]))	("hospitali"[All Fields] AND "ation"[Title/Abstract]) OR "admission"[Title/Abstract] OR "readmission"[Title/Abstract] OR "hospital admission"[Title/Abstract] OR ("Hospitalisation"[MeSH Terms] OR "Patient Admission"[MeSH Terms] OR "Patient Readmission"[MeSH Terms])
18	(("Hospitalisation"[Mesh]) OR ("Patient Admission"[Mesh])) OR ("Patient Readmission"[Mesh])	"Hospitalisation"[MeSH Terms] OR "Patient Admission"[MeSH Terms] OR "Patient Readmission"[MeSH Terms]
17	(((hospitali?ation[Title/Abstract]) OR (admission[Title/Abstract])) OR (readmission[Title/Abstract])) OR (hospital admission[Title/Abstract])	("hospitali"[All Fields] AND "ation"[Title/Abstract]) OR "admission"[Title/Abstract] OR "readmission"[Title/Abstract] OR "hospital admission"[Title/Abstract]
16	"Patient Readmission"[Mesh]	"Patient Readmission"[MeSH Terms]
15	"Patient Admission"[Mesh]	"Patient Admission"[MeSH Terms]
14	"Hospitalisation"[Mesh]	"Hospitalisation"[MeSH Terms]
13	((((((cancer[Title/Abstract]) OR (oncolog*[Title/Abstract])) OR (malignan*[Title/Abstract])) OR (neoplas*[Title/Abstract])) OR (tumo*[Title/Abstract])) OR (carcinoma*[Title/Abstract])) OR ((("Neoplasms"[Mesh]) OR ("Carcinoma"[Mesh])) OR ("Medical Oncology"[Mesh]))	"cancer"[Title/Abstract] OR "oncolog*"[Title/Abstract] OR "malignan*"[Title/Abstract] OR "neoplas*"[Title/Abstract] OR "tumo*"[Title/Abstract] OR "carcinoma*"[Title/Abstract] OR "Neoplasms"[MeSH Terms] OR "Carcinoma"[MeSH Terms] OR "Medical Oncology"[MeSH Terms]
12	(("Neoplasms"[Mesh]) OR ("Carcinoma"[Mesh])) OR ("Medical Oncology"[Mesh])	"Neoplasms"[MeSH Terms] OR "Carcinoma"[MeSH Terms] OR "Medical Oncology"[MeSH Terms]
11	(((((cancer[Title/Abstract]) OR (oncolog*[Title/Abstract])) OR (malignan*[Title/Abstract])) OR (neoplas*[Title/Abstract])) OR (tumo*[Title/Abstract])) OR (carcinoma*[Title/Abstract])	"cancer"[Title/Abstract] OR "oncolog*"[Title/Abstract] OR "malignan*"[Title/Abstract] OR "neoplas*"[Title/Abstract] OR "tumo*"[Title/Abstract] OR "carcinoma*"[Title/Abstract]
10	"Medical Oncology"[Mesh]	"Medical Oncology"[MeSH Terms]
9	"Carcinoma"[Mesh]	"Carcinoma"[MeSH Terms]

8	"Neoplasms"[Mesh]	"Neoplasms"[MeSH Terms]
7	((((((geriatr*[Title/Abstract]) OR (elderly[Title/Abstract])) OR (aged[Title/Abstract])) OR (geront*[Title/Abstract])) OR (older adult*[Title/Abstract])) OR (senior*[Title/Abstract])) OR ((((("Geriatrics"[Mesh]) OR ("Geriatric Assessment"[Mesh])) OR ("Aged"[Mesh])) OR ("Aged, 80 and over"[Mesh]))	"geriatr*"[Title/Abstract] OR "elderly"[Title/Abstract] OR "Aged"[Title/Abstract] OR "geront*"[Title/Abstract] OR "older adult*"[Title/Abstract] OR "senior*"[Title/Abstract] OR "Geriatrics"[MeSH Terms] OR "Geriatric Assessment"[MeSH Terms] OR "Aged"[MeSH Terms] OR "aged, 80 and over"[MeSH Terms]
6	((("Geriatrics"[Mesh]) OR ("Geriatric Assessment"[Mesh])) OR ("Aged"[Mesh])) OR ("Aged, 80 and over"[Mesh])	"Geriatrics"[MeSH Terms] OR "Geriatric Assessment"[MeSH Terms] OR "Aged"[MeSH Terms] OR "aged, 80 and over"[MeSH Terms]
5	(((((geriatr*[Title/Abstract]) OR (elderly[Title/Abstract])) OR (aged[Title/Abstract])) OR (geront*[Title/Abstract])) OR (older adult*[Title/Abstract])) OR (senior*[Title/Abstract])	"geriatr*"[Title/Abstract] OR "elderly"[Title/Abstract] OR "aged"[Title/Abstract] OR "geront*"[Title/Abstract] OR "older adult*"[Title/Abstract] OR "senior*"[Title/Abstract]
4	"Aged, 80 and over"[Mesh]	"aged, 80 and over"[MeSH Terms]
3	"Aged"[Mesh]	"Aged"[MeSH Terms]
2	"Geriatric Assessment"[Mesh]	"Geriatric Assessment"[MeSH Terms]
1	"Geriatrics"[Mesh]	"Geriatrics"[MeSH Terms]

CINAHL Search Strategy:

#	Query	Limiters/Expanders	Last Run Via
S23	S5 AND S11 AND S17 AND S22	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S22	S20 OR S21	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete

S21	S18 OR S19	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S20	AB adverse event OR AB adverse reaction OR AB side effect	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S19	(MH "Medication Side Effects (Saba CCC)")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S18	(MH "Adverse Drug Event+")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S17	S15 OR S16	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S16	S12 OR S13 OR S14	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
			Search Screen - Advanced Search
		Search modes - Boolean/Phrase	Database - CINAHL Complete
S15	AB hospitali?ation OR AB admission OR AB readmission OR AB hospital admission	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S14	(MH "Readmission")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S13	(MH "Patient Admission")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S12	(MH "Hospitalisation+")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S11	S9 OR S10	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S10	S6 OR S7 OR S8	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S9	AB cancer OR AB oncolog* OR AB malignan* OR AB neoplasm* OR AB tumo* OR AB carcinoma*	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S8	(MH "Oncology+")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases

		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S7	(MH "Carcinoma+")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S6	(MH "Cancer Patients")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S5	S3 OR S4	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S4	S1 OR S2	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S3	AB geriatr* OR AB elderly OR AB geront* OR AB older adult* OR AB senior*	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
			Search Screen - Advanced Search
		Search modes - Boolean/Phrase	Database - CINAHL Complete
S2	(MH "Aged+")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete
S1	(MH "Geriatric Assessment+")	Expanders - Apply equivalent subjects	Interface - EBSCOhost Research Databases
		Search modes - Boolean/Phrase	Search Screen - Advanced Search
			Database - CINAHL Complete

Appendix 3: PICOST Table

<table>
<tr><th colspan="7">PICOST TABLE</th></tr>
<tr><th colspan="2">Patient/ Population</th><th>Intervention/ Indicator</th><th>Control/ Compare</th><th>Outcome</th><th>Study</th><th>Time/Type of Study</th></tr>
<tr><td>Geriatric</td><td>Oncology</td><td>Adverse drug effect</td><td rowspan="5">N/A</td><td rowspan="2">Hospitalisation</td><td rowspan="5">Quantitative data</td><td rowspan="5">N/A</td></tr>
<tr><td>Elderly</td><td>Cancer</td><td>Adverse drug event</td></tr>
<tr><td>Aged</td><td>Carcinoma</td><td>Side effect</td><td rowspan="2">Admission</td></tr>
<tr><td>Older adult</td><td>Neoplasm</td><td>Polypharmacy</td></tr>
<tr><td rowspan="2">Senior</td><td rowspan="2">Malignancy</td><td>Toxicity</td><td rowspan="2">Readmission</td></tr>
<tr><td>Inappropriate prescribing</td></tr>
</table>

Appendix 4: Adapted Cochrane data collection tool

Ospidéal Ollscoile Phort Láirge
University Hospital Waterford
Regional Cancer Centre South East

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Cochrane Data collection form for intervention reviews: RCTs and non-RCT

Version 3, April 2014

This form can be used as a guide for developing your own data extraction form. Sections can be expanded and added, and irrelevant sections can be removed. It is difficult to design a single form that meets the needs of all reviews, so it is important to consider carefully the information you need to collect, and design your form accordingly. Information included on this form should be comprehensive, and may be used in the text of your review, 'Characteristics of included studies' table, risk of bias assessment, and statistical analysis.

Using this form, or an adaptation of it, will help you to meet MECIR standards for collecting and reporting information about studies for your review, and analysing their results (see MECIR standards C43 to C55; R41 to R45).

Notes on using data extraction form:

- Be consistent in the order and style you use to describe the information for each report.
- Record any missing information as unclear or not described, to make it clear that the information was not found in the study report(s), not that you forgot to extract it.
- Include any instructions and decision rules on the data collection form, or in an accompanying document. It is important to practice using the form and give training to any other authors using the form.

Review title or ID	
Study ID *(surname of first author and year first full report of study was published e.g. Smith 2001)*	
Report ID	
Report ID of other reports of this study including errata or retractions	
Notes	

General Information

Date form completed *(dd/mm/yyyy)*	
Name/ID of person extracting data	

Reference citation	
Study author contact details	
Publication type *(e.g. full report, abstract, letter)*	
Notes:	

Study eligibility

Study Characteristics	Eligibility criteria *(Insert inclusion criteria for each characteristic as defined in the Protocol)*	Eligibility criteria met? Yes No N/A	Location in text or source *(pg & ¶/fig/table/other)*
Type of study	Randomised Controlled Trial	☐ ☐ ☒	
	Quasi-randomised Controlled Trial	☐ ☐ ☒	
	Controlled Before and After Study Contemporaneous data collection Comparable control sites At least 2 x intervention and 2 x control clusters	☐ ☐ ☒	
	Interrupted Time Series At least 3 time points before and 3 after the intervention Clearly defined intervention point	☐ ☐ ☒	
	Other design (specify):	☒ ☐ ☐	Retrospective Cohort Study
Participants		☒ ☐ ☐	
Types of intervention		☐ ☐ ☐	
Types of comparison		☐ ☐ ☐	
Types of outcome measures		☐ ☐ ☐	
INCLUDE ☐		EXCLUDE ☐	

Reason for exclusion	
Notes:	

DO NOT PROCEED IF STUDY EXCLUDED FROM REVIEW

Characteristics of included studies

Methods

	Descriptions as stated in report/paper		**Location in text or source** *(pg & ¶/fig/table/other)*
Aim of study *(e.g. efficacy, equivalence, pragmatic)*			
Design *(e.g. parallel, crossover, non-RCT)*			
Unit of allocation *(by individuals, cluster/ groups or body parts)*			
Start date			
End date			
Duration of participation *(from recruitment to last follow-up)*			
Ethical approval needed/ obtained for study	☐ Yes ☐ No ☐ Unclear		
Notes:			

Participants

	Description *Include comparative information for each intervention or comparison group if available*	Location in text or source *(pg & ¶/fig/table/other)*

Population description *(from which study participants are drawn)*		
Setting *(including location and social context)*		
Inclusion criteria		
Exclusion criteria		
Method of recruitment of participants *(e.g. phone, mail, clinic patients)*		
Informed consent obtained	☐ Yes ☐ No ☐ Unclear	
Total no. randomised *(or total pop. at start of study for NRCTs)*		
Clusters *(if applicable, no., type, no. people per cluster)*		
Baseline imbalances		
Withdrawals and exclusions *(if not provided below by outcome)*		
Age		
Sex		
Race/Ethnicity		
Severity of illness		
Co-morbidities		
Other relevant sociodemographics		
Subgroups measure		

Subgroups reported		
Notes:		

Intervention groups

Copy and paste table for each intervention and comparison group

Intervention Group 1

	Description as stated in report/paper	Location in text or source *(pg & ¶/fig/table/other)*
Group name		
No. randomised to group *(specify whether no. people or clusters)*		
Theoretical basis *(include key references)*		
Description *(include sufficient detail for replication, e.g. content, dose, components)*		
Duration of treatment period		
Timing *(e.g. frequency, duration of each episode)*		
Delivery *(e.g. mechanism, medium, intensity, fidelity)*		
Providers *(e.g. no., profession, training, ethnicity etc. if relevant)*		
Co-interventions		
Economic information *(i.e. intervention cost, changes in other costs as result of intervention)*		

Resource requirements *(e.g. staff numbers, cold chain, equipment)*		
Integrity of delivery		
Compliance		
Notes:		

Outcomes

Copy and paste table for each outcome.

Outcome 1

	Description as stated in report/paper		Location in text or source *(pg & ¶/fig/table/other)*
Outcome name			
Time points measured *(specify whether from start or end of intervention)*			
Time points reported			
Outcome definition *(with diagnostic criteria if relevant)*			
Person measuring/ reporting			
Unit of measurement *(if relevant)*			
Scales: upper and lower limits *(indicate whether high or low score is good)*			
Is outcome/tool validated?	☐ Yes ☐ No ☐ Unclear		
Imputation of missing data *(e.g. assumptions made for ITT analysis)*			

Assumed risk estimate *(e.g. baseline or population risk noted in Background)*		
Power *(e.g. power & sample size calculation, level of power achieved)*		
Notes:		

Other

Study funding sources *(including role of funders)*		
Possible conflicts of interest *(for study authors)*		
Notes:		

Risk of Bias assessment

(See Handbook Chapter 8. Additional domains may be added for non-randomised studies.)

Domain	Risk of bias Low High Unclear	Support for judgement *(include direct quotes where available with explanatory comments)*	Location in text or source *(pg & ¶/fig/table/other)*
Random sequence generation *(selection bias)*	☐ ☐ ☐		
Allocation concealment *(selection bias)*	☐ ☐ ☐		
Blinding of participants and personnel *(performance bias)*	☐ ☐ ☐	Outcome group: All/	
(if separate judgement by outcome(s) required)	☐ ☐ ☐	Outcome group:	

Blinding of outcome assessment *(detection bias)*	☐ ☐ ☐	Outcome group: All/	
(if separate judgement by outcome(s) required)	☐ ☐ ☐	Outcome group:	
Incomplete outcome data *(attrition bias)*	☐ ☐ ☐	Outcome group: All/	
(if separate judgement by outcome(s) required)	☐ ☐ ☐	Outcome group:	
Selective outcome reporting? *(reporting bias)*	☐ ☐ ☐		
Other bias	☐ ☐ ☐		
Notes:			

Data and analysis

Copy and paste the appropriate table for each outcome, including additional tables for each time point and subgroup as required.

For RCT/CCT

Dichotomous outcome

	Description as stated in report/paper	Location in text or source *(pg & ¶/fig/table/other)*
Comparison		
Outcome		
Subgroup		
Time point *(specify from start or end of intervention)*		

Results	Intervention		Comparison		
	No. with event	Total in group	No. with event	Total in group	
Any other results reported *(e.g. odds ratio, risk difference, CI or P value)*					
No. missing participants					
Reasons missing					
No. participants moved from other group					
Reasons moved					
Unit of analysis *(by individuals, cluster/groups or body parts)*					
Statistical methods used and appropriateness of these *(e.g. adjustment for correlation)*					
Reanalysis required? *(specify, e.g. correlation adjustment)*	☐ Yes ☐ No ☐ Unclear				
Reanalysis possible?	☐ Yes ☐ No ☐ Unclear				
Reanalysed results					
Notes:					

For RCT/CCT

Continuous outcome

	Description as stated in report/paper						Location in text or source *(pg & ¶/fig/table/other)*
Comparison							
Outcome							
Subgroup							
Time point *(specify from start or end of intervention)*							
Post-intervention or change from baseline?							
Results	Intervention			Comparison			
	Mean	SD *(or other variance, specify)*	No. participants	Mean	SD *(or other variance, specify)*	No. participants	
Any other results reported *(e.g. mean difference, CI, P value)*							
No. missing participants							
Reasons missing							
No. participants moved from other group							
Reasons moved							
Unit of analysis *(individuals, cluster/ groups or body parts)*							

Statistical methods used and appropriateness of these *(e.g. adjustment for correlation)*					
Reanalysis required? *(specify)*	☐ Yes	☐ No	☐ Unclear		
Reanalysis possible?	☐ Yes	☐ No	☐ Unclear		
Reanalysed results					
Notes:					

For RCT/CCT

Other outcome

	Description as stated in report/paper				Location in text or source *(pg & ¶/fig/table/other)*
Comparison					
Outcome					
Subgroup					
Time point *(specify from start or end of intervention)*					
No. participant	Intervention		Control		
Results	Intervention result	SE (or other variance)	Control result	SE (or other variance)	
	Overall results		SE (or other variance)		

Any other results reported			
No. missing participants			
Reasons missing			
No. participants moved from other group			
Reasons moved			
Unit of analysis *(by individuals, cluster/groups or body parts)*			
Statistical methods used and appropriateness of these			
Reanalysis required? *(specify)*	☐ Yes ☐ No ☐ Unclear		
Reanalysis possible?	☐ Yes ☐ No ☐ Unclear		
Reanalysed results			
Notes:			

For Controlled Before-and-After study (CBA)

	Description as stated in report/paper	Location in text or source *(pg & ¶/fig/table/other)*
Comparison		
Outcome		
Subgroup		

Time point *(specify from start or end of intervention)*					
Post-intervention or change from baseline?					
No. participants	Intervention		Control		
Results	Intervention result	SE *(or other variance, specify)*	Control result	SE *(or other variance, specify)*	
	Overall results		SE *(or other variance, specify)*		
Any other results reported					
No. missing participants					
Reasons missing					
No. participants moved from other group					
Reasons moved					
Unit of analysis *(individuals, cluster/ groups or body parts)*					
Statistical methods used and appropriateness of these					

Reanalysis required? *(specify)*	☐ Yes ☐ No ☐ Unclear		
Reanalysis possible?	☐ Yes ☐ No ☐ Unclear		
Reanalysed results			
Notes:			

For Interrupted Time Series study (ITS)

	Description as stated in report/paper		Location in text or source *(pg & ¶/fig/table/other)*
Comparison			
Outcome			
Subgroup			
Length of time points measured *(e.g. days, months)*			
Total period measured			
No. participants measured			
No. missing participants			
Reasons missing			
	Pre-intervention	Post-intervention	
No. time points measured			
Mean value *(with variance measure)*			
Any other results reported			

Unit of analysis *(individuals or cluster/ groups)*					
Statistical methods used and appropriateness of these					
Reanalysis required? *(specify)*	☐ Yes ☐ No ☐ Unclear				
Reanalysis possible?	☐ Yes ☐ No ☐ Unclear				
Individual time point results					
Read from figure?	☐ Yes ☐ No				
Reanalysed results	Change in level	SE	Change in slope	SE	
Notes:					

Other information

	Description as stated in report/paper	**Location in text or source** *(pg & ¶/fig/table/other)*
Key conclusions of study authors		
References to other relevant studies		
Correspondence required for further study information *(from whom, what and when)*		
Notes:		

Definitions

Assumed risk estimate	An estimate of the risk of an event or average score without the intervention, used in Cochrane 'Summary of findings tables'. If a study provides useful estimates of the risk or average score of different subgroups of the population, or an estimate based on a representative observational study, you may wish to collect this information.
Bias	A systematic error or deviation in results or inferences from the truth. In studies of the effects of health care, the main types of bias arise from systematic differences in the groups that are compared (selection bias), the care that is provided, exposure to other factors apart from the intervention of interest (performance bias), withdrawals or exclusions of people entered into a study (attrition bias) or how outcomes are assessed (detection bias). Reviews of studies may also be particularly affected by reporting bias, where a biased subset of all the relevant data is available.
Change from baseline	A measure for a continuous outcome calculated as the difference between the baseline score and the post-intervention score.
Clusters	A group of participants who have been allocated to the same intervention arm together, as in a cluster-randomised trial, e.g. a whole family, town, school or patients in a clinic may be allocated to the same intervention rather than separately allocating each individual to different arms.
Co-morbidities	The presence of one or more diseases or conditions other than those of primary interest. In a study looking at treatment for one disease or condition, some of the individuals may have other diseases or conditions that could affect their outcomes.
Compliance	Participant behaviour that abides by the recommendations of a doctor, other health care provider or study investigator (also called adherence or concordance).
Contemporaneous data collection	When data are collected at the same point(s) in time or covering the same time period for each intervention arm in a study (that is, historical data are not used as a comparison).
Controlled Before and After Study (CBA)	A non-randomised study design where a control population of similar characteristics and performance as the intervention group is identified. Data are collected before and after the intervention in both the control and intervention groups
Exclusions	Participants who were excluded from the study or the analysis by the investigators.
Imputation	Assuming a value for a measure where the true value is not available (e.g. assuming last observation carried forward for missing participants).
Integrity of delivery	The degree to which the specified procedures or components of an intervention are delivered as originally planned.

Interrupted Time Series (ITS)	A research design that collects observations at multiple time points before and after an intervention (interruption). The design attempts to detect whether the intervention has had an effect significantly greater than the underlying trend.
Post-intervention	The value of an outcome measured at some time point following the beginning of the intervention (may be during or after the intervention period).
Power	In clinical trials, power is the probability that a trial will obtain a statistically significant result when the true intervention effect is a specified size. For a given size of effect, studies with more participants have greater power. Note that power should not be considered in the risk of bias assessment.
Providers	The person or people responsible for delivering an intervention and related care, who may or may not require specific qualifications (e.g. doctors, physiotherapists) or training.
Quasi-randomised controlled trial	A study in which the method of allocating people to intervention arms was not random, but was intended to produce similar groups when used to allocate participants. Quasi-random methods include: allocation by the person's date of birth, by the day of the week or month of the year, by a person's medical record number, or just allocating every alternate person.
Reanalysis	Additional analysis of a study's results by a review author (e.g. to introduce adjustment for correlation that was not done by the study authors).
Report ID	A unique ID code given to a publication or other report of a study by the review author (e.g. first author's name and year of publication). If a study has more than one report (e.g. multiple publications or additional unpublished data) a separate Report ID can be allocated to each to help review authors keep track of the source of extracted data.
Sociodemographics	Social and demographic information about a study or its participants, including economic and cultural information, location, age, gender, ethnicity, etc.
Study ID	A unique ID code given to an included or excluded study by the review author (e.g. first author's name and year of publication from the main report of the study). Although a study may have multiple reports or references, it should have one single Study ID to help review authors keep track of all the different sources of information for a study.
Theoretical basis	The use of a particular theory (such as theories of human behaviour change) to design the components and implementation of an intervention
Unit of allocation	The unit allocated to an intervention arm. In most studies individual participants will be allocated, but in others it may be individual body parts (e.g. different teeth or joints may be allocated separately) or clusters of multiple people.

Unit of analysis	The unit used to calculate N in an analysis, and for which the result is reported. This may be the number of individual people, or the number of body parts or clusters of people in the study.
Unit of measurement	The unit in which an outcome is measured, e.g. height may be measured in cm or inches; depression may be measured using points on a particular scale.
Validation	A process to test and establish that a particular measurement tool or scale is a good measure of that outcome.
Withdrawals	Participants who voluntarily withdrew from participation in a study before the completion of outcome measurement.

Sources:

Cochrane Collaboration Glossary, 2010. Available from www.cochrane.org/glossary.

Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from handbook.cochrane.org.

Last JM (editor), A Dictionary of Epidemiology, 4th Ed. New York: Oxford University Press, 2001.

Schünemann H, Brożek J, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendation. Version 3.2 [updated March 2009]. The GRADE Working Group, 2009.

Appendix 5: Baseline data collection form and report

Feidhmeannacht na Seirbhíse Sláinte Health Service Executive	UHW PHARMACY DEPARTMENT **Geriatric Oncology Medicines Optimisation Form** **Version 1.3**	University College Cork, Ireland Coláiste na hOllscoile Corcaigh

Patient Name:			MRN:		
Consultant:			DOB:		
Diagnosis:			Stage:		
Viral Screen (if required):			Allergies:		
ECOG:			G8:		
Co-morbidities:	1.		Medical History:	1.	
	2.			2.	
	3.			3.	
	4.			4.	
	5.			5.	
Anti-cancer Treatment Plan:			Ancillary Medications		Dose Reduction at baseline? Y / N

Geriatric Oncology Clinic Visit Date:		**Medicines Reconciliation**			
Height(cm)		**Community Pharmacy:** **Patient Reported Adherence:** **Dosage Aids:**			
Weight(kg)					
BSA (m^2)		**Medication**	**Dose**	**Frequency**	**Route**
Serum Creatinine (µmol/L)					
Creatinine Clearance (mL/min)					
Bilirubin (µmol/L)					
ALT (U/L)					
AST (U/L)					
Hb (g/dl)					
WBC ($x10^9$/L)					
Neutrophils ($x10^9$/L)		**OTC and Herbal Products/Remedies**			
Platelets ($x10^9$/L)					
Electrolytes:					
Other:					
Comments		Med Rec Source:			

Drug Interactions					
Drug A	Drug B	Interaction	Source	Severity	Recommendation
General Recommendations					

Potentially Inappropriate medications		
Drug	**Rationale**	**Reference**
START Criteria Medications		

Anticholinergic Burden Score					
Medication	Anticholinergic Burden Score	Cumulative Anticholinergic Burden Score	Recommended Alternative	Alternative Anticholinergic Burden	New Cumulative Score
Falls in past 3 months? (Y/N)		Number of falls in past 3 months (if applicable):			
Anticholinergic burden (ACB) refers to the cumulative effects of anti-cholinergic medication. Each medicine that has anticholinergic properties contributes a score of 1, 2 or 3 to the overall ACB score. A patient with a **cumulative ACB score of ≥ 3** has severe anticholinergic burden with increased risk of confusion/cognitive dysfunction and falls. ACB Scoring: 1. Mild → 2. Moderate → 3. Severe					

Completed by:

Date:

Patient consent to Medicines Optimisation Study: **Y/N**

Appendix 6: Outpatient clinic letter template

Ospidéal Ollscoile Phort Láirge
University Hospital Waterford
Regional Cancer Centre South East

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Department of Oncology
Dr. Anne Horgan
Tel:
Secretary email:
Fax:
Geriatric Oncology Assessment and Liaison (GOAL)Clinic

Private and Confidential
Recipient

Ref:

Re: Patient Name, Address
DOB: MRN:
Mobile: Landline:
Diagnosis:
Comorbidities:
Medications:
Allergies:

Dear Dr.

Patient Name attended Dr. Horgan's GOAL clinic recently, and kindly consented to our medication optimisation study in older adults with cancer. Please find summary of comprehensive geriatric pharmacological assessment below:
SACT Treatment Plan:

Ancillary medications:

Additional monitoring:

Drug-drug Interactions:

Potentially Inappropriate Medication:

Medication	Rationale	Reference

START Medication:

Medication	Rationale	Reference

Anticholinergic Burden:

Anticholinergic burden (ACB) refers to the cumulative effects of anti-cholinergic medication.
Each medicine that has anticholinergic properties contributes a score of 1, 2 or 3 to the overall ACB score.
A patient with a **cumulative ACB score of ≥ 3** has severe anticholinergic burden with increased risk of confusion/cognitive dysfunction and falls.
ACB Scoring: 1. Mild → 2. Moderate → 3. Severe

Medication	ACB	Cumulative ACB

Summary of recommendations:

UHW implemented recommendations:

GP recommendations for consideration:

Please feel free to implement the suggested changes as you feel appropriate.

Kind regards,



Darren Walsh
Senior Pharmacist (Cancer Services), Pharmacy Department, University Hospital Waterford, Dunmore Road, Waterford X91 ER8E
Geriatric Oncology Assessment and Liaison (GOAL) Clinic Pharmacist, UHW
PhD Candidate, School of Pharmacy, UCC
| [redacted] |

Appendix 7: Ethical approval

Initial ethics approval:

Ospidéal Ollscoile Phort Láirge
University Hospital Waterford
Regional Cancer Centre South East

UCC
University College Cork, Ireland
Coláiste na hOllscoile Corcaigh

Research Ethics Office Old School of Nursing
University Hospital Waterford
Tel: 051- 842026/051-842391

21st February 2022

Mr. Darren Walsh
Pharmacy Dept.
University Hospital Waterford

STUDY TITLE: "Evaluating the Impact of Pharmacist Interventions in a Geriatric Oncology Setting"

STUDY STATUS: APPROVED

Dear Mr. Walsh,

The Research Ethics Committee Co-ordinator, REC, HSE, South East reviewed the above study.

Expedited ethical approval has been granted for the above study and constitutes full ethical approval.

The following documents were reviewed and approved:

1. Research Ethics Standard Application Form
2. Research Protocol
3. Data Collection Form
4. Participant Information Leaflet
5. Participant Consent Form
6. Declaration Form
7. C.V. of Principle Investigator – Mr. Darren Walsh
8. GDPR Certificate – Mr. Darren Walsh

In addition this study will be outlined at the next planned Research Ethics Committee Meeting for the HSE, South Eastern Area by the Research Ethics Committee Coordinator and any comments made at this meeting in relation to your study shall be communicated to you in writing.

It is a requirement of the REC, HSE, South East that you send copy of your study results to the Research Ethics Office on completion.

Yours sincerely,



REC office re -issue 10.25

Ms Caroline Lamb
Research Ethics Committee Coordinator
Health Service Executive, South Eastern Area

The Research Ethics Committee, HSE, South East is a recognized Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human use) Regulations 2004 and as such is authorized to undertake ethical review of clinical trials of all descriptions and classes for the Republic of Ireland.
The Research Ethics Committee, HSE, South East issues ethical approval on the basis of information provided. It is the responsibility of the researcher to notify the Research Ethics Office of any changes to a study to ensure that the approval is still relevant.

Protocol amendment 1:

Oifig Eitice Taighde
Ospidéal Ollscoile
Port Láirge
X91 ER8E

Research Ethics Office
University Hospital Waterford
Waterford
X91 ER8E

https://hseresearch.ie/

22nd August 2023

Mr. Darren Walsh
Pharmacy Department
University Hospital Waterford
Dunmore Road
Waterford

AMENDMENT

STUDY TITLE: "Evaluating the Impact of Pharmacist Interventions in a Geriatric Oncology Setting".

STUDY AMENDMENT STATUS: APPROVED

Dear Mr. Walsh,

The Research Ethics Committee Chairperson, REC, HSE, South East reviewed the above study amendment for:

1. "Aims and Objectives updated - Objectives updated to be more specific with regards to the methodology and structure employed to achieve the aim of the study".
2. "Exclusion criteria updated – added "Patients acutely admitted with an unplanned hospitalisation within 72 hours of attending clinic" as an exclusion criteria to reduce selection bias and reporting bias as the patients are unlikely to be admitted with an adverse drug event in this setting, and are unable to benefit from a medication review due to timing bias"
3. "Planned durations – Duration revised from 6 years to reflect early progress made in research"
4. "Study endpoint – Secondary endpoints updated to better reflect data gathered from latest evidence base that emerged since the study commencement date"
5. "References updated – Most up-to-date versions of references updated"

Ethical approval has been granted for this amendment and constitutes full ethical approval.

The following documents were reviewed and approved:

- Amendment Form (Received 14th August 2023)
- Cover Page (Received 14th August 2023)
- Revised Study Protocol (Received 10th August 2023)

This study was outlined at the Research Ethics Committee Meeting for the HSE, South Eastern Area by the Research Ethics Committee Coordinator.

It is a requirement of the REC, HSE, South East that you send copy of your study to the Research Ethics Office on completion.

Yours sincerely,



Prof. Ruairi MacNiocaill
Chairperson
Health Service Executive, South Eastern Area

The Research Ethics Committee, HSE, South East is a recognized Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human use) Regulations 2004 and as such is authorized to undertake ethical review of clinical trials of all descriptions and classes for the Republic of Ireland.
The Research Ethics Committee, HSE, South East issues ethical approval on the basis of information provided. It is the responsibility of the researcher to notify the Research Ethics Office of any changes to a study to ensure that the approval is still relevant.

Protocol amendment 2:

Oifig Eitice Taighde
Ospidéal Ollscoile
Port Láirge
X91 ER8E

Research Ethics Office
University Hospital Waterford
Waterford
X91 ER8E

https://hseresearch.ie/

Mr. Darren Walsh
Pharmacy Dept.
University Hospital Waterford
Dunmore Road
Waterford

23rd September 2025
Original Reference: 22.09
Amendment No. 1 Reference: 23.45
Amendment No. 2 Reference: 25.60

AMENDMENT

STUDY TITLE: "Evaluating the Impact of Pharmacist Interventions in a Geriatric Oncology Setting"

Amendment Number: 2

STUDY AMENDMENT STATUS: APPROVED

Dear Mr. Walsh,

The Research Ethics Committee, REC, HSE, South East reviewed the above study amendment for the:

- Addition of co-investigator, Dr. Edel Burton, School of Pharmacy, University College Cork, to the research team.

Ethical approval has been granted for this amendment in advance of the next scheduled REC meeting and constitutes full ethical approval.

The following documents were reviewed and approved:

1. Amendment Application Form
2. Cover Page_v1.2
3. Study Protocol_v1.2_29.07.2025

In addition this study will be outlined at the next planned Research Ethics Committee Meeting for the HSE, South Eastern Area by the Research Ethics Committee Coordinator and any comments made at this meeting in relation to your study shall be communicated to you in writing.

It is a requirement of the REC, HSE, South East that you send copy of your study to the Research Ethics Office on completion.

Yours sincerely,



Prof. Ruairi MacNiocaill
Research Ethics Committee Chairperson
Health Service Executive, South Eastern Area

The Research Ethics Committee, HSE, South East is a recognized Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human use) Regulations 2004 and as such is authorized to undertake ethical review of clinical trials of all descriptions and classes for the Republic of Ireland.
The Research Ethics Committee, HSE, South East issues ethical approval on the basis of information provided. It is the responsibility of the researcher to notify the Research Ethics Office of any changes to a study to ensure that the approval is still relevant.

Appendix 8: Adverse drug event case summary template

1. Demographic details

- **Age:**
- **Gender**:

---

2. Clinical Background

- **Primary Diagnosis**:
- **Relevant Medical History**:
- **Allergies**:
- **Renal Function (e.g., eGFR)**:
- **Liver Function (e.g., ALT, AST, Bilirubin)**:

---

3. Suspected Drug(s)

- **Drug Name**:
- **Dose**:
- **Route**:
- **Frequency**:
- **Start Date**:
- **Stop Date**:

(Repeat for each suspected drug)

---

4. Concomitant Medications

- *(List all other medications the patient was taking at the time of the event)*

---

5. Description of Adverse Event

- **Detailed Description of Event**:
- **Severity**:
- **Outcome**: (e.g., recovered, ongoing, fatal)
- **Management of Event**: (e.g., drug withdrawn, dose reduced, treatment given)

---

6. Laboratory and Diagnostic Findings

- *(Include relevant lab results, imaging, or other diagnostics that support the event)*

---

7. Additional Notes

- **Other Possible Causes**:
- **Relevant Literature or Known ADRs**:

Any Preventability Factors Identified

Medication

Cause for unplanned hospitalisation

Question	Yes	No	Do Not Know	Score
1 Are there previous conclusive reports on this reaction?	1	0	0	
2. Did the adverse event appear after the suspected drug was administered?	2	-1	0	
3. Did the adverse event improve when the drug was discontinued or a specific antagonist was administered?	1	0	0	
4. Did the adverse event reappear when the drug was readministered?	2	-1	0	
5. Are there alternative causes that could on their own have caused the reaction?	-1	2	0	
6. Did the reaction reappear when a placebo was given?	-1	1	0	
7. Was the drug detected in blood or other fluids in concentrations known to be toxic?	1	0	0	
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	1	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	1	0	0	
10. Was the adverse event confirmed by any objective evidence?	1	0	0	
	Total Score:			
LADR - **Use the algorithm below to determine avoidability**	**Avoidability:**			

Appendix 9: Drug-drug interactions

SACT (n=89)		Supportive care (n= 169)		Regular/PRN medications (n= 654)	
Medication	**n**	**Medication**	**n**	**Medication**	**n**
Cytotoxic chemotherapy/ Targeted therapy	**59**	**Prophylaxis**	**147**	**Cardiac medications**	**237**
Oxaliplatin	19	Dexamethasone	75	Diuretics	129
Capecitabine	11	Loperamide	27	ACEi/ARB	21
Carboplatin	11	Netupitant	19	Antiplatelets	20
Fluorouracil	5	Palonosetron	12	Calcium channel blockers	14
Sorafenib	5	LMWH	7	Amiodarone	11
Bevacizumab	2	Granisetron	4	Statins	10
Olaparib	2	Chlorphenamine	3	Beta Blockers	9
Sunitinib	2			Anticoagulants	7
Dabrafenib	1	**Symptom control**	**22**	Ranolazine	7
Paclitaxel	1	Levomepromazine	8	Digoxin	5
		Metoclopramide	7	Ivabradine	3
		Ondansetron	4	Isosorbide mononitrate	1
Hormone therapy	**30**	Domperidone	2		
Enzalutamide	9	Cyclizine	1	**Psychotropic medications**	**95**
Prednisolone	6			SSRI	50
Triptorelin	6			Amitriptyline	9
Bicalutamide	3			Benzodiazepines	9
Abiraterone	2			Olanzapine	8
Degarelix	2			Risperidone	5
Darolutamide	1			Dosulepin	4
Leuprorelin	1			Mirtazapine	4
				Quetiapine	2

SACT (n=89)		Supportive care (n= 169)		Regular/PRN medications (n= 654)	
Medication	**n**	**Medication**	**n**	**Medication**	**n**
				Trazodone	2
				SNRI	1
				Prochloperazine	1
				Gastrointestinal	**77**
				PPI	63
				Senna	10
				Cholestyramine	3
				Alginic acid	1
				Analgesics	**62**
				Opioids	42
				NSAID	17
				Gabapentinoids	3
				Respiratory	**55**
				Beta agonists	47
				Corticosteroids (Inhaled)	8
				Endocrine	**43**
				SGLT2i	20
				Metformin	12
				GLP-1 RA	3
				Gliclazide	3
				Glimepiride	2

SACT (n=89)		Supportive care (n= 169)		Regular/PRN medications (n= 654)	
Medication	**n**	**Medication**	**n**	**Medication**	**n**
				Levothyroxine	2
				Insulin degludec	1
				Other	**30**
				Quinine	10
				Folic acid	5
				Tacrolimus	4
				Iron	3
				Fexofenadine	3
				Omega-3	2
				Brinzolamide	1
				Tocilizumab	1
				Vitamin E	1
				Central Nervous system	**19**
				Z-drugs	11
				Phenobarbital	3
				Primidone	3
				Promethazine	2
				Genitourinary	**14**
				Tamsulosin	5
				Tolterodine	4
				Dutasteride	3
				Mirabegron	2

SACT (n=89)		Supportive care (n= 169)		Regular/PRN medications (n= 654)	
Medication	**n**	**Medication**	**n**	**Medication**	**n**
				Musculoskeletal	**12**
				Calcium carbonate	5
				Allopurinol	2
				Bisphosphonate	2
				Colecalciferol	2
				Glucosamine	1
				Antimicrobials	**10**
				Azithromycin	8
				Trimethoprim	1
				Valaciclovir	1

Key: SACT – Systemic Anticancer Therapy; LMWH – Low Molecular Weight Heparin; ACEi – Angiotensin Converting Enzyme inhibitor; ARB – Angiotensin Receptor Blocker; SSRI – Selective Serotonin Reuptake Inhibitor; SNRI – Serotonin Noradrenaline Reuptake Inhibitor; PPI – Proton Pump Inhibitor; NSAID – Non-steroidal Anti-inflammatory Drugs; SGLT2i – Sodium-Glucose Cotransporter-2 inhibitor; GLP-1 RA; Glucagon-like Peptide-1 Receptor Agonist

Appendix 10: Potentially inappropriate medication

Potentially inappropriate medications					
Medication	**n**	**Medication**	**n**	**Medication**	**n**
Antiplatelet	20	Anticoagulant	8	Antimuscarinics (inhaled)	4
PPI/ H2 antagonist	18	Benzodiazepines	8	Amitriptyline	4
Statin/Ezetimibe	13	Urinary alpha blocker	8	Gabapentanoids	4
NSAID	12	Beta Blocker	7	Paracetamol	4
Diuretic	12	Bisphosphonate	7	SGLT2i	4
Z-drugs	12	Calcium Channel Blocker	6	Sulfonylurea	4
Formulation-specific issue	11	Dexamethasone	6	DMARD	3
Opioid	11	First-generation antihistamine	6	Prophylactic antimicrobial	3
SSRI	11	Calcium	5	Quinine	3
Metformin	10	Folic acid	5	Alginic acid	2
Antiemetic	9	Herbal remedy	5	ARB	2
Ferrous fumarate	2	Colestyramine	1	Loperamide	1
Isosorbide	2	Denosumab	1	Nicotine 24-hour patch	1
Melatonin	2	Dosulepin	1	Omega-3	1
ONS	2	Doxazosin	1	Olanzapine	1
Tolterodine	2	Dutasteride	1	Oxaliplatin	1
Allopurinol	1	Fexofenadine	1	Primidone	1
Betahistine	1	Lenalidomide	1	Risperidone	1
Colchicine	1	Levothyroxine	1	Vitamin D_3	1

Key: PPI – Proton Pump Inhibitor; H2 antagonist – Histamine-2 receptor antagonist; NSAID – Non-steroidal Anti-inflammatory Drugs; SSRI – Selective Serotonin Reuptake Inhibitor; SGLT2i – Sodium-Glucose Cotransporter-2 inhibitor; DMARD – Disease-modifying Antirhuematic Drug; ARB – Angiotensin Receptor Blocker; ONS – Oral Nutritional Supplement

Appendix 11: Potentially omitted medication

Potentially omitted medication					
Medication	**n**	**Medication**	**n**	**Medication**	**n**
PPI/H2 antagonist	38	G-CSF	3	Chlorphenamine	1
Laxatives	12	Isphagula	3	DMARD	1
Anticoagulant	10	LAMA/LABA inhaler	3	Folic acid	1
Denosumab	10	Allopurinol	2	Hydrocortisone	1
Opioids	9	Calcium/Colecalciferol	2	Insulin degludec	1
Intravenous Iron	8	Cardioselective beta blocker	2	Levetiracetam	1
Silodosin	8	Paracetamol	2	Loperamide	1
ONS	8	Colecalciferol	2	Melatonin	1
Formulation change	7	ACEi	1	Mirabegron	1
Antidepressant	6	AChi	1	Spironolactone	1
DPP4i	6	Antihistamine eye drop	1	Tamsulosin	1
Antiemetic	5	Betahistine	1	Vitamin B_{12}	1
Pancreatin	4	BMX	1		

Key: PPI – Proton Pump Inhibitor; H2 antagonist – Histamine-2 receptor antagonist; ONS – Oral Nutritional Supplement; DPP4i - Dipeptidyl peptidase 4 inhibitor; G-CSF - Granulocyte-Colony Stimulating Factor; LAMA – Long Acting Antimuscarinnic; LABA – Long acting Beta-agonist; ACEi – Angiotensin Converting Enzyme inhibitor; AChi - Acetylcholinesterase inhibitor; BMX – Benylin Maalox Lidocaine; DMARD – Disease-modifying Antirhuematic Drug

Appendix 12: Anticholinergic medications at baseline

Medications with anticholinergic properties					
Medication	**n**	**Medication**	**n**	**Medication**	**n**
Dexamethasone	69	Glycopyrronium (inhaled)	6	Methotrexate	2
Loperamide	28	Prednisolone	6	Trazodone	2
Codeine	20	Amitriptyline	5	Venlafaxine	2
Metoclopramide	19	Isosorbide mononitrate	5	Aclidinium	1
Metformin	18	Olanzapine	5	Bumetanide	1
Furosemide	13	Paroxetine	4	Colchicine	1
Alprazolam	12	Promethazine	4	Desloratadine	1
Tramadol	11	Tiotropium (inhaled)	4	Diphenhydramine	1
Lansoprazole	10	Diazepam	3	Domperidone	1
Mirtazapine	10	Digoxin	3	Dosulepin	1
Morphine sulphate	10	Diltiazem	3	Hydrocortisone	1
Atropine	9	Fexofenadine	3	Hyoscine butylbromide	1
Chlorphenamine	9	Fluoxetine	3	Ipratropium (inhaled)	1
Famotidine	9	Loratadine	3	Levomepromazine	1
Oxycodone	9	Omeprazole	3	Metoprolol	1
Sertraline	9	Pantoprazole	3	Phenobarbital	1
Cyclizine	8	Tapentadol	3	Pramipexole	1
Atenolol	7	Tolterodine	3	Prochlorperazine	1
Escitalopram	7	Umeclidinium (inhaled)	3	Quetiapine	1
Cetirizine	6	Carbamazepine	2	Risperidone	1
Citalopram	6	Fesoterodine	2	Triazolam	1

Appendix 13: COVID Statement

The findings reported in Chapter 4 relate to research conducted in 2018, prior to the COVID-19 pandemic, therefore this research was not impacted by the pandemic.

The findings reported in Chapter 6 pertain to clinical activity in the medical oncology outpatient clinic between July 2022 and October 2024 with the follow up period ending in April 2025. A report from the National Cancer Registry of Ireland found that the pandemic had no lasting impact on cancer survival, and by 2022 the number of diagnosed cases had returned to expected levels. Therefore, it is reasonable to conclude that the pandemic did not impact on the recruitment, data collection, data analysis or data extraction discussed in this thesis.

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