Engaging frail and seriously ill patients as partners in research:

A multiple methods study

Claire Ludwig RN, MA

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School of Nursing,
Faculty of Health Sciences,
University of Ottawa

There is no respect for others without humility in one's self.

Henri Frederic Amiel

Every person that you meet knows something you don't; learn from them.

H. Jackson Brown Jr.

Preface

Claire Ludwig (CL), the named doctoral candidate, conceptualized all aspects of this dissertation, and is responsible for the integrity of the data and its interpretation. CL led all components of the dissertation studies, including data collection and analysis, and drafting each manuscript.

Contributions of Collaborators

Elements	Chapter 2	Chapter 3	Chapter 4
Study conceptualization, design and review	DS, IDG, WG	DS, IDG, WG	DKW, DS, IDG, WG
Auditing data analysis and/or interpretation	DS, IDG, JL, WG	DS, JL	DKW
Title and abstract screening by second reviewer	JL	N/A	N/A
Revision of manuscripts	DS, IDG, JL, WG	DS, IDG, JL, WG	DKW, DS, IDG, WG
Final approval of manuscripts*	DS, IDG, JL, WG	DS, IDG, JL, WG	DKW, DS, IDG, WG

***Meg Carley** assisted with the manuscript formatting and preparation.

DS – Dr. Dawn Stacey RN PhD FAAN FCAHC FCAN holds a Research Chair in Knowledge Translation to Patients and is a Distinguished University Professor in the School of Nursing at the University of Ottawa. She is a Senior Scientist and Scientific Director of the Patient Decision Aids Research Group at the Ottawa Hospital Research Institute.

IDG – Dr. Ian D. Graham PhD FCAHS FNYAM FRSC is a Professor, Faculty of Medicine, School of Epidemiology and Public Health, University of Ottawa, and Senior Scientist, Ottawa Hospital Research Institute. Dr. Graham's research interests include knowledge

translation/mobilization (implementation) science; the role of sex, gender and other intersectional considerations in implementation science; the development, quality and implementation of practice guidelines; mixed and multiple methods, and knowledge synthesis. A core component of his research program focuses on understanding how engaging patients and other stakeholders in the research process (known as integrated knowledge translation) works and the impact it produces.

WG – Dr. Wendy Gifford, RN PhD is a Full Professor in the School of Nursing, Faculty of Health Sciences, University of Ottawa, Loyer-DaSilva Research Chair in Community and Public Health Nursing, and Co-Director of the Center for Research on Health & Nursing. Her program of research focuses on promoting health equity with disadvantaged and marginalized groups, with a particular focus working with First Nations, Inuit, and Metis for culturally safe health care. She recognizes that healthcare is founded on systemic settler racism that continues to disenfranchise and marginalize Indigenous Peoples today, which has increasingly situated her research within critical decolonizing methodologies and approaches.

DKW – Dr. David K. Wright, RN PhD is an Associate Professor in the School of Nursing, Faculty of Health Sciences, University of Ottawa. He is the academic lead for Palliative Care and Nursing Ethics within the Centre for Research on Health and Nursing. He holds specialty certification in hospice palliative care nursing from the Canadian Nurses Association and works clinically at a residential palliative care facility (hospice) in Montreal. A core component of his research program focuses on palliative care approaches in diverse contexts such as intensive care, forensic psychiatry, and prison.

JL – Josee Lavoie, MSW RSW is a Clinical Social Worker in Geriatric Psychiatry at the Royal Ottawa Mental Health Centre. Her practice is dedicated to working with the frail elderly

population who have concurrent mental health issues. She is a strong advocate for inclusivity and equity of access to health and social care for vulnerable populations.

Dissertation Abstract

Background: Commitment to patient engagement in research provides significant opportunities to advance our understanding of patients' experience whilst fostering sensitivity and progress in research. Yet, people who are frail or seriously ill are rarely given the opportunity to partner across the course of a research study. Little is known about their impact on the conduct of research and the best ways of 'meaningfully' involving them as research partners. A series of studies using multiple methods were conducted to explore meaningful engagement of frail and seriously ill patients as partners in research.

Study 1: A systematic review with narrative synthesis was conducted to describe the engagement of frail and seriously ill patients as research partners across the research cycle. Thirty eligible studies showed emerging evidence that research partnerships with frail and seriously ill patients can be achieved successfully. Frailty and serious illness present legitimate concerns due to the vulnerability of patient-partners but can be successfully mitigated when researchers ensure timing and methods of engagement are flexible and practical, and emotional needs of patient partners are consistently addressed.

Study 2: A qualitative sub-analysis of the prior systematic review was conducted to identify ethical considerations of engaging frail and seriously ill patients as research partners. Findings revealed that researchers and patients should work together to clarify the intent and outcomes of the partnership, actively address relational and intellectual power differentials, recognize and minimize the potential for unintended harm, and strive to maximize the benefits of partnership.

Study 3: An analytic autoethnography was conducted to explore how patient engagement is embodied and situated during serious illness. Findings provide a unique contribution to the

discourse on representation and contested identity. Current concerns of tokenism are countered through recognition of ways in which patients 'find' and 'make' meaning through research partnerships. Partnering with seriously ill patients offers enormous potential to advance research through harnessing the power of embodied knowledge production.

Conclusion: This dissertation highlights the importance of ensuring that the voices of frail and seriously ill patient-partners' are heard first-hand. It further demonstrates, the current methodological imperative of patient engagement requires novel approaches to both enacting and evaluating patient engagement.

Acknowledgements

I am indebted to many people who supported me throughout both my PhD and my illness, particularly as the two became inextricably entwined. I have been humbled by their generosity, guidance and support.

I will be forever grateful to my supervisor Dr. Dawn Stacey – she is the reason I stepped out of my comfort zone in healthcare administration to pursue my PhD. I witnessed 'research in action' and the importance of authentic stakeholder engagement from my very first meeting with her. Her wisdom, understanding and support has been immeasurable. I also extend my heartfelt gratitude to my committee members Dr. Ian D. Graham and Dr. Wendy Gifford. Dr. Graham challenged me constantly to think broader and be a better academic, re-connected me to my inner sociologist, and fostered my deep appreciation of why research must always serve those for whom it is produced. Dr. Gifford encouraged me to trust my instinct and believe in myself; her confidence in my abilities kept me going during those early days where I doubted myself. I am profoundly grateful to my committee for their kind and constant consideration of my circumstances.

Dr David K. Wright held a very special place in my PhD studies, particularly as I grappled with my autoethnography. He was incredibly generous in offering up his time to mentor me through the process. I am so thankful for his insightful feedback, academic support and for his kindness and compassion.

I am truly beholden to the faculty members of the School of Nursing at the University of Ottawa who enact and validate the importance of multiple forms of knowledge production. Further appreciation goes to my peers in the PhD program who challenged me and helped to shape my ideas, and to my friend Dr. Michelle Crick whose wisdom and irreverent wit, in

combination with the stories of her own PhD journey, inspired raucous laughter and taught me not to take myself too seriously.

Finally, I dedicate this work to my family and friends, both near and far. To my two amazing daughters, Hesther and Ophelia, who never wavered in their belief that I could do this, I only ever wanted to make them proud of me. For Patrick and Sharon, who have nourished and nurtured me more than they will ever know. And to my spouse, Josee, who picked me up and carried me during those darkest of hours so that I might complete this dissertation.

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List of Abbreviations Used

AIDS	Acquired Immune Deficiency Syndrome
CIHR	Canadian Institutes of Health Research
CINAHL	Cumulative Index to Nursing and Allied Health Literature
EMBASE	Excerpta Medica Database
FSI	Frail and/or Seriously Ill
IAP2	International Association of Public Participation
LGBTQ+	Lesbian, Gay, Bisexual, Transgender, and Queer and/or Questioning. “Plus” (+) represents other sexual identities such as pansexual, Two-Spirit, and intersexual
MEDLINE	Medical Literature Analysis and Retrieval System Online
MeSH	Medical Subject Headings
MMAT	Mixed Methods Appraisal Tool
PAR	Participatory Action Research
PCORI	Patient-Centred Outcomes Research Institute
PEIR	Patient Engagement in Research
PICOS	Population/participants, Interventions, Comparators, Outcomes, and Study designs
PPI	Patient and Public Involvement
PRISMA-P	Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols
PROSPERO	Prospective Register of Systematic Reviews
PSP	Priority Setting Partnership
PsycINFO	Psychological Information Database
SC	Steering committee

CHAPTER 1: Introduction

The purpose of this chapter is to orient the reader to the research problem, key concepts, objectives, guiding theoretical framework, and the current state of knowledge related to engaging frail and seriously ill patients as partners in research. First, I provide context for the research problem and introduce key concepts. Second, I summarize the current state of knowledge, identify gaps in the literature, and provide justification for this dissertation. Third, I describe the guiding conceptual model and a summary of methods. Lastly, I describe the structure of this dissertation.

1.1 Context

Demand for better health care from individuals experiencing frailty and serious illness has highlighted significant gaps in our knowledge of patient-centred care. Current commitment to patient engagement in research not only provides significant opportunities to advance our understanding of the medical and healthcare needs of the frail and seriously ill, it also serves to foster sensitivity and progress in the conduct of research. 'Patient engagement' as an umbrella term is often used to denote a relatively new paradigm in the way that research is conceptualized and conducted; moving patients from a "passive role as research participant to one where they are involved in research activities traditionally handled only by researchers" [1; p.308].

Through focusing on engagement with patients, there is a shift from the researcher as sole expert to one where researchers and patients are both experts, working together to solve problems and generate knowledge [2]. Patients' experiential knowledge of disease is not accessible to most researchers, but if leveraged appropriately, has the potential to complement researchers' analytical skills and scientific perspective [3, p.676]. The concept of partnering with patients in research has been incorporated into clinical guideline development [4], systematic reviews, and improvements to health services [5].

A systematic review of 142 studies by Domecq et al. (2014) established that, in most instances, it is possible to partner with patients across the continuum of health research; however, engagement tends to be focused in the early stages of the study (e.g. setting of research priorities, proposal development). Similarly, a more recent scoping review examining methods and outcomes of patient engagement revealed that, in the absence of a validated framework, efforts to engage patients continue to be limited to the early stages of engagement and do not appear to be maintained throughout the lifecycle of most research projects [7]. The level of patient engagement in the process varies in intensity and complexity, and takes a number of different forms, e.g., participation in research meetings, membership on advisory boards, and contribution to education and dissemination activities [6, 7].

The international interest in patient engagement has been spurred on by the belief that it can enhance the relevance, validity, and quality of research [6, 8]. Research developed in this way is considered to be more applicable to the needs of patients, more likely to be utilized [9] and provides justification for research funded by public money [10, 11]. The involvement of patients as partners in the design, execution and evaluation of health research is now an expectation of major funding programs [11, 12].

From a theoretical perspective, "patient engagement is increasingly recognized as a distinct and important body of work for researchers to be aware of and understand, in the same way as other areas of knowledge" [13, p.69]. However, evidence to inform the implementation of meaningful patient engagement in research remains limited, and there has been inconsistency in how the philosophy and practice of patient engagement has been embedded across different health sectors [6, 13-15]. Definitions of patient engagement and conceptions of how it improves outcomes vary extensively. In response to these shortcomings, a significant number of

conceptual frameworks have been developed. A recently published systematic review identified over 60 frameworks in use internationally [16]. The sheer number of patient engagement frameworks published in the peer reviewed literature have led to additional confusion for researchers working to operationalize the concept [6, 17]. Critics have referred to this as "muddles" of patient engagement rather than models of patient engagement, and cite a lack of conceptual clarity as a contributory factor towards their limited application in the research environment [18].

Conceptually, there is increasing momentum towards engagement across the full spectrum of research activities with "patients serving as advisors to researchers, as consultants for specific aspects of research design and/or outcomes selection, and/or as co-investigators with responsibility and intellectual contribution equal to that of the trained clinical researchers" [1; p.308]. Whilst there appears to be a drive towards more collaborative relationships whereby patients are considered equal members of the research team, the lack of consistency in how patient engagement is conceived and operationalized, particularly where patients serve as research partners or co-investigators, requires further consideration. The variability in approaches demands further scrutiny in order to avoid tokenistic patient engagement and foster an understanding of the barriers and facilitators to implementing approaches more akin to partnership across the spectrum of health research [19-21].

While all the levels of engagement are important, for this dissertation I am focusing specifically on patient engagement related to frail and seriously ill patients as research partners. The partnership role appears to be more difficult to enact for research teams but is increasingly promoted as the exemplar by research funders (in spite of limited evaluation).

The vulnerability of certain groups such as frail and seriously ill patients provides additional complexity to engagement processes, particularly with regard to prolonged and more intensive patient engagement [22-24]. For the purpose of this dissertation, I am focused on patients who are frail, seriously ill, or both frail and seriously ill. I used the following definitions. Frailty is classified as: a) a geriatric condition involving functional decline, with increasing vulnerability to adverse events including mortality, morbidity, disability, hospitalization, and nursing home admission [25], or b) the presence of multiple chronic conditions such as arthritis, heart failure, renal failure, and pulmonary disease leading to changes in functional ability [26], or c) the presence of cognitive decline and dementia [25, 27]. Serious illness is defined as a condition that carries a high risk of mortality, negatively impacts quality of life and daily function, and/or is burdensome in symptoms or treatments [28]. Examples of serious illnesses are cancer (metastatic or hematologic), advanced liver disease, advanced renal disease, and advanced pulmonary diseases [28].

1.2 Engaging Frail and Seriously Ill Patients as Research Partners

Inclusivity is an important principle in meaningful patient engagement and places emphasis on equity of involvement in research [29-31]. Whilst a number of reviews have concentrated on descriptions of the process and methods of patient engagement, much less attention has been directed towards providing detailed accounts of patient characteristics [6, 7, 17, 24]. This oversight makes it difficult to gauge the inclusion of diverse patient groups in the process.

The practical and ethical issues related to involving frail or sick patients in research appears to deter research teams from engaging them as partners in research [22, 23]. A recent systematic review investigating the engagement of cancer patients in research determined that

the focus of most studies appeared to be on the methodological challenges and limitations of engaging this population [32]. Such findings may continue to deter teams from including this population. With an increased emphasis on inclusivity and meaningful engagement, investigation is needed to identify how and when frail and seriously ill patients are engaged in research. These very patients may have the most to contribute to our knowledge of health and illness, and the most to gain from the knowledge that they have helped to co-create [24, 30, 33, 34]. Further inquiry is required to better understand the implications of their partnering with researchers in order to determine whether the benefits of the research partnership outweigh potential harms.

1.3 Achieving *Meaningful* Patient Engagement

There are compelling reasons for investigating the impact of patient engagement in research, especially if we are to identify the best ways of involving patients 'meaningfully' in different activities and mitigate the possibility of deleterious effects of their engagement [8]. Reviews summarizing current knowledge have typically focused on the methods and impacts of patient engagement, the benefits and challenges, as well as key areas for research, including demonstrating impact, and ensuring commitment from institutions and research funders to support and resource engagement activities [6, 7, 17, 22]. However, most studies appear to be self-reported by research teams and little is known about the patients' experience, particularly in terms of how patients themselves define meaningful engagement [8, 35-37]. Where patients are involved in authorship it remains difficult to ascertain their voice. Moreover, having researchers speak for them has been deemed "problematic because of their position in the social hierarchy" vis-à-vis the researcher [37, p. 40].

Studies that have sought direct patient feedback tend to be conducted in the areas of chronic disease where input is solicited from patient advocacy groups, advisory committees, and

patients with chronic health conditions [38-40]. A survey from the Patient-Centred Outcomes Research Institute (PCORI) reported meaningful engagement as securing trust and participation, regular contact, concern for the individual, and dialogue [39]. A case study of meaningful engagement conducted and co-authored with asthma patients in a European collaborative identified five key principles to avoid tokenistic engagement: involve early, involve deeply, have patients' feedback on project progress, include patients in dissemination and help patients convey their own story [38]. Hamilton et al. (2018) conducted a mixed-methods study to develop a questionnaire examining meaningful engagement from the perspective of patients with arthritis. A qualitative secondary analysis of the interview data was used to generate a framework for meaningful patient engagement in research. The Patient Engagement in Research (PEIR) Framework identified eight themes: procedural requirements, convenience, contributions, support, team interaction, research environment, feel valued and benefits [42]. The limited data that exists appears to suggest that the relational component of engagement, (i.e., the dynamic interaction between patients, researchers and others on the team) is where patients identify what is meaningful to them [43].

As identified, the majority of studies on patient engagement in research appear to be limited to patients with chronic health conditions. There is scant evidence on what constitutes meaningful engagement of frail and seriously ill patients as partners in research, particularly as reported from the patient perspective. Most of the evidence of the preferences of frail and seriously ill patients engaged in research tends to come from commentaries, editorials, reports, or opinion pieces [44, 45]. Where studies have sought the patient voice, the issue of representation is compounded because frail and seriously ill patients are often represented by caregivers or advocacy groups, particularly in the dementia and palliative populations [46, 47]. In this sense,

patients themselves are rendered voiceless. Given the current state of evidence, it is difficult to know: 1) whose views are represented (i.e., patients, caregivers, or community advocates), and 2) the extent to which the commentary is grounded in formal analysis, as opposed to being mired at the level of advocacy and rhetoric [44, 47, 48]. Further evaluation is required to build the evidence base about what constitutes meaningful patient partnership for those patients who are frail and seriously ill with the evidence shaped from the patient's voice.

1.4 Evaluating Meaningful Patient Partnership in Research

Efforts to evaluate meaningful patient engagement are increasingly perceived as problematic because they are predicated on a construction of patient engagement as a therapeutic intervention rather than as a method employed during the research process itself [49]. The search for discrete and measurable motivations and outcomes is challenging because patient engagement is a multi-faceted and complex phenomenon, particularly at more intensive levels of engagement [37]. Evaluation of patient-partnership in research often fails to capture the nuances of the evolving and dynamic nature of the interactions. Anecdotal or case study evidence tells only part of the story and does not have the depth to fully address the intricacies and meaning patients bring to, and derive from, the partnership process.

There is a need for more reflective perspectives of patient engagement [37, 50], particularly from patients themselves. However, in order to provide a more reflective account of what constitutes meaningful partnership in research from a patient perspective, there is a need to disentangle the patient voice from the voices of caregivers, advocacy groups, and researchers. The current methodological imperative requires novel approaches to inquiry in order to access the patient voice and enable a more comprehensive understanding of meaningful patient partnership.

1.5 Purpose

The overarching purpose of this dissertation is to explore the meaningful engagement of frail and seriously ill patients as partners in research. This multiple methods dissertation is aimed at addressing the following objectives:

- Study 1 – synthesize the current evidence on the engagement of frail and/or seriously ill patients as research partners across the research cycle.
- Study 2 - identify the ethical considerations related to engaging frail and seriously ill patients as partners in research.
- Study 3- explore from the patient's perspective how partnering in research is embodied and situated at a time of serious illness, and understand how patient-partnership in research is shaped within wider cultural meanings and social trends.

1.6 Reflexivity and Paradigmatic Position

I situate myself as someone who has received education in a number of different but related disciplines: nursing, healthcare management, critical medical sociology, and psychology. During the conceptualization and conduct of this dissertation, I was also a patient dealing with a serious and potentially life-limiting illness. I am, for want of a better term, "the consummate inter-disciplinarian" straddling a space between academia, clinical practice, and illness. This positionality has unintentionally provided me with a view from an "in-between space" [51]. A space which, paradoxically, has made me more attuned to how knowledge about patient engagement is both conducted and constructed. It has further exposed me to the complexities of enacting patient partnerships and cemented my commitment to producing knowledge that has explicit implications for practice.

My epistemological foundation for this dissertation rests within pragmatism and draws heavily on Dewey's work on experience and inquiry which values applied knowledge over purely abstract or theoretical knowledge [52]. For pragmatists, knowledge should be useful and actionable [53]. Dewey espoused a non-cartesian view of world, valuing both objective and subjective knowledge and the interactions between them [52]. Pragmatism endorses the use of the methodologies and methods most suitable and practical for answering complex questions [54]. Pragmatism further accepts that individual context and experience means there are multiple realities, so adopting a pragmatic approach to exploring complex phenomena is not only logical, it ensures rigour [55]. Moreover, contemporary pragmatism supports an embodied reflexivity in making meaning [56]. Pragmatism does not require a particular method or methods mix; the focus is to investigate the phenomenon of interest using the most appropriate research method [55]. Of pertinence for this dissertation, pragmatism has been identified as a fitting paradigm for patient-partnerships in research, with knowledge created based on interactions between the individual and their environment [54, 57].

1.7 Guiding Conceptual Framework

This dissertation was guided by a conceptual framework developed utilizing existing frameworks for patient and public engagement [17, 58] and ethical principles [59, 60]. The framework addresses patient engagement during the stages of the research process, the level of engagement at any specified stage, and ethical principles and practices that flow throughout the research stages and levels of engagement (Table 1.1).

1.7.1 Stages and Levels of Patient Engagement: The first component of the conceptual framework was developed, in part, by a prior systematic review of patient and service user engagement in health research and addresses patient engagement at different stages of the

research cycle with associated activities [17]. The second component addresses the level of engagement in the decision-making process as defined by the International Association of Public Participation (IAP2) Spectrum of Public Participation. The IAP2 spectrum denotes five levels of engagement (inform, consult, involve, collaborate, and empower). The focus on engagement in this dissertation was at the levels of involve (e.g., working directly with patients throughout the process to ensure concerns and aspirations are consistently understood and considered) and collaborate (e.g., contributing to shared decision-making across the research process) [58].

1.7.2 Ethics as an Integral Component for Patient Engagement. In an attempt to enhance existing frameworks and capture the complexities inherent in partnering with patients in research, a third component has been added to the framework above to provide a foundational element that addresses ethical principles and practices of patient engagement. This third foundational element is comprised of 2 components: 1) Beauchamp and Childress' Ethical Principles (respect for autonomy, non-maleficence, beneficence, and justice) [59] , and 2) the principles of Relational Ethics (engagement, respect, embodied knowledge, and environment) [60]. See Table 1.1.

Table 1.1 Guiding Conceptual Framework for Engaging Frail and Seriously Ill Patients in Research

Stages of Research Cycle*	**Level of Engagement****	
Foundational phase • Research priority setting – specific to disease, condition, or syndrome • Setting evidence-based patient engagement strategies – specific to disease, condition, or syndrome **Preparatory phase** • Agenda setting at the individual study level • Proposal development • Ethics application – including well-defined consent procedures • Acquiring funding/grant application **Execution phase** • Study design & procedures • Recruitment strategies & tools • Data collection • Data analysis (reviewing & interpreting data) **Translation phase** • Dissemination • Implementation • Evaluation	**Involve** • Working directly with (patients) throughout the process to ensure concerns and aspirations are consistently understood and considered	**Collaborate** • Partnering in each aspect of the decision (e.g., contributing to shared decision-making *across the research process)*
Ethical Foundation **Principles**: respect for autonomy, non-maleficence, beneficence, and justice [59] **Relational Ethics**: engagement, respect, embodied knowledge, and environment [60]		

*Adapted from Phases and Stages of Patient and Service User Engagement in Research. [17]
**Adapted from IAP2 Spectrum of Public Participation [58]

Beauchamp and Childress (2019) provide a framework to capture the major moral considerations for the ethical conduct of patient engagement. The framework offers many practical advantages for application by providing researchers with a common language through

which to identify and address bioethical issues. Furthermore, the framework is widely incorporated into medical and health sciences curricula and has been adopted extensively by research institutions for governance and regulation of research [59]. The four moral principles are: 1) respect for autonomy (the obligation to respect the decision-making capacities of autonomous persons based on their beliefs and actions); 2) non-maleficence (the obligation to avoid causing harm); 3) beneficence (the obligations to provide benefits and to balance those benefits against risks); and 4) justice (obligations of fairness in the distribution of benefits and risks) [59].

Relational ethics is composed of: 1) engagement (characterized by openness, trust, and responsiveness, with an understanding of perspective and vulnerability); 2) respect (acknowledgment of power differences, values, beliefs, knowledge, and experiences); 3) embodiment (focus on both the mind and body); 4) environment (context where ethical reflection happens) [61]. Relational ethics complements Beauchamp and Childress' bio-medical ethical principles which have been critiqued as a static binary/non-binary approach to ethical decision-making [62]. Relational ethics, on the contrary, is described as an "action ethic" [60, p. 486]. The approach focuses on the relationships between people as the center of ethical interest and the knowledge that is shared between them [63]. It is throughout the relationship between health care provider and patient where connections are made, with particular attention given to the moral space within the relationship [64]. Relational ethics does not disregard ethical principles or codes of ethics, it rather builds upon and embraces them, allowing for the complexities of the health care environment to be explicitly acknowledged [60]. A focus on relational ethics does not negate the need to distinguish between different types of ethics or to adhere to the ethical

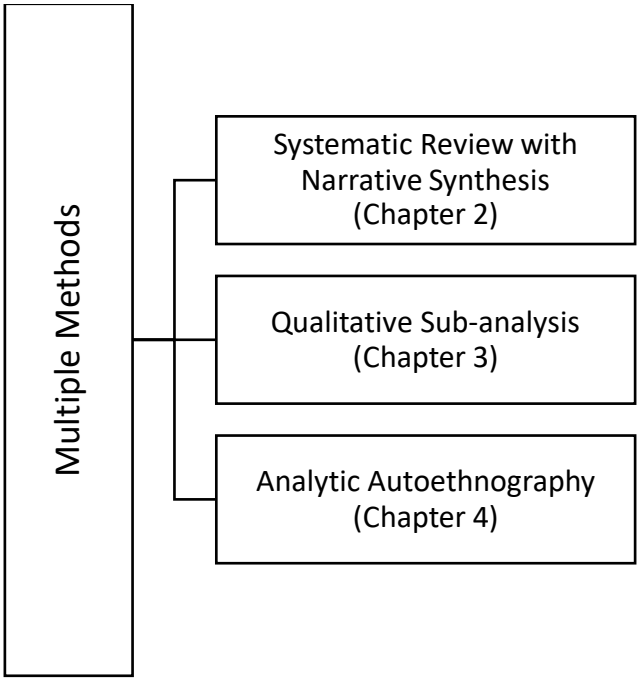
principles such as respect for autonomy, non-maleficence, beneficence, and justice; it does however situate relationships at the centre of our ethical practice [64].

Investigating meaningful patient engagement of frail and seriously ill patients through a relational ethics lens offers novel ways of thinking, inquiring, and addressing the challenges presented in defining the concept [43]. Moreover, it supports a deeper understanding of patient-partnership as a dynamic and evolving relationship, and facilitates inquiry into issues of differential relational power, diversity and difference, and the inherent vulnerability of patients in shaping the moral climate in which engagement takes place.

1.8 Research Design

The proposed dissertation is a qualitative multiple methods study comprised of three separate but integrated components: 1) systematic review of qualitative, quantitative, and mixed methods studies with narrative synthesis, 2) qualitative sub-analysis of the prior systematic review with a focus on the ethical considerations of engaging frail and seriously ill patients as partners in research, and 3) an analytic autoethnography during a time of serious illness where I was engaged as a partner in research. The components of this multiple methods study are captured in Figure 1.1 below. In keeping with a pragmatist epistemology, the purpose of using multiple methods was to combine methodologies in order to capture diverse aspects of the engagement of frail and seriously ill patients as partners in research [65]. This approach is more commonly used to answer broader research questions and provide a more holistic understanding of the phenomena [65].

Figure 1.1 Engaging Frail and Seriously Ill Patients as Partners in Research: A Multiple Methods Study



Multiple methods are defined as two or more complete projects that are independently planned and conducted with separate, but complementary, research questions that are consistent with the overall aim [66, p. 3]. This differs from mixed-methods research whereby two or more methods are used to study the same question in a singular project [66]. Multiple method studies facilitate triangulation of findings across the studies to produce results that are more robust than single method studies [65]. Methodological triangulation entails the combination of two or more research methods into one study and can compensate for potential weaknesses in single research methods [65, 67]. The reflexivity between the components of this multiple methods study assists in informing aspects of the analysis of the core aim of this dissertation which explores meaningful engagement of frail and seriously ill patients as partners in research [66].

Engagement of patients as research partners is a multi-faceted phenomenon, grounded in context and relationships. Given its complexity, a singular study does not go far enough in answering the question of what constitutes the meaningful engagement of frail and seriously ill patients as partners in research. In order to fully benefit from the potential of a multiple-method design, integration needs to be at the epistemological, theoretical and methodological levels [68, p. 288]. Given concerns regarding the quality of narrative synthesis in addressing complex issues [69], there is a need to address the issue of commensurability of the literature review in this study and its use in providing a foundation for this dissertation. Due to the limited reporting on patient characteristics in the patient engagement literature, it was important to identify those studies where frail and seriously ill patients had been engaged as partners in research. The narrative synthesis of the studies included in the systematic review was undertaken in a manner that is akin to the synthesis of a set of interviews in a primary qualitative study. The systematic review raised additional questions about the ethical considerations of engaging frail and seriously ill patients as partners in research and in essence served to stimulate further inquiry in much the same way that prompts are used in an interview setting. By utilizing an analytic autoethnographic approach, as opposed to more constructivist approaches to autoethnography, e.g., evocative, performative [70], I have stayed close to my epistemological roots. The methodological approaches taken in this dissertation also honor a commitment to respecting multiple frames of knowledge and knowledge production, which is a key tenet of patient-engaged research.

1.9 Structure of this Dissertation

This dissertation is centered around a series of manuscript-based papers. Following this introduction, **Chapter Two** presents a published systematic review and narrative synthesis of qualitative, quantitative, and mixed-method studies engaging frail and seriously ill patient-

partners in research [71]. Broadly, this literature review addresses how and when frail and seriously ill patients are engaged in research as partners and provides an account of the barriers and facilitators to their partnering. It also provides an understanding of the impact of the research partnership on them as individuals, on the researchers, and on the research itself.

Chapter Three presents a published sub-analysis of studies included in the systematic review (Chapter Two) exploring the ethical considerations for researchers when they are engaging frail and seriously ill patients as partners in research [72]. Broadly, this component is a qualitative analysis of the related ethical issues from studies included in Chapter Two.

Chapter Four presents an autoethnography of my own experience as a patient-partner with a serious and potentially life-limiting illness engaged in research during a period in which I was acutely and seriously ill. Relatedly, this component provides a first-person account of the engagement of a seriously ill patient as a partner in research. The account is rendered and analysed in the 'patient voice' as an attempt to complement (or counter) the existing narrative where others speak on behalf of patients about meaningful engagement of frail and seriously ill patients as partners in research.

Chapter Five is an integrated discussion in which the findings from each study component are amalgamated to enrich the findings of the overall phenomenon of meaningful engagement of frail and seriously ill patient-partners in research. Findings across studies are discussed within the broader literature. The implications of the dissertation are highlighted with relevance to nursing education and research.

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CHAPTER 2: Partnering with Frail or Seriously Ill Patients in Research: A Systematic Review

Authors:

Claire Ludwig

Ian D. Graham

Wendy Gifford

Josee Lavoie

Dawn Stacey

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Plain English Summary

Patients are experts by experience and are becoming more active as partners on research teams. Patients who are frail and/or seriously ill do not appear to be engaged as research partners to the same extent as those living with more stable illness. The aim of this systematic review was to explore how frail and/or seriously ill patients have been engaged as partners in research.

In 30 studies, frail and/or seriously ill patients were engaged as research partners. They identified: research questions and outcomes important to patients; developed tools and processes more related to patients' needs and experiences; helped collect and/or interpret findings; presented research results; and provided study oversight. Barriers to patients' partnering were mostly related to concerns about their fragile health, their ability to process information and their likely limited ability to partner for the duration of the study due to declining health or death. When frail and/or seriously ill patients were engaged as partners in research, patients had a renewed sense of purpose and felt emotional support, research was more related to patients' needs, and researchers gained greater insight into the lived experience of illness and suffering. Overall, it appears that frail and/or seriously ill patients can and should be included as research partners. Researchers can work to avoid unduly harming patient partners by being flexible and ensuring patients' physical and emotional needs are addressed during the research process.

Abstract

Background: The expectation to include patients as partners in research has steadily gained momentum. The vulnerability of frail and/or seriously ill patients provides additional complexity and may deter researchers from welcoming individuals from this patient population onto their teams. The aim was to synthesize the evidence on the engagement of frail and/or seriously ill patients as research partners across the research cycle.

Methods: A systematic review was conducted using PRISMA guidelines. A search strategy included MEDLINE®, EMBASE®, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and PsycINFO from database inception to April, 2019. Eligible studies were peer-reviewed qualitative, quantitative, and mixed methods research reporting on the engagement of frail and/or seriously ill patients as partners on research teams. The Mixed Methods Appraisal Tool was used to appraise study quality. Narrative analysis was conducted.

Results: Of 8763 citations, 30 were included. Most studies included individuals with cancer on the research team (60%). Barriers included: lack of time and resources (50%), discontinuity in contribution (37%), and concerns for well-being (33%). Facilitators included: trust and mutual respect (60%), structural accessibility (57%), flexibility in timing and methods of engagement (43%), and attention to care and comfort, (33%). Perceived impacts for patients included: renewed personal sense of agency (37%) and emotional/peer support (37%). Impacts for researchers included sensitization to the lived experience of disease (57%) and an increased appreciation of the benefits of patient engagement (23%). Research design, execution, and outcomes, developed with patients, were deemed more suitable, relevant and reflective of patients' priorities.

Conclusions: There is emerging evidence to suggest that research partnerships with frail and/or seriously ill patients can be achieved successfully. Patients mostly report benefit from partnering with research teams. Frailty and/or serious illness do present legitimate concerns for their well-being but appear to be successfully mitigated when researchers ensure that the purpose of engagement is well-defined, the timing and methods of engagement are flexible, and the practical and emotional needs of patient partners are addressed throughout the process.

Systematic review registration: The systematic review protocol was registered with the International Prospective Register of Systematic Reviews PROSPERO (CRD42019127994)

Keywords: Patient engagement, public patient involvement, systematic review, integrated knowledge translation, co-production

2.1 Background

Over the past two decades, the commitment to engaging patients as partners in research has steadily gained momentum. International interest in patient engagement has been fostered by the belief that it can enhance the relevance, validity, and quality of research [1]. It is further postulated that research developed in this way will be more applicable to the needs of patients and hence more readily applied [2, 3]; thereby, legitimizing research that is often publicly funded [4, 5]. Patient engagement has become a moral and ethical imperative and, in some jurisdictions, particularly with marginalized communities, patient engagement also serves as a pre-requisite for research ethics approval [6-8]. The engagement of patients as partners in the design, execution and evaluation of health research is now an expectation of several principal funding programs [5, 9].

In Canada, as in many other countries, most major national and provincial research funding bodies promote engagement of patients throughout the entire process, from determining the research question to dissemination of the research results [10, 11]. A systematic review of 142 studies [2] established that, in most instances, it was possible for patients to contribute their expertise across the continuum of research; however, their engagement tended to be focused in the early stages of the study. The level of patient engagement in the process has varied in intensity and complexity depending on the nature of the research and information needs [11]. A more recent scoping review examining methods and outcomes of patient engagement confirmed that, in the absence of a validated framework, most efforts to engage patients continued to be limited to the early stages of engagement and did not appear to be maintained throughout the lifecycle of most research projects [12].

2.1.1 Engaging patients as research partners

Patients are broadly defined as individuals with personal experience of a health condition [11]. There are numerous terms used for the concept of patient engagement in research including, but not limited to: 'integrated knowledge translation', 'patient and public involvement', 'participation', 'patient engagement', 'public and patient engagement' and 'co-production'[13, 14]. Patient engagement can be considered along a continuum from consultation at one end of the spectrum to partnership at the other end of the spectrum of engagement [15]. Research partnership is identified as patient membership on the research team, contributing to shared decision-making across the research process, engaged in the planning, execution and dissemination of research findings [15].

When partnering with patients, there is a shift from the researcher as sole expert to one where researchers and patients are both experts, working together to solve problems and co-generate knowledge [16]. Patients' experiential knowledge (of illness) is not accessible to most researchers, but if leveraged appropriately, has the potential to complement researchers' analytical skills and scientific perspective [17, p.676]. The concept of partnering with patients as equal team members has been demonstrated in clinical guideline development [18], by systematic review teams [19], and in the area of health and services improvement [20]. However, there are ongoing concerns about the need to balance rights to participation with efficiency and outcomes, [21, 22], particularly in disciplines that may lack the necessary infrastructure to support patient-facing activities (e.g., preclinical research) [23, 24].

2.1.2 Partnering with Frail and/or Seriously Ill Patients

Inclusivity is an important principle in meaningful research partnerships with patients and places emphasis on equity of engagement in research [25, 26]. Whilst a number of reviews have

concentrated on descriptions of the process and methods for various levels of patient engagement, little attention has been directed towards providing detailed accounts of patient characteristics [2, 12, 15, 27]. This oversight makes it difficult to gauge the inclusion of individuals from diverse patient populations.

The vulnerability of certain groups, such as frail and/or seriously ill patients (e.g., elderly patients with limited functional capacity, patients with high symptom burden, palliative patients), provides additional complexity to the engagement processes for prolonged and more intensive patient partnerships [27-29]. Frailty is classified as: a) geriatric condition involving functional decline, with increasing vulnerability to adverse events including mortality, morbidity, disability, hospitalization, and nursing home admission [30], or b) presence of multiple chronic conditions such as arthritis, heart failure, renal failure, and pulmonary disease leading to changes in functional ability [31], or c) presence of cognitive decline and dementia [30, 32]. Older adults living with frailty are a diverse group of patients that exhibit physical and/or cognitive impairments. Serious illness is defined as a condition that carries a high risk of mortality, negatively impacts quality of life and daily function, and/or is burdensome in symptoms or treatments [33]. Examples of serious illnesses are cancer (e.g., metastatic or hematologic), advanced liver disease, and advanced pulmonary diseases [33].

Patients who are frail and/or seriously ill have unique needs associated with symptoms related to their condition and/or treatment side effects which may offer researchers' access to a lived experience of illness that is qualitatively different than those with more stable or chronic conditions [29]. Practical issues related to engaging frail and/or seriously ill patients as research partners appears to deter research teams from inviting, or even considering them for membership on the research team [28]. A recent scoping review exploring engagement of geriatric oncology

patients found little evidence of patients' inclusion as research partners [29]. Little is known about the engagement of frail and/or seriously ill patients as partners on research teams.

2.1.3 Aim

The aim was to synthesize the evidence on the engagement of frail and/or seriously ill patients as research partners across the research cycle. The specific objectives were to: a) describe the contribution of frail and/or seriously ill patient partners to the stages of the research cycle (and associated research activities), b) identify the barriers and facilitators to partnering encountered by frail and/or seriously ill patients, and researchers, and c) describe the perceived positive and negative impacts of including frail and/or seriously ill patient partners in research from the perspective of patients, researchers, and the research itself.

2.2 Methods/Design

2.2.1 Study Design

A systematic review of qualitative, quantitative, and mixed methods studies was conducted with narrative synthesis. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [34] guided the reporting. The study protocol was developed prior to the literature search and registered via PROSPERO (CRD42019127994).

2.2.2 Guiding Conceptual Framework

The systematic review was guided by a conceptual framework comprised of two components (see Table 2.1). The first component utilizes a modified version of the Patient Service User Engagement in Research Framework originating from a prior systematic review by Shippee et al. (2015), and addresses patient engagement at different stages of the research cycle and associated activities. The second component addresses the level of engagement in the decision-making process as defined by the International Association of Public Participation

(IAP2) Spectrum of Public Participation (*see Supplementary file 1 for additional detail* [Appendix 3]) [35]. The IAP2 spectrum denotes five levels of engagement (inform, consult, involve, collaborate, and empower) and has been used in Canada, Australia, New Zealand, Indonesia, Italy, Southern Africa and the USA to outline levels of engagement and promote best practices in patient and public engagement [36].

Table 2.1 Guiding Conceptual Framework for Engaging Frail and/or Seriously Ill Patients in Research

Stages of Research Cycle*	IAP2 Spectrum of Public Participation†
Foundational phase • Research priority setting – specific to disease, condition, or syndrome • Setting evidence-based patient engagement strategies – specific to disease, condition, or syndrome Preparatory phase • Agenda setting at the individual study level • Proposal development • Ethics application – including well-defined consent procedures • Acquiring funding/grant application Execution phase • Study design & procedures • Recruitment strategies & tools • Data collection • Data analysis (reviewing & interpreting data) Translation phase • Dissemination • Implementation • Evaluation	Inform • Providing balanced and objective information to assist in understanding the problem, alternatives, opportunities and/or solutions Consult • Seeking/obtaining feedback on analysis, alternatives and/or decisions Involve • Working directly with (patients) throughout the process to ensure concerns and aspirations are consistently understood and considered Collaborate • Partnering in each aspect of the decision (e.g., contributing to shared decision-making *across the research process)* Empower • Patients and members of the public provide final decision.

*Modified from Shippee et al. (2015) [15]

†Based on the IAP2 Spectrum of Public Participation (2014) [35]

2.2.3 Data Sources and Search Strategy

An electronic search strategy was developed with the assistance of an experienced health sciences librarian (KF) and adapted for the following databases: MEDLINE® (via Ovid), Cumulative Index to Nursing and Allied Health Literature (CINAHL via EBSCO), Excerpta Medica database (EMBASE® via Ovid), and PsycINFO® (via Ovid). The search strategy included a combination of key words and medical subject headings (MeSH) terms such as "patient engagement", "patient involvement", "patient-oriented research" (*see Supplementary file 2 for the complete Medline search strategy* [Appendix 4]). Reference lists of the included studies were manually reviewed to maximize the breadth of the review. There were no date limitations. The search strategy was executed from April 4, 2019 to April 6, 2019.

2.2.4 Eligibility criteria

The population, intervention, control, outcomes, study design (PICOS) criteria were used to assess study eligibility [34] (see Table 2.2). All original studies of any design were eligible if they included frail and/or seriously ill patients as research partners at the level of involvement, collaboration, or empowerment throughout the research cycle (see Table 2.1). There were no language restrictions. In order to limit duplication, all systematic reviews were excluded after manually searching the reference lists of relevant reviews. Commentaries and editorials were excluded as well as studies that did not provide any details on patient perspectives or patient condition and when no full text was available.

Table 2.2 Study Eligibility Criteria: Modified (PICOS) Framework

PICOS [34]	Inclusion Criteria	Exclusion Criteria
Participants (P)	• Frail and/or seriously ill adult patients as per definitions for frailty and serious illness (e.g., elderly patients exhibiting physical and/or cognitive impairments, patients with high symptom burden due to acute illness or treatment effects, acute episodic illness, palliative patients; patients susceptible to adverse events including mortality, morbidity, disability, hospitalization, and nursing home admission).	• Studies where patients were excluded due to frailty of condition (physical and or cognitive) or deemed too ill to participate during acute episodes of serious illness or treatment. • Patients not identified as frail or seriously ill, i.e., survivors, chronic disease (focus on single disease without description of acuity/severity of condition). • Participants from broader community or public engagement (with no descriptors of frailty and serious illness) • Patients for whom there were no descriptors of physical characteristics or cognitive status. • Pediatric and youth patients (<18yrs).
Phenomenon of Interest (I)	• Engagement of frail and/or seriously ill patients as partners in research, i.e., at the level of involvement, collaboration, empowerment.	• Engagement of patients as objects of study, i.e., doing research *on* or *to*. • Engagement that took the form of informing patients of research activities, or at the level of consultation only.
Comparator (C)	No comparator	
Outcome (O)	• Methods and timing of engagement (i.e., stage(s) of research process). • Level of engagement. • Engagement strategies, factors associated with barriers and facilitators to engagement. • Positive and/or negative impacts of engagement on patient(s), researcher(s), research and/or ethical concerns.	• Primary research outcomes where patients were research participants only.
Study Type (S)	• Peer-reviewed qualitative, quantitative, or mixed methods studies.	• Letters. • Commentaries/editorials. • Studies reported in non-peer reviewed journals. • Conference abstracts/ presentations. • Dissertations. • Review articles.
Language	No language restrictions.	

2.2.5 Study Selection

Search results were uploaded to Covidence Systematic Review Software [37]. Following the removal of duplicates, citations were screened independently by two reviewers (CL, JL) based on title and abstract (level 1 screening) and full-text articles (level 2 screening). The studies were assessed against the inclusion and exclusion criteria. Full-texts that did not meet the eligibility criteria were excluded and the rationale was documented in the Covidence Systematic Review Software to facilitate ease of tracking and reporting.

2.2.6 Data Extraction

Data extraction forms were developed to provide a standardized and transparent method for examining the methodology and findings from the studies [38]. The forms were piloted on a subset of relevant papers that were included in the review and refined to ensure the extraction template met the specific objectives of the review. The following general characteristics were extracted: year of publication; title, aim, study design, country of conduct; number of frail and/or seriously ill patients engaged in research; patient condition with regard to reports of serious illness and/or frailty of patients. Engagement in research was extracted on four components: a) stages of the research cycle and associated activities within those stages; b) the level of engagement in the decision-making process, i.e., involvement, collaboration, and empowerment (see Table 2.1); c) barriers and facilitators to engaging frail and/or seriously ill patients in research; d) the described impacts of engaging frail and/or seriously ill patients. Data were extracted by two independent reviewers (CL, JL) and discrepancies resolved through discussion. A third party (DS) was available in the event that consensus could not be reached.

2.2.7 Data Analyses

Narrative descriptions were reported for all studies. Data were synthesized in accordance with the guiding conceptual framework, i.e., engagement during the research cycle and by level of engagement. No meta-analyses were conducted as the aim was to identify the scope and types of patient engagement. Additionally, the heterogeneity across studies regarding the design, patient populations, methods, measures used, and a lack of numeric outcomes reported inhibited meta-analyses.

2.2.8 Quality Assessment

Two independent reviewers (CL, JL) critically appraised included studies using the updated Mixed Methods Appraisal Tool (MMAT) [39]. The MMAT has been content validated, tested for inter-rater reliability and is increasingly utilized in the quality appraisal of systematic reviews of mixed studies [40-43]. Scores are based on criteria, which differ according to study type. Each study was appraised according to the criteria met and were ranked as having low, moderate, or high quality. But they were not excluded on the basis of low quality because the overall aim was to identify the scope and types of patient engagement. Reviewers resolved discrepancies through discussion and consensus.

2.3 Results

2.3.1 Search and Selection Results

There were 14,062 citations retrieved from electronic searching (see Figure 2.1) [44]. After removing duplicates, 8,763 original articles were screened, 431 full text reports were reviewed for eligibility, and 28 studies plus two additional studies identified through manual screening of reference lists in the included studies for a total of 30 studies met eligibility criteria.

Included studies were published between 2006-2019, with a trend of increasing publications over time; 73% of studies were published within the last five years since 2014 (see Figure 2.2).

Figure 2.1 PRISMA Flow Diagram

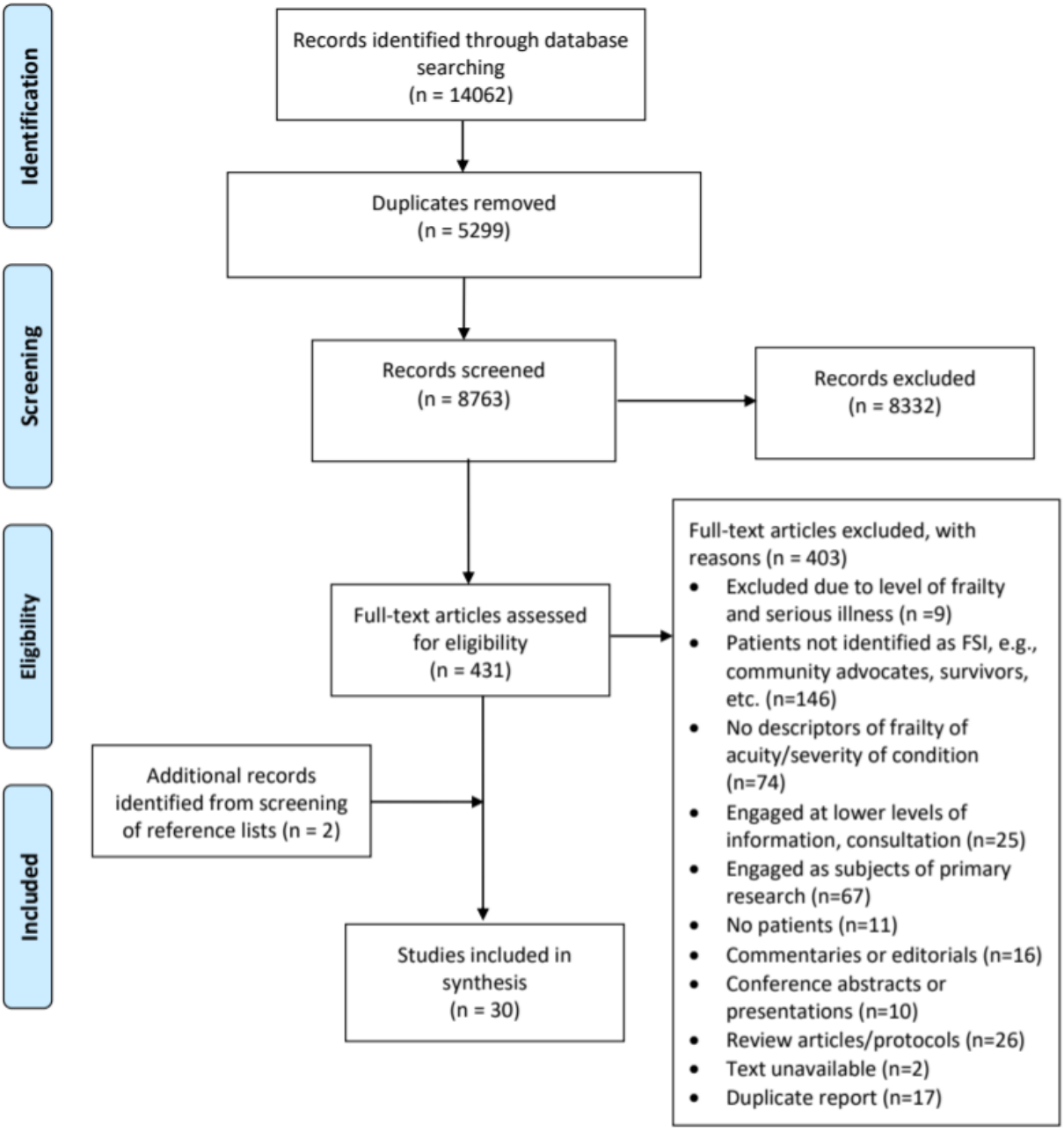
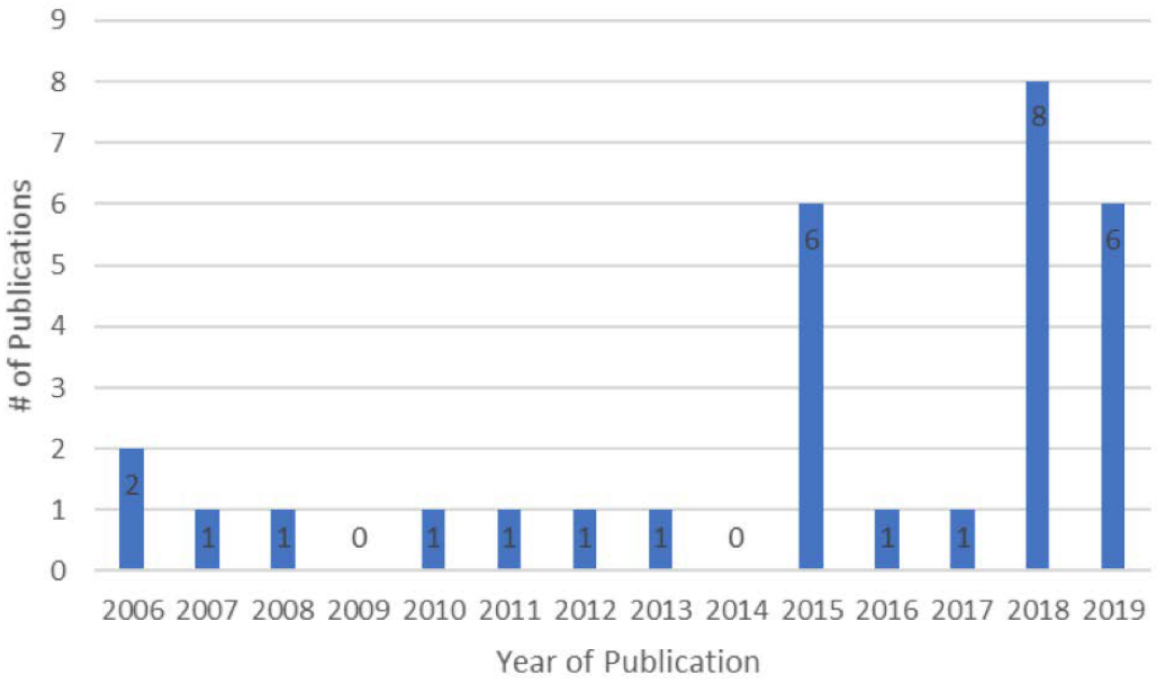


Figure 2.2 Number of Publications by Year (2006-2019)



2.3.2 Characteristics of Included Studies

Of 30 studies, 20 used qualitative methods (67%), 2 used quantitative methods (7%), and 8 used mixed methods (27%) (see Table 2.3). All studies were published in English. Studies originated from: United Kingdom (n=18 studies), Canada (n=5), Denmark (n=3), United States (n=2), the Netherlands (n=1), and Malawi (n=1).

The number of patients in the studies ranged from one [45] to 168 [46] with a median of 16 patients. There were 11 (37%) studies where patients were engaged as a group with caregivers and/or other stakeholders (e.g., ex-patients, survivors, patient representatives/ advocates, or members of the public) [7, 24, 47-55].

Table 2.3 Characteristics of Included Studies

Author, year, country of origin	Study objective related to this systematic review (from text)	Methodological approach and data collection	# FSI patients engaged
Absolom 2015 [56] UK	To provide an overview of how research collaborations with patient representatives have developed over time and how patient involvement has played a crucial role the success of local and national cancer research programs (eRapid study).	Qualitative; case study	14 patients on treatment, cancer survivors 2 additional patients on research S/C
Arain 2015 [47] UK	To explore different ways of involving consumers in cancer research in one regional network.	Quantitative; descriptive	15 patients on treatment, ex-patients, cancer survivors, caregivers
Bates 2018 [69] Malawi	To report on experiences and lessons learnt using Photovoice in Blantyre, Malawi to encourage its wider use in research and practice.	Qualitative; participatory action research (PAR)	6 patients with palliative care needs
Bethell 2018 [67] Canada	To engage persons with dementia, friends, family, caregivers, and health and social care providers to identify and prioritize their questions for research related to living with dementia and prevention, diagnosis, and treatment of dementia.	Mixed methods; James Lind Alliance Research Priority Setting Partnership (PSP) methods	7 persons with dementia 1 additional person with dementia on research S/C
Bethell 2019 [68] Canada	To engage people with lived or clinical experience of frailty and produce a list of research priorities related to care, support, and treatment of older adults living with frailty	Mixed methods; James Lind Alliance Research Priority Setting Partnership (PSP) methods	52 initial survey 6 interim prioritization # n/r for research S/C participation
Burns 2018 [66] US	To report outcomes of engaging patients and caregivers, identification of knowledge gaps, and prioritization of high impact research questions or recommendations related to hematopoietic cell transplantation.	Qualitative; focus groups	25 patients Patients also served on steering committee & working groups
Caldon 2010 [70] UK	To report on the process and consequences of consumer participation, rather than the findings of the illustrative (primary) research study	Qualitative; case study	2 patients
Chiu 2013 [7] Canada	To share the experience of engaging cancer patients/survivors in a participatory research study.	Mixed methods; participatory action research (PAR)	18 patients on treatment, ex-patients, cancer survivors
Collins 2015 [24] UK	To outline the challenges faced by the North Trent Cancer Research Network Consumer Research Panel model of Public & Patient Involvement.	Qualitative; case study	38 patients on treatment, ex-patients, cancer survivors
Corner 2007 [48] UK	To involve cancer patients across the UK in identifying priorities for research investment.	Qualitative; participatory action research & nominal group study	130 patients on treatment, ex-patients/cancer survivors
Cotterell 2011 [49] UK	To explore the personal impact of involvement on the lives of service users affected by cancer.	Qualitative; focus groups	64 patients on treatment, ex-patients/cancer survivors
Davis 2019 [64] UK	To consult frail older adults about services improvements and research topics associated with the design and delivery of discharge from hospital. To use successive PPIE processes to enable a permanent PPIE panel to be established.	Qualitative; focus groups and interviews	27 frail older adults

Author, year, country of origin	Study objective related to this systematic review (from text)	Methodological approach and data collection	# FSI patients engaged
Froggatt 2015 [57] UK	To describe the experiences of people's participation in patient and public involvement (PPI) in supportive and palliative care research.	Qualitative; semi-structured interviews	8 patients 1 patient on research S/C
Heaven 2016 [58] UK	To create a structure to enable meaningful, sustainable public involvement within the cmRCT framework.	Qualitative; case study	70 frail older adults
Iwata 2019 [50] US	To describe the benefits of patient-driven research in the field of head and neck oncology, review lessons learned from establishing partnerships with patients and caregivers and serve as a model for further patient-driven research endeavors.	Qualitative; case study	15 patients on treatment, ex-patients, cancer survivors
Jones 2017 [54] Canada	To identify research priorities in the management of kidney cancer.	Mixed methods; James Lind Alliance Research Priority Setting Partnership (PSP) methods	34 patients on treatment: 34 waiting surgery: 7 on research S/C (conflated with caregivers)
Jorgensen 2018 [51] Denmark	To report on the process of having current and former cancer patients involved as co-researchers.	Qualitative; case study	8 patients on treatment, ex-patients, cancer survivors
Jorgensen 2018 [52] Denmark	To investigate the impact of involving patient representatives as peer interviewers in a research project on patient empowerment.	Mixed methods; qualitative & quantitative analyses	16 patients on treatment, ex-patients, cancer survivors
Lechelt 2018 [53] Canada	To determine research priorities for patients with head and neck cancer.	Mixed methods (James Lind Alliance method for PSP)	104 patients on treatment, ex-patients, cancer survivors 5 patients on research S/C
Litherland 2018 [71] UK	To describe the involvement of people with dementia and carers as part of the IDEAL study	Qualitative; case study	3 persons with dementia
Littlechild 2015 [65] UK	To evaluate the impact of working with co-researchers from the perspective of multiple stakeholders on a project in which older people with dementia and older people from a black and minority ethnic community were involved as co-researchers.	Qualitative; case study	11 older persons with dementia and/or frailty
Parveen 2018 [45] UK	To report the process of involving a diverse range of experts-by-experience approach within the Caregiving HOPE study, and its impact on research processes and outcomes.	Qualitative; case study	1 older person with dementia
Perkins 2008 [59] UK	To determine patients' priorities for palliative care research through a questionnaire study	Quantitative; survey	19 patients 10 patients piloted tool
Piil 2019 [60] Denmark	To identify future research agendas that reflect the concerns and unexplored areas of interest for patients with life-threatening cancer, their relatives and the clinical specialists during the cancer trajectory.	Qualitative; focus groups	6 patients 2 patients on research S/C
Schölvinck 2019 [61] The Netherlands	To identify and prioritize research needs of hematological cancer patients and people who have undergone a stem cell transplantation.	Mixed methods; focus groups, interviews, questionnaire	19 patients interviewed 27 patients in focus group 146 patients surveyed 3 patients on research S/C

Author, year, country of origin	Study objective related to this systematic review (from text)	Methodological approach and data collection	# FSI patients engaged
Stephens 2015 [46] UK	To identify top 10 research priorities relating to mesothelioma, and identify those unanswered questions that involved an intervention, in order to aid translation into answerable research questions.	Mixed methods; James Lind Alliance Research Priority Setting Partnership (PSP) methods	168 patients surveyed 6 patients at consensus meeting
Stevenson 2019 [62] UK	To involve individuals with dementia as co-researchers in analysis of research findings to enhance validity through a process of applying multiple perspectives to data analysis.	Qualitative; case study	4 persons with dementia
Tanner 2012 [63] UK	To report on the process of involving older people with dementia in all stages of the research process.	Qualitative; case study	3 persons with dementia
Wright 2006 [72] UK	To provide detail of collaborative participation of patients and carers in the design and conduct of participatory research study in setting the cancer research agenda.	Qualitative; participatory approach	22 patients & caregivers
Wright 2006 [55] UK	To describe the experiences of involving palliative care patients as co-researchers in end of life research.	Qualitative; case study	15 patients

S/C = research steering committee

2.3.3 Characteristics of Patients in Included Studies

Of 30 studies, 18 (60%) included patients with specific cancer diseases: 10 heterogeneous cancers, 2 blood cancers, 2 head and neck cancers, 2 breast cancer, one kidney cancer, and one mesothelioma (see Table 2.4). Other studies included patients/persons with dementia (n=6), older adults with frailty (n=3), and palliative patients including malignant and non-malignant disease (n=3). Patient characteristics of frailty and/or serious illness were mostly reported in relation to: receipt of active treatment(s) associated with high symptom burden (n=18), receipt of palliative or end-of-life care (n=3), higher levels of cognitive impairment (n=6), and physical frailty associated with old age (n=3).

Of 30 studies, 12 (40%) reported the ages of the patient-partners [24, 48, 50, 53, 56-63] and six (6/12) of them also included patients 75 years of age and above [24, 57, 58, 61-63]. Five of 30 studies (17%) reported on ethnicity [47, 49, 50, 64, 65]; three (3/5) of which reported ethnicity more broadly in terms of "diversity" [47, 49, 65].

2.3.4 Patient Partner Research Roles: Research Stages and Activities

No studies reported engagement of frail and/or seriously ill patients at the level of empowerment, i.e., the provision of primary direction and governance to a given research endeavor. The highest level of engagement was reported in four of 30 studies (13%) where collaboration was demonstrated across all four stages of the research cycle (see Table 2.4). Patients in these studies partnered in activities including, but not limited to: delineation of the scope of the partnership, contribution to study design, co-leadership on working groups during study execution, data analysis, dissemination activities, and adoption of decision-making roles on research steering/advisory committees [48, 50, 60, 66].

Seven studies (23%) included patients in research priority setting at the broader level of biomedical specialty/disease/condition, rather than at the individual study level [46, 53, 54, 61, 64, 67, 68]. These studies included patients who were representative of the condition as partners on research steering/advisory committees and who contributed to shared decision-making across the research study cycle.

Eleven studies (37%) described collaboration with frail and/or seriously ill patients across the latter three stages of the research cycle (preparation, execution, and translation) at the individual study level [7, 45, 49, 51, 55, 56, 65, 69-72]. Patients partnered in a variety of different activities that mostly included: assistance with grant applications, input into study design, co-design of project materials, recruitment strategies, data analysis, dissemination activities, and decision-making at research steering/advisory committees. Four (13%) studies included frail and/or seriously ill patient partners from research collaboratives or networks who assisted with the identification of appropriate patient engagement strategies specific to frail and/or seriously ill populations at a broader system level. Patients described contributing to grant writing, proposal development, tool refinement, conducting interviews, representing research findings, and co-authorship on papers across different studies [24, 47, 57, 58].

Four studies (13%) described patient roles during key stages of the research process, rather than across the research cycle [52, 59, 62, 63]. Patients participated in activities at the execution stage of the research cycle, where they piloted research tools, served as peer interviewers, assisted in other forms of data collection, or interpreted data sets [52, 59, 62, 63].

Table 2.4 Patient Characteristics and Partnering Activities

Study	Disease or diagnosis	Age (years)	Ethnicity or cultural identity	Description of illness severity acuity/frailty (from text)	Highest level of engagement	Research activities where patients provided input (from text)	Stages of the research cycle			
							Foundation	Preparation	Execution	Translation
Absolom 2015 [56]	Heterogeneous cancers - including gastro-intestinal, breast, prostate, and gynecological	50-70 yrs	n/r	Patients on active treatment for cancer.	Collaborate	Grant writing; proposal development; research design; recruitment strategy development; tool refinement; implementation & dissemination. *2 patients on the steering committee (SC) which oversaw and advised the study.*		√	√	√
Arain 2015 [47]	Heterogeneous cancers	n/r	"diversity"	Patients on treatment for cancer type; including colorectal, breast, lung, brain and prostate.	Collaborate	Grant writing; proposal development; research design; tool refinement (patient information sheets for clinical trials, questionnaires); advice for increasing trial recruitment, conducting patient interviews. Patients also sat on project team.		√	√	√
Bates 2018 [69]	Heterogeneous cancers	n/r	n/r	Patients receiving palliative care for advanced cancer.	Collaborate	Engaged in data collection and data analysis, dissemination activities.		√	√	√
Bethell 2018 [67]	Dementia	n/r	n/r	Different types/stages of dementia – varying degrees of cognitive impairment.	Collaborate	Identification and prioritization of research questions. *1 person with dementia included on the steering committee which oversaw and advised the study. Persons with dementia were involved in: promoting surveys and recruitment.*	√	√	√	
Bethell 2019 [68]	Older Adults with Frailty	n/r	n/r	Those with lived experience of frailty.	Collaborate	Identification of research priorities. *People with lived experience of frailty included on steering committee which oversaw and advised the study.*	√	√	√	
Burns 2018 [66]	Hematological malignancies	n/r	n/r	Patients who have undergone hematopoietic cell transplant.	Collaborate	Identified research priorities. Provided advice on patient engagement. Patients also participated on SC and working groups throughout the entire research cycle (details and outcomes of contribution provided).	√	√	√	√
Caldon 2010 [70]	Breast cancer	n/r	n/r	Patients with cancer. One patient partner died prior to publication of the study.	Collaborate	Co-development of the project – tools, documentation, and processes. Also involved in dissemination and co-authorship.		√	√	√
Chiu 2013 [7]	Breast cancer	n/r	n/r	Some participants on active treatment.	Collaborate	Provided input through all phases of the research from grant development to dissemination of study findings. Other activities included refinement of research questions, survey development, data analysis, presentations, and co-authorship.		√	√	√

Study	Disease or diagnosis	Age (years)	Ethnicity or cultural identity	Description of illness severity acuity/frailty (from text)	Highest level of engagement	Research activities where patients provided input (from text)	Stages of the research cycle			
							Foundation	Preparation	Execution	Translation
Collins 2015 [24]	Heterogeneous cancers & palliative	22-75	n/r	Level of acuity not documented in cancer patients but includes palliative patients	Collaborate	Co-researchers across different projects from influencing the research agenda through to dissemination as co-authors and presenters at conferences.		√	√	√
Corner 2007 [48]	Heterogeneous cancers (including breast, gastrointestinal, lung, hematological, etc.) & palliative	30-70	n/r	16% on active treatment; 13 % receiving palliative care. *Inclusion of other stakeholders, e.g., caregivers, ex-patients (cancer survivors). Patients were excluded if deemed by clinical team to be too unwell, have complicating health factors or liable to be distressed by participating.*	Collaborate	Identification of research priorities. The co-researchers 'co-owned' the study with the unit, and as such had a direct influence on all aspects of the study, including data collection, analysis and dissemination of study findings.	√	√	√	√
Cotterell 2011 [49]	Heterogeneous cancers, COPD, Stills Disease, Parkinson's Disease	41-78	"diversity"	Patients receiving active treatment and patients receiving palliative care (for non-malignancies). *Inclusion of other stakeholders, e.g., caregivers, ex-patients (cancer survivors)*	Collaborate	Involved as integral members of the research team throughout the length of the study; data collection, analysis and dissemination of study findings.		√	√	√
Davis 2019 [64]	Frail older adults	n/r	Pakistani, Somalian, Yemeni	Frail older adults.	Collaborate	Identification of research topics. Provided advice on methods of patient engagement to develop sustainable infrastructure. Developed a PPI structure. *Patients/caregivers included on steering committee.*	√	√	√	
Froggatt 2015 [57]	Heterogeneous cancers	51-84	n/r	Patients experiencing recurrence of disease and those receiving ongoing treatment	Collaborate	Research partners across different studies in cancer research collaborative. Provided input regarding barriers to patient engagement. The term research partner was proposed by the co-applicant patient representative on the management group as reflecting the nature of the PPI working that was to be developed in the collaborative	√	√	√	
Heaven 2016 [58]	Frailty	75+	n/r	Older adults with frailty.	Collaborate	Engaged throughout a number of studies from grant writing/proposal development, research conduct, dissemination. Participation on research steering/advisory committees.		√	√	√
Iwata 2019 [50]	Head and neck cancers	35-74	10% Asian, Hispanic or Latino	Included patients on active treatment. *Inclusion of other stakeholders, e.g., caregivers, ex-patients (cancer survivors).*	Collaborate	Engaged in identification of research priorities, hypothesis generation, feedback on tools and processes, clinical flow and dissemination.	√	√	√	√
Jones 2017 [54]	Kidney cancer	n/r	n/r	Included patients on current active treatment and those awaiting surgical treatment.	Collaborate	Identifying and prioritizing research questions. *7 Patients/caregivers included on steering committee; contributed throughout study design and execution; defining the scope of the partnership, development of the protocol,*	√	√	√	

Study	Disease or diagnosis	Age (years)	Ethnicity or cultural identity	Description of illness severity acuity/frailty (from text)	Highest level of engagement	Research activities where patients provided input (from text)	Stages of the research cycle			
							Foundation	Preparation	Execution	Translation
						identifying potential partners and stakeholders, and oversight of the process.				
Jorgensen 2018 [51]	Heterogeneous cancers	n/r	n/r	Included patients on active treatment. *Inclusion of other stakeholders, e.g., a caregiver, ex-patients (cancer survivors).*	Collaborate	Engaged throughout research cycle: co-application on grants, literature review participation, outcome and tool development, feedback on the conduct of the research, presentations, co-authorship.		√	√	√
Jorgensen 2018 [52]	Heterogeneous cancers	n/r	n/r	Included peer interviewer with advanced age and stage of illness. *Co-researchers also included caregivers, ex-patients (cancer survivors).*	Collaborate	Involved in study design, conduct of research (conducting peer interviews), data analysis.		√	√	
Lechelt 2018 [53]	Head and neck cancers	n/r	n/r	Broad spectrum of patients, varying tumor types and sites, including newly diagnosed, those on current active treatment. *Inclusion of other stakeholders, e.g., caregivers, ex-patients (cancer survivors).*	Collaborate	Identification of research priorities. *5 patients on the steering committee which established consensus on desired scope and inclusion/exclusion criteria for the project regarding: respondent groups, question categories; tumor types/site; developed the survey; oversaw all aspects of the project.*	√	√	√	
Litherland 2018 [71]	Dementia	n/r	n/r	Different types/stages of dementia – varying degrees of cognitive impairment.	Collaborate	Engaged in shaping project materials, providing feedback on questionnaires and interview processes, reviewing emerging theoretical themes, and presenting project findings.		√	√	√
Littlechild 2015 [65]	Dementia	n/r	"diversity"	Older persons with varying types/stages of dementia – varying degrees of cognitive impairment.	Collaborate	Engaged at all stages of the study, including: designing the research method and tools, identifying key themes and findings at the analysis stage, dissemination activities.		√	√	√
Parveen 2018 [45]	Dementia	n/r	n/r	Different types/stages of dementia – varying degrees of cognitive impairment	Collaborate	Engaged in discussing study progress, findings and interpretation of data		√	√	√
Perkins 2008 [59]	Heterogeneous cancers	65 median	n/r	Included palliative patients with a prognosis of 6 months or less.	Involve	Patient input into identification of research domains, piloting of questionnaires prior to prioritization of research questions.	§	√	√	
Piil 2019 [60]	Primary malignant brain tumor and acute leukemia	22-59	n/r	Life threatening cancer diagnosis, characterized by poor and uncertain prognosis, undergoing aggressive and intensive oncological treatments resulting in a complex symptom burden.	Collaborate	Identifying and prioritizing research questions. *Patients included on steering committee and contributed throughout study design & execution; defining scope of the partnership, development of the protocol, identifying potential partners and stakeholders, and oversight of the process. Additional details included in published study protocol [86].*	√	√	√	√
Schölvinck 2019 [61]	Hematological malignancies	19-75+	n/r	Patients from all disease phases and types.	Collaborate	Identification and prioritization of research questions and outcomes. *Patient representatives*	√	√	√	

Study	Disease or diagnosis	Age (years)	Ethnicity or cultural identity	Description of illness severity acuity/frailty (from text)	Highest level of engagement	Research activities where patients provided input (from text)	Stages of the research cycle			
							Foundation	Preparation	Execution	Translation
						included on the research steering/advisory committee.				
Stephens 2015 [46]	Mesothelioma	n/r	n/r	Patients with high symptom burden.	Collaborate	Identification and prioritization of research questions. *Patients sat on the research advisory committee which oversaw and advised the study.* .	√	√	√	
Stevenson 2019 [62]	Dementia	<65-75+	n/r	Cognitive impairment - early to mid-stage dementia.	Involve	Engaged in deriving meaning from the data, identifying and connecting themes.			√	
Tanner 2012 [63]	Dementia	60-77	n/r	Cognitive impairment – progressive during the study.	Involve	Engaged as co-researchers involved in conducting interviews.			√	
Wright 2006 [72]	Heterogeneous cancers	n/r	n/r	Includes patients undergoing treatment. *Inclusion of other stakeholders, e.g., caregivers, ex-patients (cancer survivors).*	Involve	Engaged in the design and conduct of the study (including co-facilitation of focus groups). Also engaged in subsequent data analysis and dissemination activities.		√	√	√
Wright 2006 [55]	Disease/s not specified (palliative)	n/r	n/r	Patients receiving palliative care.	Collaborate	Engaged in the design and conduct of the study. Co-research role throughout the course of the study.		√	√	√
						Totals: n (%)	13 43 %	28 93 %	30 100 %	18 60 %

n/r = not reported; § - Research prioritization reported in prior publication [87]

2.3.5 Barriers and Facilitators to Partnering with Patients

System Level Factors

The most commonly cited barrier for researchers to partner in research with frail and/or seriously ill patients was resource constraints, including financial concerns, human resource capacity for support, and the time commitment required for meaningful engagement (15/30) [7, 24, 45, 47, 51, 52, 55, 56, 58, 62, 64, 65, 69, 71, 72] (see Figure 2.3). Researchers also cited lack of formal infrastructure and policy, poorly defined governance mechanisms, and inconsistent processes to support meaningful patient partnerships as a system level barrier (4/30) [24, 45, 49, 51].

Both patients and researchers reported the need to establish consistent, formal compensation frameworks in order to recognize patient contribution and reimburse patients for their time, travel, and incidental costs (11/30) [7, 45, 47, 51, 53, 56, 58, 60, 65, 69, 71]. Researchers stressed the importance of having a rigorous macro and micro level infrastructure with appropriate policy and governance mechanisms to support successful and meaningful patient partnership beyond a singular study (11/30) [24, 45, 47, 49-51, 55, 58, 62, 64, 67]. Relatedly, studies made direct reference to the significance of ensuring that funding for patient engagement is integrated into the research structure in order to facilitate and sustain patient engagement activities (8/30) [24, 45, 47, 51, 56, 62, 64, 71].

Team Level Factors

Lack of role clarity and expectations related to the contribution of patients throughout the research cycle was cited as a barrier to meaningful engagement by both patients and researchers (6/30) (see Figure 2.3) [24, 49, 51, 56, 62, 65].

The most commonly cited facilitator to meaningful engagement with frail and/or seriously ill patients as partners in research was to establish a collaborative team environment built on trust, mutual respect, and openness (18/30) [7, 24, 45, 49-52, 55, 56, 60-63, 65, 69-72]. Researchers also stressed the importance of promoting structural accessibility as a facilitator to meaningful engagement, with an emphasis on inclusivity and diversity of representation (i.e., ensuring that patient partners were representative of varied ethnocultural and socioeconomic groups) (17/30) [7, 24, 45, 46, 48-51, 55, 56, 58, 65, 67-69, 71, 72]. The importance of regular contact, ongoing support, feedback, and team de-briefing was recognized as a requirement to effective partnership for both patients and researchers (15/30) [7, 24, 45, 49-52, 55, 56, 61, 63, 64, 69-71]. Flexibility in the timing, methods and modes of contribution (13/30) [7, 45, 49, 51, 55, 56, 59, 62-66, 71], clarity in roles and the expected contribution of patients throughout the partnership (10/30) [24, 47, 49-52, 56, 57, 62, 70], and clear and transparent processes for all members of the team (9/30) [24, 45, 48, 51, 52, 63, 65, 66, 70] were cited by both patients and researchers as key facilitators to the process. Facilitating communication through provision of multiple mechanisms for input and feedback, and limiting overly technocratic jargon was also perceived as vital to enabling patients' contribution (9/30) [7, 24, 46, 50, 53, 56, 57, 63, 70].

Researcher Level Factors

The most commonly cited perceived barrier of researchers to partnering with frail and/or seriously ill patients in research was related to their concerns about patients' potential lack of continuity in contributions throughout the research cycle due to deterioration in patients' health or cognition, or death (11/30) (see Figure 2.3) [7, 46, 49-51, 53, 55-57, 63, 69]. The second most common barrier was researchers' uncertainty about the value or overall benefit of patient engagement, particularly given the outcomes of the partnership on research may not be visible

for some time (9/30) [24, 47-50, 55, 58, 62, 71]. Other researcher barriers were perception that research outputs identified by patient partners may not be fully aligned with the initial objectives of the project or might be too costly to implement (4/30) [24, 52, 61, 65], concern for placing additional or perceived unnecessary burden on patients (3/30) [48, 59, 69], and lack of familiarity and confidence in patient engagement, particularly where patients assume a partnership role (2/30) [58, 71].

Facilitators were researchers' willingness to share decision-making with patients as essential to partnering with patients (10/30) [7, 24, 49, 51-53, 58, 66, 67, 70]. Another facilitator was researchers' knowledge and expertise of patient engagement practices as vital to mitigating potential harms of engagement (9/30) [7, 24, 50, 51, 60, 64, 69-71].

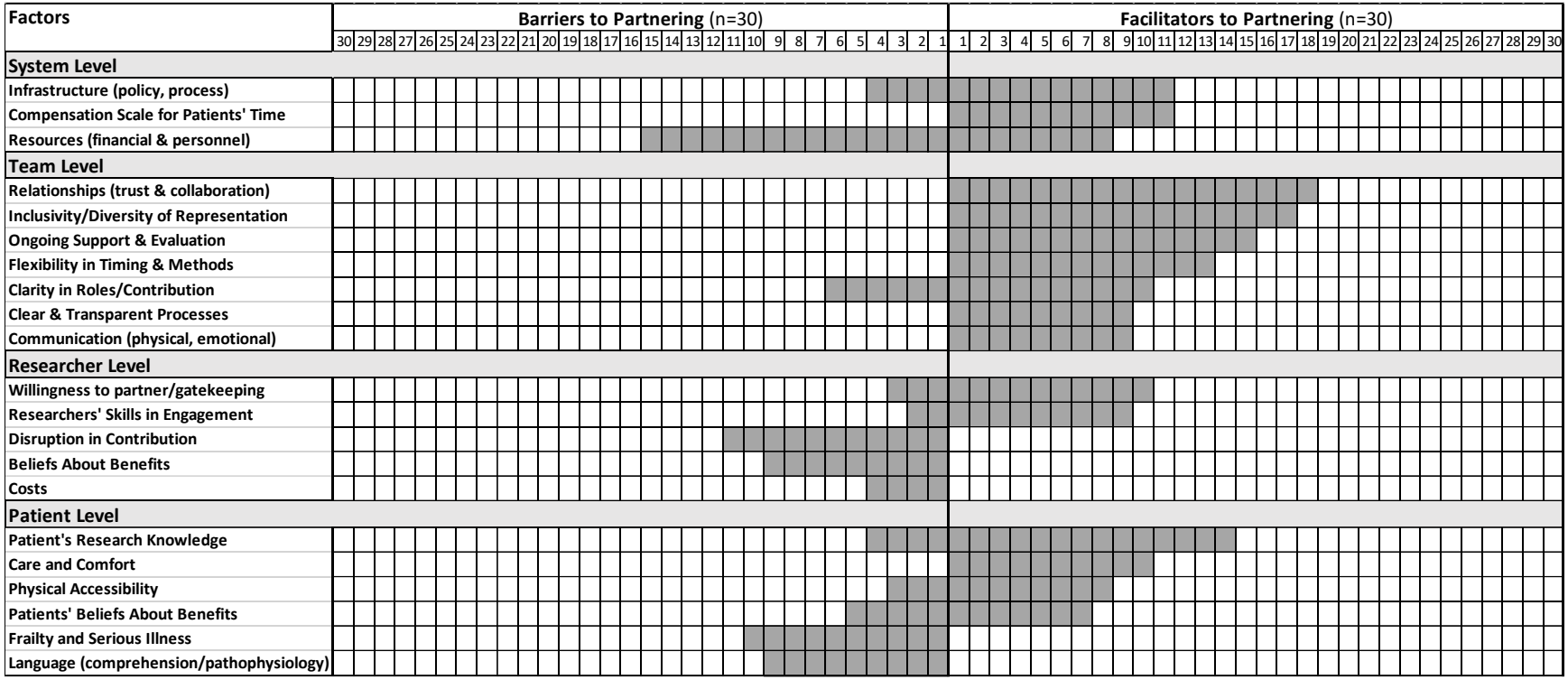
Patient Level Factors

The most common patient level barrier was being frail and/or experiencing severe illness or limited cognitive status (10/30) [46, 48, 55, 59, 60, 63, 67-69, 72] (see Figure 2.3). The second most common barrier was communication difficulties due to diminished capacity for comprehension, heightened emotional distress due to subject matter material, or pathophysiology (9/30) [24, 46, 50, 57-59, 61, 63, 67]. Other barriers were patients' apprehension about the impact of their engagement and their capacity to influence action and outcomes of the research process (5/30) [46, 49, 50, 57, 71], perceived reservations about the extent to which patient partners possess the requisite knowledge and skills for research (4/30) [24, 52, 62, 65], and limited accessibility and concerns related to patients' potential difficulty to physically attend meetings (3/30) [7, 50, 64].

Skills building by providing basic training for patients in research methods and research ethics, was cited by both patients and researchers as a key facilitator to building confidence in

contribution and partnership (14/30) [7, 47, 50-52, 55, 56, 58, 62, 63, 65, 69, 70, 72]. Another facilitator for engagement was the provision of practical and emotional support, and comfort (e.g., refreshments, quiet spaces) (10/30) [7, 45, 49, 50, 53, 55, 62, 63, 69, 71]. Other facilitators for patients were ensuring physical accessibility to meeting spaces (8/30)[7, 45, 55, 62-64, 69, 71], and patients' altruistic beliefs that their involvement would improve care and outcomes for others (7/30) [49-51, 56, 64, 65, 70].

Figure 2.3 Themes and Sub-themes of Barriers and Facilitators to Partnering with Frail and/or Seriously Ill Patients



Reported in one study for each square

2.3.6 Impacts

Perceived impact on patients

The most commonly cited positive impact to partnering in research was described by patients as a renewed sense of personal agency in the face of debilitating disease and loss of self-esteem (11/30) [7, 49, 56, 57, 62-65, 69-71] (see Table 2.5). Patients also described positive impacts stemming from relationships formed with other patients and members of the research team which appeared to provide additional emotional support in their illness journey (11/30) [7, 45, 49, 50, 57, 60, 62, 63, 65, 70, 71]. Patient partnership was cited as having a positive beneficial impact for patients in relation to incorporation of their priorities for research questions and meaningful outcomes (10/30) [7, 24, 50, 53, 58, 59, 61, 64, 66, 70]. The development of new skills and knowledge (8/30) [51, 52, 56, 57, 65, 70-72] and acquisition of knowledge about their own disease/condition were also perceived by patients to be positive personal impacts (3/30) [57, 62, 70].

Perceived negative impacts for patients were cited as potential physical and/or cognitive fatigue related to the effort required during engagement (5/30) [7, 49, 55, 57, 69]. Increased emotional vulnerability and the potential for distress in reliving their illness and related negative experiences were also cited as perceived negative impacts to patient as partners (5/30) [7, 55, 57, 69, 72].

Perceived impacts on researchers

Perceived positive impacts of partnering with frail and/or seriously ill patients in the research process were cited as increasing researchers' awareness, and sensitizing them to the lived experience of illness and suffering (17/30) [7, 48, 50, 51, 55-57, 60-66, 69-71]. Partnering with patients was reported to challenge negative or ambiguous views held by researchers about

the utility of patient engagement (7/30) [48, 51, 55, 59, 65, 71, 72]. The potential to enhance interpersonal skills and promote inter-disciplinary collaboration (4/30) were also cited as positive impacts to researchers engaging frail and/or seriously ill patients as partners in research [51, 65, 70, 71].

The negative impacts described by researchers engaging frail and/or seriously ill patients as partners in research were described in relation to the potential strain on scarce resources (particularly related to funding and the human resource capacity required to support patient engagement activities) (15/30) [7, 24, 45, 47, 51, 52, 56, 58, 62-65, 69, 71, 72]. The additional complexity of the process and time required for engaging patient partners was also cited as a potential impediment to advancing project objectives and meeting timelines closely aligned with research funding cycles (2/30) [7, 45].

Perceived impact on the research

Researchers partnering with frail and/or seriously ill patients cited positive impacts on the research itself, with the design, execution and end of grant translation of research perceived as more applicable to those populations for whom the research is intended to serve (13/30) [7, 45, 51, 55, 57, 58, 62-65, 70-72]. On a more tangible level, including patients in the research process was also described as having a positive impact on the development of research tools (e.g., consent and data collection tools), processes (e.g., recruitment and retention), and methods that were more appropriate for use with frail and/or seriously ill patients (13/30) [7, 45, 47, 50, 51, 56, 58, 63, 65, 69-72]. Research produced with patient partners was also perceived to incorporate outcomes more relevant for frail and/or seriously ill populations (11/30) [45, 47, 55, 60, 62-66, 70, 72], and generated new ideas and direction for researchers and funders (11/30) [24, 46, 48, 50, 53, 56, 59, 61, 67, 68, 70]. Research produced with patients is also perceived to produce

outputs that are more accessible to patients (9/30) [24, 45, 48, 50, 56, 58, 62, 69, 70], was more reflective of the lived experience of illness, frailty, and/or treatment impacts (6/30) [24, 48, 53, 54, 67, 68]; facilitated democratization of the allocation of scarce funds (2/30) [48, 68], and increased transparency and accountability for public funds (1/30) [57].

Table 2.5 Impacts of Patient Engagement (N=30 studies)

Patient Level - Perceived Impacts	
Positive Impacts	Negative Impacts
11 (37%) Renewed sense of purpose/agency [7, 49, 56, 57, 62-65, 69-71]	
11 (37%) Emotional/peer support [7, 45, 49, 50, 57, 60, 62, 63, 65, 70, 71]	5 (17%) Emotional vulnerability or emotional distress [7, 55, 57, 69, 72]
10 (33%) Incorporation of patients' priorities for research and outcomes [7, 24, 50, 53, 58, 59, 61, 64, 66, 70]	
8 (27%) Develop new knowledge and skills [51, 52, 56, 57, 65, 70-72]	5 (17%) Physical/cognitive fatigue [7, 49, 55, 57, 69]
3 (10%) Acquire insights into disease and treatment [57, 62, 70]	
Researcher – Perceived Impacts	
Positive Impacts	Negative Impacts
17 (57%) Sensitizes researchers to experiential knowledge not gained at the bench or the bedside. Recognizing human experience [7, 48, 50, 51, 55-57, 60-66, 69-71]	
7 (23%) Challenges negative/ambiguous beliefs and perceptions of utility of patient partnerships [48, 51, 55, 59, 65, 71, 72]	
4 (13%) Increase interpersonal skills and highlighted significance of partnerships in research [51, 65, 70, 71]	
	15(50%) Investment and expenditure of time and resources [7, 24, 45, 47, 51, 52, 56, 58, 62-65, 69, 71, 72]
	2 (7%) Complexity/intensity of the process may serve as an impediment to meeting project timeline [7, 45]
Research Level - Perceived Impacts	
Positive Impacts	Negative Impacts
13 (43%) Improves/informs research design, execution, and translation [7, 45, 51, 55, 57, 58, 62-65, 70-72]	
13 (43%) Research tools (e.g., consent and data collection form), processes (e.g., recruitment and	

retention), and methods are more relevant [7, 45, 47, 50, 51, 56, 58, 63, 65, 69-72]	
11 (37%) Outcomes are identified as being more relevant to patients [45, 47, 55, 60, 62-66, 70, 72]	
11 (33%) Patients' input offers directions for researchers and research funding agencies – generation of new ideas [24, 46, 48, 50, 53, 56, 59, 61, 67, 68, 70]	
9 (30%) Research outputs are more accessible to the public [24, 45, 48, 50, 56, 58, 62, 69, 70]	
6 (20%) Research priorities ranked by patients reflect applicability to the lived experience of illness, frailty, and/or treatment [24, 48, 53, 54, 67, 68]	
2 (7%) Democratization of allocation of research resources [48, 68]	
1 (3%) Increased transparency and accountability for publicly-funded research [57]	

2.3.7 Study Quality

All 30 studies provided evidence of relevant sources of data appropriate for the research question and used a research design relevant to address the research question. Of the 20 qualitative studies (66%) in the review, most were rated as high quality using the MMAT [48-51, 55, 57, 60, 62, 63, 65, 66, 69, 72]. Seven (7/20) of the qualitative studies were rated moderately lower because it was difficult to determine whether interpretation of the results was sufficiently substantiated by data [24, 45, 56, 58, 64, 70, 71]. For the two quantitative studies (6.7%) [47, 59], there was a risk of nonresponse bias in both studies, particularly in one study where those deemed too ill were excluded from the opportunity to participate [59]. For the eight mixed methods studies (26.7%) [7, 46, 52-54, 61, 67, 68], five had risk of nonresponse bias [53, 54, 61, 67, 68] and three reported interpretation of the qualitative results that was not sufficiently substantiated by the data [46, 53, 67] (see Table 2.6).

Table 2.6 Quality Appraisal Results Using MMAT [39]

MMAT Items	Screening Questions		Methodological Quality Criteria														
			Qualitative Studies					Quantitative Studies					Mixed Methods				
	Are the data sources relevant to address the research question?	Is the process for analyzing data relevant to address research question?	Is the qualitative approach appropriate to answer the research question?	Are the qualitative data collection methods adequate to address the research question?	Are the findings adequately derived from the data?	Is the interpretation of results sufficiently substantiated by data?	Is there coherence between qualitative data sources, collection, analysis & interpretation?	Is the sampling strategy relevant to address the research question?	Is the sample representative of the target population?	Are the measurements appropriate	Is the risk of nonresponse bias low?	Is the statistical analysis appropriate to answer the research question??	Is there an adequate rationale for using mixed methods design to address research question?	Are the different components of the study effectively integrated to answer research q?	Are outputs of the integration of qual & quant components adequately interpreted?	Are divergences and inconsistencies between quant and qual results adequately addressed?	Do the different components of the study adhere to quality criteria of each tradition?
Qualitative Studies (n=20)																	
Absolom 2015 [56]	Y	Y	Y	Y	Y	CT	Y										
Bates 2018 [69]	Y	Y	Y	Y	Y	Y	Y										
Burns 2018 [66]	Y	Y	Y	Y	Y	Y	Y										
Caldon 2010 [70]	Y	Y	Y	Y	Y	CT	Y										
Collins 2015 [24]	Y	Y	Y	Y	CT	CT	Y										
Corner 2007 [48]	Y	Y	Y	Y	Y	Y	Y										
Cotterell 2011 [49]	Y	Y	Y	Y	Y	Y	Y										
Davis 2019 [64]	Y	Y	Y	Y	Y	CT	Y										
Froggatt 2015 [57]	Y	Y	Y	Y	Y	Y	Y										
Heaven 2016 [58]	Y	Y	Y	Y	Y	CT	Y										
Iwata 2019 [50]	Y	Y	Y	CT	Y	Y	Y										
Jorgensen 2018 [51]	Y	Y	Y	Y	Y	Y	Y										
Litherland 2018 [71]	Y	Y	Y	Y	Y	CT	Y										
Littlechild 2015 [65]	Y	Y	Y	Y	Y	Y	Y										
Parveen 2018 [45]	Y	Y	Y	Y	Y	CT	Y										
Piil 2019 [60]	Y	Y	Y	Y	Y	Y	Y										
Stevenson 2019 [62]	Y	Y	Y	Y	Y	Y	Y										

MMAT Items	Screening Questions		Methodological Quality Criteria														
			Qualitative Studies					Quantitative Studies					Mixed Methods				
	Are the data sources relevant to address the research question?	Is the process for analyzing data relevant to address research question?	Is the qualitative approach appropriate to answer the research question?	Are the qualitative data collection methods adequate to address the research question?	Are the findings adequately derived from the data?	Is the interpretation of results sufficiently substantiated by data?	Is there coherence between qualitative data sources, collection, analysis & interpretation?	Is the sampling strategy relevant to address the research question?	Is the sample representative of the target population?	Are the measurements appropriate	Is the risk of nonresponse bias low?	Is the statistical analysis appropriate to answer the research question??	Is there an adequate rationale for using mixed methods design to address research question?	Are the different components of the study effectively integrated to answer research q?	Are outputs of the integration of qual & quant components adequately interpreted?	Are divergences and inconsistencies between quant and qual results adequately addressed?	Do the different components of the study adhere to quality criteria of each tradition?
Tanner 2012 [63]	Y	Y	Y	Y	Y	Y	Y										
Wright 2006 [72]	Y	Y	Y	Y	Y	Y	Y										
Wright 2006 [55]	Y	Y	Y	Y	Y	Y	Y										
Quantitative Descriptive (n=2)																	
Arain 2015 [47]	Y	Y						Y	Y	Y	CT	Y					
Perkins 2008 [59]	Y	Y						Y	Y	Y	N	Y					
Mixed Methods (n=8)																	
Bethell 2018 [67]	Y	Y	Y	Y	Y	CT	Y	Y	Y	Y	CT	Y	Y	Y	Y	Y	CT
Bethell 2019 [68]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	CT	Y	Y	Y	Y	Y	Y
Chiu 2013 [7]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Jones 2017 [54]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	CT	Y	Y	Y	Y	Y	Y
Jorgensen 2018 [52]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Lechelt 2018 [53]	Y	Y	Y	Y	Y	CT	Y	Y	Y	Y	CT	Y	Y	Y	Y	Y	CT
Schölvinck 2019 [61]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Stephens 2015 [46]	Y	Y	Y	Y	Y	CT	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	CT

Y= Yes, N= No, CT= Can't tell

2.4 Discussion

The overall aim of this review was to synthesize the evidence on the engagement of frail and/or seriously ill patients as research partners across the research cycle. The 30 studies included in the review provide an indication of an upward trend in the inclusion of frail and/or seriously ill patients as partners in research over the past decade, with a marked increase in the number of studies in the past five years. Most studies included patients with cancer, with fewer studies partnered with patients who had dementia and/or frailty, or patients with palliative care needs. There was evidence of research partnerships with frail and/or seriously ill patients across the research cycle. These activities engaged patients on research related to setting priorities, selecting outcomes considered important to patients, grant review, tool development, research conduct, and dissemination of findings. These findings lead to the following three key points for discussion.

2.4.1 Barriers, Facilitators and Impacts to Engaging Frail and/or Seriously Ill Patient in Research

The barriers and facilitators to partnering with frail and/or seriously ill patients (e.g., funding, infrastructure, role clarity, capacity building for both patients and researchers, structural inclusivity, trust and willingness to collaborate) are similar to those reported in other systematic reviews of the engagement of non-frail and non-seriously ill patients [2, 12, 22, 28, 73-75]. When engaging frail and/or seriously ill patients as partners across the research cycle, the degree of illness and/or frailty, and potential instability in patients' health warrants more concern for wellbeing, but it should not serve to prevent initial or ongoing engagement [69]. Patients with high symptom burden and/or at end-of-life have expressed willingness and capacity for engagement in the development, conduct and dissemination of research [55, 59, 60, 69, 73, 74].

However, it is essential to confront researchers', clinicians and caregivers' concerns about over-burdening already frail and/or sick patients so that active and passive gatekeeping to engagement is minimized. Patients should be provided with the opportunity to accept or refuse opportunities to be engaged in research partnership in a manner that minimizes potential harm to them. The emphasis on how research partnership can and should be achieved is crucial in addressing the reservations that teams have in engaging frail and/or seriously ill patients beyond the level of consultation only.

Both patients and researchers should work to ensure clarity in patients' roles and their expected contribution throughout the study so that their input is not perceived as tokenistic [47, 50, 56]. Unintended symbolic or inauthentic gestures with frail and/or seriously ill patients assumes a greater level of magnitude, particularly when quality of life is already compromised or life-span may be limited. Providing flexibility in the timing and methods for frail and/or seriously ill patients to contribute to the research process is critical to enabling partnerships given fluctuations in health and/or cognition [49, 64, 71]. Research teams have discussed the need for flexibility by engaging different patients who are representative of the frail and/or seriously ill population at different points and for different tasks during the project, such as design and grant writing, tool development, peer interviews, and dissemination [7, 48, 56, 68]. Enabling partnership with frail and/or seriously ill patients requires research teams to pay extra attention to the care and comfort of their patient partners, (e.g., providing refreshments, assisting with the logistics of attending meetings, ensuring comfortable and quiet rooms, and regular touch points) [7, 45, 49, 50, 56, 63, 69, 71]. The need to provide practical and emotional support has also been recognized in recent scoping reviews of patient and caregiver engagement in dementia research and palliative care research [28, 74].

There is ongoing deliberation about the paucity of evaluation of patient engagement in research, especially the long-term impacts related to research implementation and ongoing use of research findings [12, 22, 74, 76]. Interestingly, no reports of negative impacts on the research itself were found in the studies included in this review, which may reflect a bias in over-reporting positive impacts of patient engagement, or may suggest that evaluation efforts are more focused on short and intermediate term impacts of partnering with patients [77]. Insufficient evaluation and poor reporting of the negative impacts of patient engagement are described elsewhere in the literature and point to lack of methods and rigorous evaluation tools [22, 78]. Without validated evaluation frameworks and consistent identification of both positive and negative outcomes, there is a risk that anecdotal accounts, and perceived barriers to partnership will dominate the discourse of engagement and undermine the successes [77, 79].

Given the population of focus, it was surprising to have identified few negative impacts on patients. Negative outcomes were primarily defined as potential depletion of physical and emotional resources, and the likelihood of experiencing emotional distress through reliving painful illness experiences, exposure to undesirable information, or experiencing the direct suffering of others [56, 69]. It is difficult to establish whether the limited number of negative impacts identified is due to lack of evaluation or lack of reporting [12, 22, 28]. However, while a limited number of negative impacts were cited, the possible magnitude of these impacts should not be under-estimated and every effort is required by research teams to mitigate these potentially deleterious impacts. Similarly, when examining the potential impact on researchers partnering with frail and/or seriously ill patients, it is interesting to note that researchers described exposure and sensitization to the lived experience of illness and suffering, yet failed to acknowledge the concomitant emotional labor and associated burden that invariably comes with

exposure to suffering [65, 80]. Issues of loss and grief are readily acknowledged for patient-partners following a decline in health or the death of others on the team [7]. However, it would appear that feelings of grief and loss, and the subsequent impact to emotional well-being, is not as readily acknowledged for researchers [80]. Failure to address these issues may leave many researchers ill-prepared to deal with emotionally demanding and difficult situations, cause unintended harm, and serve as a deterrent for both patients and researchers alike.

Evaluating the impact of partnering with frail and/or seriously ill patients is essential; limited evidence suggests that patients experienced several positive impacts, particularly when more intensive levels of engagement occurred. The potential emotional benefits described by patient partners (e.g., a renewed sense of purpose whilst coping with a disease over which they have little control, and/or the emotional support from peers on the research team) may in fact serve as a protective factor against emotional distress and vulnerability, and may also serve to quell researchers' hesitation in partnering with them [7, 45, 56, 69, 70].

2.4.2 Discontinuity of Contribution

Consistent and predictable contribution is an important consideration for teams embarking on a partnership with patients, more so for those involving frail and/or seriously ill patients on research teams. Concern for well-being is critical and is cited as a barrier to both initial and ongoing engagement. Discontinuity of contribution is a commonly anticipated barrier to engaging those most frail and/or ill (i.e., patients receiving palliative care, those with progressive dementia, or experiencing aggressive disease progression) [49, 63]. Patients' contribution will be lost or interrupted most often due to deterioration in their health or death, and it is incumbent on researchers to mitigate this. Paradoxically, discontinuity of contribution is rarely acknowledged when related to an improvement in condition, and yet, with advances in

treatment approaches, particularly within oncology, many serious illnesses beyond the acute treatment phase are now considered chronic conditions [81]. If the purpose of including frail and/or seriously ill patients as partners in research is to provide access to the lived experience of their illness and leverage that knowledge to shape the research that is produced, the concept of discontinuity of contribution needs to be expanded to include situations when patient partners move from serious illness into remission, cure, or survivorship. The transition from serious illness to a period of more stable illness undoubtedly shifts the perspective and lived experience of patients. As such, it may be argued that over time they become less able to speak to the immediate lived experience of serious illness and more acute suffering. As patients are invited to participate in all stages of the research process, it is important to ensure patients within various stages of the illness trajectory are provided with equal opportunity to partner in the very research that is intended to benefit them [82].

2.4.3 Weighing up the Costs of Partnership

There are moral, ethical, and practical reasons to engage frail and/or seriously ill patients as partners in research [83]; but researchers need to consider whether the impact or benefits of their engagement is warranted by the supplementary costs they will inevitably incur [77]. Facilitators for partnering with frail and/or seriously ill patients will invariably involve additional investments of time, money, and human resources to compensate for the accompanying administrative and emotional burden that research teams undertake in the endeavor [2, 28, 75]. Appropriate funding must be made available to teams dedicated to engaging frail and/or seriously ill patients as research partners, particularly when factoring in the need to address patients' emotional and physical needs throughout the course of engagement [7, 69]. Therefore,

it is necessary to optimize efforts at patient engagement to ensure expertise of patients who truly represent illness across the trajectory, particularly with regard to frailty and/or serious illness.

2.4.4 Strengths and Limitations

The diversity of nomenclature describing patient engagement combined with a deficiency of standardized reporting and lack of specific indexing may have resulted in some relevant studies being undetected [2, 15]. There are distinctions between what constitutes a "patient," "service user," or member of the "public," which pose additional methodological challenges for identification, recruitment and reporting [84]. Moreover, trajectories of disease progression, acute episodic exacerbation, and aggressive treatment regimens create challenges for defining frail and/or seriously ill patients [85]. To mitigate the challenges generated by issues of nomenclature and the potential fluidity of patients' condition, the search strategy was designed intentionally to be broad in order to cast a wide net for potentially relevant papers.

Further effort was taken to review the reference lists of the included studies and recently published reviews on patient engagement. To mitigate potential bias two independent reviewers were involved during study screening, data extraction, and critical appraisal. The reviewers met numerous times throughout the review process to discuss and remain consistent. All supporting files were reviewed, attention was paid to descriptors of patient condition, and associated published study protocols, where available, were traced and reviewed. Of particular relevance, one of the reviewers was a patient who was representative of being seriously ill, experiencing illness and high treatment burden at the time of the review. The second reviewer works in a direct clinical role with frail and vulnerable populations. Co-authors have clinical expertise in oncology, palliative care, frail elderly care, integrated knowledge translation, systematic review methods, and community based participatory research and were instrumental in further

addressing clinical and methodological issues during the review. There were few studies reporting on the engagement of frail and/or seriously ill patients. Hence, in the spirit of transparency and inclusion, none of the lower quality studies were excluded. Interestingly, quality issues in the quantitative studies were related to the potential for non-response bias whereby those deemed too ill were not engaged as research partners.

2.4.5 Conclusion

Engaging frail and/or seriously ill patients as research partners has offered research teams a unique insight into understanding what it is like to live with a debilitating and fragile condition to develop research that more accurately addresses their needs. This review provides limited, but promising evidence that it is possible to successfully engage frail and/or seriously ill patients as partners in research without causing them harm. However, researchers need to ensure the purpose of engagement is well-defined, the timing and methods of inclusion are flexible, and the practical and emotional needs of patient partners are addressed. This review also highlights the need for more rigorous reporting of patient characteristics alongside the experiences, benefits, harms and impacts of their engagement in order to build best practices for engaging this vulnerable population.

List of abbreviations

CINAHL: Cumulative Index to Nursing and Allied Health Literature

EMBASE: Excerpta Medica Database

IAP2: International Association of Public Participation

MEDLINE: Medical Literature Analysis and Retrieval System Online

MMAT: Mixed Methods Appraisal Tool

PCORI: Patient-Centered Outcomes Research Institute

PICOS: Population/participants, Interventions, Comparators, Outcomes, and Study designs

PRISMA-P: Preferred Reporting Items for Systematic Reviews and Meta-Analyses **Protocols**

PROSPERO: Prospective Register of Systematic Reviews

PsycINFO: Psychological Information Database

Declarations

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Consent for publication

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Authors' contributions

CL, DS, IDG and WG contributed to the conception of this review. All authors contributed to its design. CL led and coordinated the development and writing of the paper. IDG, DS, JL, and WG participated throughout the development and writing of the review by contributing intellectual content and feedback on drafts of the manuscript. All authors read and approved the final manuscript.

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Authors' Information

CL is a PhD Candidate in Nursing, Faculty Health Sciences at University of Ottawa. Her research interests are focused on integrated knowledge translation and how frail and/or seriously ill patients are engaged as knowledge users in research. The objectives and rationale for this review were initially conceived when she was a patient partner in a research study during a period of serious illness and acute treatment for a life-limiting disease. She was involved in all aspects of this review and has been active in dissemination of the preliminary findings.

IDG is Senior Scientist in the Clinical Epidemiology Program of the Ottawa Hospital Research Institute and Professor in the School of Epidemiology and Public Health at University of Ottawa. His extensive research focuses on knowledge translation and conducting applied research on strategies to increase implementation of research findings.

WG is Associate Professor at the University of Ottawa School of Nursing and Co-Director of the Centre for Research on Health and Nursing. Her program of research focuses on

leadership and knowledge mobilization/translation to improve health care delivery and patient outcomes, and includes working with Indigenous communities in Canada.

JL is a Clinical Social Worker in Geriatric Psychiatry at the Royal Ottawa Mental Health Centre. Her practice is dedicated to working with the frail elderly population who have concurrent mental health issues. She is a strong advocate for inclusivity and equity of access to health and social care for vulnerable populations.

DS is Professor in the School of Nursing at the University of Ottawa and Senior Scientist at the Ottawa Hospital Research Institute, and currently holds a University Research Chair in Knowledge Translation to Patients. Her substantial research is focused on advancing the science of knowledge translation to patients and enhancing patient engagement in shared decision making.

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Table Legends

Figure Legends

Supplementary Files

CHAPTER 3: Ethical Considerations for Engaging Frail and Seriously Ill Patients as Partners in Research: Sub-analysis of a Systematic Review

Authors:

Claire Ludwig

Ian D. Graham

Josee Lavoie

Wendy Gifford

Dawn Stacey

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Plain English Summary

There are ethical, political and moral reasons to engage patients as partners in research; with evidence to suggest that research produced with patients is more relevant and responsive to their needs. Barriers to engaging patients in research have focused on practical issues but researchers feel poorly prepared to deal with the ethical issues of partnering with patients, particularly those who are frailer and sicker. The aim of this study was to identify ethical considerations related to engaging frail and seriously ill (FSI) patients as partners in research. We conducted a sub-analysis of a recent systematic review of 30 studies that engaged FSI patients as partners in research. Of 30 studies, 25 reported on ethical issues. To enhance autonomy (act independently), common themes were helping patients choose desired level of involvement, addressing power issues, and increasing knowledge and understanding of research. For non-maleficence (cause no harm), common themes were protecting patient-partners from financial burden, physical suffering, and emotional suffering. Beneficence (do good) included putting things right for others, showing value-added, and supporting patient-partners. To enhance justice, three themes were achieving appropriate representation (including across the illness trajectory), mutual respect for contributions, and avoiding over-reliance on individual patients/patient groups or relying on others to speak for FSI patients. When partnering with FSI patients, researchers should ensure processes are in place to identify and address ethical issues. Researchers and patients should work together to clarify intent of the partnership, recognize and minimize the potential for unintended harm, and maximize the benefits of partnership.

Abstract

Background: The commitment to engage patients as partners in research has been described as a political, moral and ethical imperative. Researchers feel ill-equipped to deal with potential ethical implications of engaging patients as partners. The aim of this study is to identify the ethical considerations related to engaging frail and seriously ill (FSI) patients as partners in research.

Methods: We conducted a sub-analysis of a prior systematic review of 30 studies that engaged FSI patients as partners in research. Studies were included if they reported ethical considerations associated with partnering. We performed deductive content analysis, data were categorized according to Beauchamp and Childress' Principles of Biomedical Ethics (2019): autonomy, non-maleficence, beneficence, and justice.

Results: 25 studies were included. Common ethical considerations reported in relation to the principles were: *autonomy* – promoting desired level of involvement, addressing relational and intellectual power, facilitating knowledge and understanding of research; *non-maleficence* – protection from financial burden, physical and emotional suffering; *beneficence* – putting things right for others, showing value-added, and supporting patient-partners; and, *justice* – achieving appropriate representation, mutual respect for contributions, and distributing risks and benefits.

Conclusions: When partnering with FSI patients, research teams need to establish shared values and ensure processes are in place to identify and address ethical issues. Researchers and patients should work together to clarify the intent and outcomes of the partnership, actively address power differentials, recognize and minimize the potential for unintended harm, and strive to maximize the benefits of partnership.

Systematic review registration: The protocol for the original systematic review has been registered with the International Prospective Register of Systematic Reviews PROSPERO (CRD42019127994)

Keywords: Patient engagement, public and patient involvement, integrated knowledge translation, ethics, research co-production, patient-partners.

Key Points for Decision Makers

There is mounting pressure on researchers to meaningfully engage patients across the research lifecycle. In spite of increasing evidence on the practical considerations for patient engagement, researchers report feeling ill-equipped to identify and deal with the ethical implications of more intensive and prolonged engagement – particularly with those patients who are frailer and sicker.

This sub-analysis of a prior systematic review identified the ethical considerations of partnering with frail and seriously ill patients in research. Researchers and patients should ensure there are mechanisms in place to identify and pro-actively address ethical issues throughout the course of their partnership. Due consideration must be afforded to mitigating inadvertent harms, maximizing personal benefits to patient-partners, and recognizing and responding to diminished or impaired autonomy so that patients can negotiate their role in the partnership.

3.1 Introduction

Patient engagement in research has been promoted as a political, moral and ethical imperative. It is defined as "the active, meaningful, and collaborative interaction between patients and researchers across all stages of the research process, where research decision making is guided by patients' contributions as partners, recognizing their specific experiences, values, and expertise" [1p.682]. The practice of patient engagement is driven largely by two overarching justifications [2]. First, it provides a morally acceptable means to an end, with evidence suggesting that it increases the quality and relevance of the research through the incorporation of patients' unique insights into living with a disease or condition. Second, it is a morally acceptable end in itself, because it is perceived to embed the values and preferences of the community and increase transparency and accountability for the research that is produced [2]. Engaging patients as partners in health research is considered "essential to the ethical foundation of research practice and evidence-based medicine because it ensures that those who have the most important stake in health research will play a significant role in knowledge creation and translation" [3, p.63].

The relevance-based rationale of engaging patients as research partners supports the ethical principle of beneficence, appealing to a focus on the greater good by promoting better patient outcomes [4, 5]. The rationale of promoting transparency and public accountability in research draws on democratic theory and greater citizen involvement, thereby countering medical paternalism and the dominance of 'expert knowledge' [4, 6]. Representation and inclusivity function as central tenets of public and patient engagement and are increasingly built into standards to guide practice [7]. Given democratic and relevance-based rationales, patient

engagement is now commonly incorporated into the eligibility requirements for receipt of government-funded health research [8, 9].

The growing emphasis on more meaningful and inclusive engagement of patients as partners in research has led to recent reports from researchers who describe feeling ill-equipped to deal with the potential associated ethical concerns [10, 11]. An investigation of early career researchers' views of patient engagement identified ethical concerns related to: 1) professionalization of patients involved in research (with risks of patients becoming less diverse); 2) adequate remuneration of patients; 3) fair recognition of patients' experiential knowledge; and 4) tokenism (engaging patients only for symbolic appeal) [10]. In the absence of clear ethical standards to guide the process and to identify and resolve ethical issues as they emerge, current efforts aimed at engaging patients as partners in research run the risk of unintentional harm to those patients involved, particularly those deemed more vulnerable [10-12]. A recent systematic review examining the practical issues and impacts of engaging frail and/or seriously ill (FSI) patients as partners in research established that the vulnerability and frailty of certain patient groups (e.g., frail elderly, patients with high symptom burden from disease/and or treatment, patients with dementia, palliative patients) provides additional complexity to partnering across the research cycle [13]. The practical issues associated with engaging FSI patient-partners may heighten perceived ethical concerns and deter research teams from partnering with them.

Aim

The aim of this study is to identify the ethical considerations related to engaging frail and seriously ill patients as partners in research.

3.1.1 Guiding Ethical Framework

Given the complexities of competing ethical positions and definitions, Beauchamp and Childress' principles were utilized as the guiding ethical framework [14]. The framework consists of four broad principles: respect for autonomy, non-maleficence, beneficence, and justice [15]. The principles-based approach suggests a universalizable set of principles for bioethical discourse and is flexible to accommodate local values and practices [16]. It is important to note that primacy is not afforded to any one principle [15].

According to Beauchamp and Childress [15] *respect for autonomy* acknowledges the right for individuals to hold views, make choices, and take actions based on their beliefs and actions. It also means granting individuals the right to privacy and confidentiality. It contains both negative and positive obligations. A positive obligation requires disclosure of information and other factors that allow individuals to make autonomous decisions, (e.g., clinicians and researchers disclose all relevant information to allow the patient-partner to achieve their desired level of involvement). A negative obligation requires that autonomous actions should not be constrained by others and diminish a person's ability to exercise autonomy (e.g., a patient-partner should not be fearful of alienating a clinician who is providing their treatment(s) and who is an investigator on the study). *Non-maleficence* asserts an obligation to abstain from causing harm to others (e.g., efforts are made to avoid physically or emotionally overburdening patient-partners). *Beneficence* asserts that one must make a positive move to produce some good or benefit for another (e.g., emotional support from the research team may serve as a tangible benefit for patient-partners). *Justice* is based on the notion of fairness and equity. Fairness entails treating all people with equal respect and concern. Equity requires distributing the benefits and burdens of research participation in such a way that no segment of the population is unduly

burdened by the harms of research or denied the benefits of the knowledge generated from it (e.g., ensuring appropriate inclusion of diverse patient populations).

The contribution of patients engaged as partners in research (i.e., doing research with) differs significantly from that of a research participant where one is the subject of the study. Patient engagement varies in intensity and takes many different forms e.g., focus groups, surveys, participation in research meetings, membership on advisory boards, and contribution to dissemination activities [17]. Patient engagement also occurs along a continuum, ranging from less intensive engagement (informing or consulting) to more intensive engagement (involving, collaborating, empowering) which is more indicative of partnership [18]. When partnership occurs, there is a shift from researcher as sole expert to one where researchers and patients are both experts, working together to solve problems and co-generate knowledge [19].

3.2 Methods

The systematic review methods were described in detail in the original study and in PROSPERO (CRD42019127994). In summary, a search was conducted of the MEDLINE®, EMBASE®, CINAHL, and PsycINFO databases from journal inception to April 2019. Key words were combined with medical subject headings (MeSH) terms related to "patient engagement", "patient involvement", "patient-oriented research", "integrated knowledge translation," etc. Two authors (CL, JL) independently reviewed abstracts and full-text articles, extracted data from included articles and conducted quality appraisal of each study (i.e., qualitative, quantitative, and mixed methods). The authors have an appreciation of the ethical issues of partnering with frail and seriously ill patients from lived experience (CL) and clinical practice (JL).

For this sub-analysis, eligible studies from the original review (N=30 studies) had to report on ethical considerations associated with engaging FSI patient-partners in research. Two authors (CL, JL) identified this subset of studies from the original review. Discrepancies were resolved through discussion. Any data relevant to the biomedical ethical framework was extracted from the methods and results sections of included studies.

Two authors independently analyzed all data using deductive content analysis [20, 21]. Content analysis was used to identify themes by: reviewing the texts from included studies, creating themes from the text, and establishing consensus [20]. Themes were then organized under the four principles in the biomedical ethical framework of Beauchamp and Childress: respect for autonomy, non-maleficence, beneficence, and justice [15]. Results were audited by a third author (DS), who has considerable experience of research partnerships with frail and seriously ill patients; discrepancies were resolved through discussion.

3.3 Results

Of the 30 studies in the original systematic review, 25 reported on ethical issues of FSI patient-partners [22-46] (see Table 3.1 for exemplars).

3.3.1 Respect for Autonomy

Six themes were identified under the principle of respect for the autonomy of patients as research partners in 24 (96%) studies [22-45] (see Table 3.1). Researchers were instrumental in *promoting the desired level of involvement* of the patient-partners [22, 25, 27, 29, 30, 32-34, 36-38] by extending them the courtesy of contributing to the research study according to their willingness and ability [38]. Roles and activities were tailored to the availability, time, and interests of patient-partners [22, 25, 30, 33], with opportunities provided for greater responsibility as they gained confidence and expertise [32, 36]. The need for researchers to be

flexible and responsive to changes in patient-partners' condition was a key facilitator to respecting the autonomy of FSI patient-partners [34, 37] and ensured that patient-partners continued to make informed, non-coerced decisions to initiate or remain partnered in the study [27] including the ability to withdraw effortlessly at any given time [29].

Another theme was *addressing relational and intellectual power* [22, 25-27, 33, 34, 37, 43, 44]. Practical strategies to address relational power differentials included identifying potential patient-partners through a neutral party [27] and external facilitation of meetings to ensure that patient-partners were comfortable to share opinions without influence [26, 34, 37, 43]. One study reported financial compensation may serve as a threat to autonomy because of the potential to shift the perspective of patient-partners, asserting subtle pressure to commit more time on the research project [26]. For intellectual power, sensitivity in the use of complex clinical and academic language is required as it may impede understanding [22, 25, 33, 37, 44] and reinforce power differentials as described in a study where patients with cancer were speaking from a subjective and experiential standpoint in a research environment where objectivity was the accepted mode of working [25].

Facilitating knowledge and understanding of research through access to training and education about the research role, research methods and approaches was the third most common theme for autonomy [26, 28, 30-36]. In a dementia study, the academic leads reported a desire to directly support patient partners in applying their own skills and ideas [36].

Respect for autonomy was reported in relation to *ensuring intentional engagement* with transparency in the purpose and expected outcomes of the partnership [22-27, 29]. Studies reported that patient-partners find it difficult to effectively integrate into project activities when their role and purpose lacks clarity [22, 24, 25, 27]. This sometimes required reinforcing the

distinction between patients' roles as research partners versus participants providing data [27]. Written information provided upfront was described as allowing patients to enter into the research partnership in an intentional manner [22].

Guarding against disclosure of health and other personal information was another key theme for respecting autonomy [26-29, 36, 37, 45]. Some studies in which patient-partners had a role in conducting research involving direct contact with study participants reported patient-partners had a tendency to disclose personal information to participants diagnosed with cancer [28, 29, 45], impaired cognition, or dementia [36, 37]. Non-verbal disclosure of markedly fragile health status was described in a study where a patient with advanced cancer served as a peer interviewer [45]. Disclosure of personal and potentially sensitive financial information in a group setting striving for consensus on payment of patient-partners was further described as potentially problematic [26].

Recognizing and responding to diminishing and impaired autonomy due to deterioration in physical health or cognitive decline was described in studies where FSI patients were partnered in palliative care research [39], dementia research [36, 37, 40], frailty research [41], and cancer studies [42]. Efforts to protect those at highest risk of loss of autonomy included measures such as having clinicians involved in the study familiar with the needs of patients receiving palliative care [39] or ensuring academic researchers were comfortable working with patient-partners with dementia [37]. Initial and ongoing formal consent mechanisms were reported in some studies not only for study participants but for FSI patient-partners [36, 41]. Emerging or severe health and cognition issues were reported as a factor in withdrawal or initial exclusion from the research partnership [40, 42].

3.3.2 Non-maleficence

Of 25 included studies, 20 (80%) reported ethical considerations related to non-maleficence with four themes focused on protecting patient-partners from financial hardship, physical suffering, emotional suffering, and guarding against causing offence [22, 23, 25, 26, 28-30, 32-39, 41, 43-46] (see Table 3.1). A common theme was *protection from financial burden* by being a research partner [22, 26, 28, 30, 33, 35, 37, 39, 41, 43, 46]. Efforts to protect patient-partners from negative financial impacts were described as a need to ensure the partnership was cost-neutral for patients with all out-of-pocket expenses compensated (e.g., travel and parking) [33, 35, 37, 39, 46]. Honorariums were provided in some studies to compensate for patient-partners' contribution, including time spent preparing for meetings, reviewing documentation, and training [30, 33, 43]. The need to address patients' individual circumstances was reported to ensure some patient-partners were not inadvertently disadvantaged more than others, particularly where costs for support were higher [26], e.g. reimbursement costs for caregivers who were required to escort patient-partners due to physical and cognitive impairments [41]. Costs for out-of-town events (e.g., hotel accommodation) were higher for FSI patient-partners when requiring additional time for rest and recovery [28, 43].

Studies reported the need to *protect FSI patient-partners from physical suffering* [22, 25, 28, 29, 32, 34, 37-39, 43, 44]. Researchers described addressing potential physical discomfort by anticipating and planning activities in accordance with patient-partners' needs for comfort and accessibility in meeting spaces [34, 37-39] and ensuring activities did not place additional burden on those who were fatigued through illness or treatment [39, 43]. One study reported a pre-arranged signal, such as the raising of a hand, for patient-partners to use when they were fatigued or unable to continue in co-facilitating focus groups [29]. Studies stressed the need for

researchers to be able to respond to those with rapidly deteriorating health conditions and to ensure that the practical and physical demands did not exceed the capacity of patient-partners [25, 32, 44].

Non-maleficence also required *protecting patient-partners from emotional suffering* [23, 25, 28, 29, 32, 37, 43]. Studies described the potential emotional impact of patient-partners learning about poor prognoses or unsuccessful treatment outcomes related to their own condition and further stressed the responsibility of researchers to be mindful of how information is presented [23]. Formal debriefing mechanisms were identified as a way to respond to emotional distress, particularly when patient partners had progressive and/or palliative illnesses [25, 29, 37, 43]. One study described the need to ensure that patient-partners were safeguarded from overly bureaucratic attitudes and expressions of powerlessness sometimes expressed by clinicians and researchers [23].

The moral *obligation to guard against causing offence* to patient-partners was reported in two studies [23, 37]. Lack of awareness of certain conditions and lack of confidence in dealing with illness was described as contributing to researchers' fears of not responding appropriately or potentially offending patients on the research team [37]. Guarding against contributing to a perceived lack of worth or feeling used was reported as essential in mitigating offence to patient-partners, particularly when referred to as the "usual suspects" [23].

3.3.3 Beneficence

Four themes were identified in 14 (56%) studies under the principle of beneficence and a positive obligation to produce some benefit or good for patient-partners [22-28, 34-39, 43] (see Table 3.1). Patient-partners described wanting to channel their own experiences with illness and/or with the health system into *putting things right* [22, 23, 25, 26, 34, 35, 43], therefore

researchers need to create the conditions to facilitate this occurring. In the face of progressive and debilitating illness, patient-partners described the desire to create something innovative, contribute to new treatments or programs [22, 23], improve existing services [35], and influence positive changes for future generations of patients [43].

Another common subtheme was *demonstrating value-added* of including FSI patient-partners [24-27, 34, 35, 37]. Studies reported having mechanisms for patients to be able to see the positive results of their input, know that their voices mattered, and feel that their work had meaningfully contributed [24, 25, 34]. It was important for patients and researchers to maintain a connection to the lived experience of patients so that tangible positive changes were seen in research processes and patient outcomes [26, 37]. Studies further reported that patients' input added authority to the findings and generated new insights into the findings [27, 35].

Providing support to patient-partners is another theme indicating beneficence [23, 25, 27, 28, 34-39]. FSI patient-partners described great benefits from the supportive relationships that evolved within the group [23, 35], with support sometimes extending beyond the life of the study [38, 39] . The power of peer support within one research group was described as offering a transformative function by empowering patient-partners to embrace an identity that was positively associated with living with dementia and use it in their interactions with others [36].

Feeling supported was a theme related to beneficence that extended to study participants who described an emotional connection with patient-partners conducting research [35]. The emotional connection between patient-partners and participants was further described as providing a sense of safety leading to more candid responses from participants during the interview process [36].

The final theme under the principle of beneficence for FSI patient-partners was *nurturing opportunities for patient-partners to be able to obtain supplementary personal benefits.* These additional benefits were described as restorative by providing patient-partners with new roles, increasing confidence and providing opportunities to learn about research and condition-specific treatments and programs [25, 27, 34, 35, 37].

3.3.4 Justice

There were three themes about justice reported in 20 (80%) studies [22-24, 26-38, 42, 43, 45, 46] (see Table 3.1). The most common theme was seeking diverse *representation* among the patient-partners (e.g., gender, age, ethnicity) [26-28, 30, 32, 33, 35, 38, 46]. The need for greater diversity was also reported in relation to socioeconomic status [34, 46] and geography [33]. To achieve diverse representation, studies reported the need to broaden the identification of patient partners through community groups rather than rely on current approaches through treatment centres and support groups [29, 33, 46]. Other disease-specific considerations included different tumour types [26, 28, 30], and patient-partners who were able to represent different stages and severity of illness/disease/condition [27, 28, 33, 40, 46]. A number of studies conflated the experience of frail and/or seriously ill patient-partners with those who are more well (e.g., those with chronic conditions, ex-patients/survivors), members of the public, and caregivers [22, 26, 28, 30, 32-35, 37, 38, 42, 43, 45, 46].

Another theme relevant to justice was ensure *mutual respect for contributions* to the research [22-24, 29, 31, 32, 35] that was described as not expecting patient-partners' contributions to become over-professionalized [26]. Other studies reported the need to actively address issues of equity within the team [34, 36, 38].

The final theme under justice was *distributing risks and benefits* [22, 34, 35, 38]. Researchers described relying on FSI patient-partners, with whom they had existing relationships, across multiple studies [22, 34, 35, 38] and acknowledged that over-reliance had the potential to place undue burden for research partnerships on individual patients or advisory groups. This practice excluded others from opportunities to contribute to the research produced and the benefits of the partnering process.

Table 3.1 Ethical Principles and Themes

Ethical principles & themes	Evidence of ethical considerations reported in studies (exemplars from text)	Frequency (N=25 studies)
Autonomy		24 (96%)
Promoting desired level of involvement	- shaping what each person was able and willing to contribute… according to his or her needs and wishes [38] - opportunity to make an informed, non-pressurized decision about whether they would like to be part [27]	11 (44%)
Addressing relational and intellectual power	- group with the co-researchers was facilitated by a staff member, external to the project, as we were concerned that the co-researchers would otherwise avoid potential critical comments [26] - patients (patient-partners) … indicated they felt disadvantaged by their lack of understanding of the complex medical issue [44]	9 (36%)
Facilitating knowledge and understanding of research	- (Patient-partners) received training and support to co-facilitate the focus groups … initial training provided a background to general research methods, specific training on focus group approaches and a discussion on the focus group question schedule [28] - Preparation sessions were held with the co-researchers to orientate them to the study, engage their views about the interview content and structure, and enable them to practice interviewing skills [36]	9 (36%)
Ensuring intentional engagement	- Researchers need to be reflective and transparent about the desired outcomes of their projects and the role of the co-researchers in reaching those outcomes, but also acknowledge… the possibility that initial plans may change [26] - Ensuring that users with dementia are not misled about the nature of their role in the research process [27]	7 (28%)
Guarding against disclosing health and other personal information	- Disclosure of own health cognitive status in an effort to connect with interviewees – publicly affirming their dementia [37] - People's financial situation is a potentially personal and sensitive issue [26]	7 (28%)
Recognizing and responding to diminishing and impaired autonomy	- cognitive and communication difficulties associated with dementia would have precluded some persons with dementia from taking part, especially those with late-stage dementia [40] - For both co-researchers and participants, we adopted a process model of consent, monitoring and reviewing consent within the	6 (24%)

Ethical principles & themes	Evidence of ethical considerations reported in studies (exemplars from text)	Frequency (N=25 studies)
	context of the research relationship and across the duration of the project [36]	
Non-maleficence		20 (80%)
Protecting from financial burden	- …making it cost-free for people to participate, but also considering people's individual situation [26] - Assistance with travel arrangements was offered, including for an accompanying person for older adults [40]	11 (40%)
Protecting from physical suffering	- Through a shared code between the co-researcher and the experienced researcher (such as the raising of a hand), the co-researcher could indicate when they were fatigued or felt unable to continue with moderating the discussion [29] - meetings should be carefully planned with reference to degree of physical frailty and/or anticipated fluctuations in physical status of co-researchers [39]	11 (40%)
Protecting from emotional suffering	- For some, this direct contact with professionals proved a challenge, perhaps in terms of hearing negative information about one's own cancer type and potential prognosis, or in the understandable personal emphasis placed on what is discussed in meetings with professionals [23] - emotional cost could be ongoing in terms of revisiting personal experiences through the studies engaged with and then more acutely with a reoccurrence. When this happened individuals often had to withdraw …, as happened for two participants [25]	7 (28%)
Guarding against causing offence	- (patient-partners) were sometimes referred to as professional users or the usual suspects. Having responded to the request to become involved, there was some confusion and annoyance at the use of these divisive terms… being undervalued left some service users feeling undermined and used [23]	2 (8%)
Beneficence		14 (56%)
Creating conditions for putting things right for others	- "I am more than willing to put effort into a project if it may benefit my daughter and future generations" [43] - to change things for the better, to be part of shaping new, and more appropriate treatment for others going through a similar experience [23]	7 (28%)
Showing value-added	- Need to demonstrate the value-added nature of its (patient partnership) impact on research processes and outcomes [24] - creation of a feedback loop allowed the patient advisors to understand that their work has meaning and their voices mattered [34]	7 (28%)
Providing support	- one (patient) was admitted to hospital towards the end of the data collection period and later died… a bereavement visit (was conducted) after death by clinician involved in the project [39] - Participants could be open about their difficulties as the (patient-partner) interviewer was seen as someone who understood and shared their problems [36]	6 (24%)
Nurturing opportunities for supplementary benefits	- Being involved has been restorative; it's given people a role, a job, and a community of interest [37] - providing benefits for the person with dementia including opportunity to exercise skills and abilities [27]	5 (20%)
Justice		20 (80%)

Ethical principles & themes	Evidence of ethical considerations reported in studies (exemplars from text)	Frequency (N=25 studies)
Seeking diverse representation	- diverse backgrounds in terms of gender, ethnicity, tumour site and their connection to cancer (patients, carers and others with specific interest in cancer research) [30] - better educated or already engaged in other community efforts, which likely influence their experience and biases [34]	16 (64%)
Ensuring mutual respect for contributions	- respect, reciprocity, and mutual benefit, the essence of collaboration is a vested interest and gain for both parties [43] - There was a perception that participants, and their groups, were peripheral to core activities and priorities [23]	12 (48%)
Distributing risks and benefits	- Same volunteers across multiple projects …may overburden some [22] - Overutilization of willing partners in other studies [38]	4 (16%)

3.4 Discussion

The overall aim of our review was to identify ethical considerations related to engaging FSI patients as partners in research. The 25 studies included in this sub-analysis of the larger systematic review provided insight into the ethical challenges facing research teams in partnering with potentially more vulnerable patients, particularly as related to respect for autonomy, non-maleficence, beneficence, and justice. Our findings lead to the following points for discussion.

The nature of complex disease, ageing processes, and aggressive treatment regimens have the potential to be a greater threat to autonomy for FSI patient-partners. Intentional and informed actions assume particular significance in terms of quality of life for patients suffering with disease and/or treatment related symptoms, living with a life-limiting illness, or those dealing with failing cognition. Intentional actions require forethought and knowledge about the series of events that will unfold in the execution of the research study [15]. It is imperative that research teams consider the purpose of partnering with patients, roles, anticipated outcomes (beneficial/harmful), and how these may evolve during the course of the study [26].

Understanding is key for autonomous action [15]. Severity of illness and impaired cognition may inhibit an individual's full understanding and requires serious consideration

during a research partnership. Given bioethical frameworks and practices most familiar to health researchers, the paradigm of informed consent has been more formally recognized by some research teams partnering with those with dementia; whereby, standardized processes for informed consent for patient-partners (similar to that utilized for research participants) have been adopted [36, 47, 48]. Protection of those with developing, impaired or diminished autonomy is a moral obligation for researchers [49] but research partnerships require an approach more analogous to negotiation in order to determine a patient's initial and ongoing ability and agreement to partner in research.. For patient-partners with diminished capacity, a process must be in place to ensure the patient appreciates the extent of their role in the research partnership. Decisions about whether a patient-partner possesses adequate understanding to continue to contribute to the study should be shared between the patient-partner and the principal investigator, thereby allowing the patient-partner to maintain their autonomy whilst ensuring the researcher fulfills their obligation to protect the patient's well-being.

The potential disparity in relational and intellectual power between the researcher and patient is a significant threat to patient-partner autonomy. Researchers should be particularly mindful of the subtle influences of relational power, especially when selecting their own patients to be patient-partners [50]. Relational power differences may be experienced more acutely by FSI patient-partners who are suffering loss of self-esteem related to illness, loss of function, or altered perception of self; all of which may make them less inclined to share negative experiences so as to preserve the caring relationship with their clinician on the research team [43, 51]. Differences in relational power may potentially silence less confident patients and inhibit their capacity to challenge the 'professional' voices around the table [52]. Strategies to reduce relational power differentials and promote participation include providing networking

opportunities outside of the study and having meetings facilitated by staff external to the core project team [26].There is also the risk that some patients may expect to receive preferential treatment if they agree to become project partners, given their direct access to their clinician [51].

Partnering with patients in research has brought new challenges to regulations governing confidentiality and control of information. Disclosure of a patient-partners' personal information, including diagnoses, to broader audiences during all phases of the research process provides additional challenges related to confidentiality [53]. Patient-partners may not be comfortable publicly disclosing personal details such as those related to their health, financial status, or sexual orientation. Discussions regarding compensation should be made at the level of the individual patient-partners, rather than during group discussion where they may feel uncomfortable to explicitly discuss their preference or go against a consensus decision [26]. Communication of life-limiting illness may also be a very sensitive issue and all parties should be aware of the power of non-verbal cues in signifying severity or advanced stage of illness [45].

There is a propensity to speak to positive impacts rather than the negative impacts of partnering with patients in research [17, 54, 55]. In principle, partnering should be something that is beneficial, or of value to others, and is critical to ethical practice involving patient-partners, but researchers must balance this against potential harms to their patient-partners. Partnering with FSI patients brings additional complexity to this moral obligation. Patients have spoken about the emotional demands of research engagement, particularly during times where they are experiencing treatment effects, exacerbation of illness, or symptoms of disease progression [25]. The impact of finding out about the shortcomings of certain treatments or disappointing results from a clinical trial need to be considered, especially when patient-partners

are receiving the same treatment [56]. Dismissive comments from members of the research team about inefficient clinical or bureaucratic processes, or expressions about the competency of colleagues can be potentially upsetting for patient-partners [23].

The lack of diversity among patients partnering in research raises justice-related concerns [4]. Equitable inclusion necessitates attention to diversity in socio-economic, gender and ethnic representation [57, 58]. Partnering with patients who are reflective of the diversity of the larger patient population ensures that research teams are not systematically excluding certain subgroups of patients from having the opportunity to influence research [4]. Ensuring patient-partners are reflective of the broader patient population must also extend to patients who are FSI, such as those with dementia or palliative diseases, or those undergoing acute treatment, who have typically been excluded [13, 29, 59, 60]. The intersection between frailty, serious illness and social determinants of health (e.g., race, socioeconomic status, sexual and gender orientation) demands further critical consideration. The question of "who" are patient-partners has important consequences for which perspectives inform research [61] and raises questions about the rationale and ethical foundation of partnering with patients in research .

Adequate representation requires the inclusion of those who possess the embodied knowledge of having an illness oneself [62]. Yet, there is a tendency towards the conflation of FSI patients with other stakeholders (e.g., patients no longer in receipt of active treatment, caregivers, community or advocacy group members) in the reporting of impact and outcomes of partnering with patients [13]. Policies and guidelines for inclusion of patient-partners compound this issue. The term 'patient' is considered an all-encompassing and inclusive label to include those with lived experience of a health concern, as well as caregivers, family members, friends and members of the public [19]. We argue that this definition is fundamentally problematic and a

threat to the principle of justice. Conflation of distinct and potentially competing perspectives into the singular term 'patient' would appear to be an inherent contradiction of the underlying justification for patient partnerships in research.

There is some evidence that the use of patient advisory groups has assisted in circumventing some of the potential barriers to partnering with FSI patients [22, 24, 30, 33]. While this offers researchers ease and convenience, there is also a risk in over-reliance on such groups [61]. Although caregivers and patient advocacy groups are increasingly called upon as a proxy, arguably they do not fully reflect the range of the patients' experience, particularly towards end-of-life or during periods of acute illness and/or treatment [63]. Patients' views shift across the trajectory of illness; lived experience is vastly different following curative treatment for a life-threatening illness, or following stabilization of an acute episodic phase of a chronic condition; the earlier phases of dementia look markedly different than the advanced stages; and approaching death versus a focus on cure or living with a chronic disease brings significantly divergent priorities [27, 64-67]. Additionally, caregivers have their own lived experience of illness, one that is informed by the embodiment of illness in those they are caring for, but also one that is shaped by their caregiving role. The fusion of the patient and caregiver voice as a singular unit is especially problematic given the unique roles that caregivers play, particularly as their loved ones become frailer and sicker [68, 69].

The tendency to unify voices for the sake of expediency does a huge disservice to patients, caregivers and the research community alike, particularly when it comes to distributing the benefits and risks of research. By continuing to privilege the voices of those who speak by proxy, we fail in our efforts to develop and adhere to appropriate ethical guidelines for researchers partnering with FSI patients. We not only fail in meeting the threshold to uphold the

principle of justice but also in upholding principles of autonomy, non-maleficence and beneficence. In considering who should speak to the patient experience, it is imperative that researchers consider the goals of the research partnership both in the context of the overall study and with regard to specific activities across the research cycle [70].

There is clearly a need to establish robust ethical standards when partnering with patients in research and to better support researchers in identifying and addressing ethical issues. Our findings further highlight ethical considerations specific to partnering with patients who are FSI. Using an established conceptual framework, such as Beauchamp and Childress' Bioethical Principles, provides a lens through which to frame the partnership and protect the well-being of vulnerable patient-partners. Researchers and patient-partners can work together to identify and mitigate ethical concerns by: co-defining the purpose and benefits of the partnership, establishing trust and understanding, knowing others' roles, respecting the right to privacy, creating a safe participatory space, addressing power imbalances within the team and decision-making processes, ensuring participation is revisited and re-negotiated with changes in health or interest, and recognizing contributions (including financial recognition) [10, 13]. Finally, as we build the evidence for ethical practice, it is imperative the process of establishing patients as partners is transparent and we are able to rigorously evaluate the partnership using validated tools, e.g., GRIPP2 [55].

3.5 Limitations and Strengths

Contrary to the practical challenges of research conducted with FSI patient-partners, the ethical implications of partnering with FSI were rarely identified as such which meant that there was some degree of subjectivity in how ethical considerations fit within each of the principles of respect for autonomy, non-maleficence, beneficence, and justice. We sought to mitigate this

challenge by having two authors review, extract, and independently analyze all data. Discrepancies were resolved by discussion and a third author audited the results. All three authors had a high degree of familiarity with the framework. A further strength of this sub-analysis is the comprehensive search strategy of the original systematic review and identification of studies reporting on FSI patients as partners in research. Although we did not formally evaluate the discrepancies between the reviewers in the deductive content analysis, the primary author (CL) appeared more attuned to issues related to respect. Researchers have an obligation to exercise care in the language used to describe patient-partners, terms such as the "usual suspect" are demeaning to patient-partners [23]. Issues of legitimacy appear to be amplified for those occupying dual role of patient-partner and researcher; considered neither 'real' patient, nor 'real' academic. The notion of multiple roles is underexplored in the literature on research co-production and clearly warrants additional investigation.

Principlism as an approach to bioethics has been criticized as being reductionist because it ignores information that may not fit neatly into the pre-determined categories [71]. However, the framework offers many practical advantages for application by providing researchers with a common language through which to identify and address bioethical issues. Furthermore, the framework is widely incorporated into medical and health sciences curricula and has been adopted extensively by research institutions for governance and regulation of research [15, 72].

3.6 Conclusion

This sub-analysis of a systematic review adds to an emerging literature base on the ethical considerations of partnering with patients in research [10, 51], specifically as it relates to engaging FSI patient-partners. The involvement of FSI patient-partners has the potential to promote autonomy, provide benefits to all, and ensure their perspective is represented on the

research team. Researchers and patients should work together to clarify the intent and outcomes of the partnership, actively address power differentials, recognize and minimize the potential for unintended harm, and strive to maximize the benefits of partnership. Failure to address ethical implications may potentially leave FSI patient-partners at risk of inadvertent harm and deny them benefits that often extend beyond the boundaries of the research study, particularly in terms of feeling supported and restoring an identity beyond that of 'patient'. However, in order to reap those benefits, FSI patients must be extended the opportunity to partner in research. By having others speak for them, or by excluding them, not only are FSI patients denied the benefits of being involved, they are also denied the benefits of contributing to the direction and outcomes of the very research intended to serve them. The previous review [13] demonstrated that partnering with patients in research is feasible with FSI patients but they must be afforded the opportunity to participate and researchers must create a supportive and accommodating environment that addresses both the practical and ethical considerations of the partnership.

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List of abbreviations

CINAHL: Cumulative Index to Nursing and Allied Health Literature

EMBASE: Excerpta Medica Database

FSI: Frail and/or Seriously Ill

MEDLINE: Medical Literature Analysis and Retrieval System Online

PROSPERO: Prospective Register of Systematic Reviews

PsycINFO: Psychological Information Database

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CL, DS, IDG and WG contributed to the conception of this review. All authors contributed to its design. CL led and coordinated the development and writing of the paper. IDG, DS, JL, and WG participated throughout the development and writing of the review by

contributing intellectual content and feedback on drafts of the manuscript. All authors read and approved the final manuscript.

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Authors' Information

CL is a PhD Candidate in Nursing, Faculty Health Sciences at University of Ottawa. Her research interests are focused on integrated knowledge translation and how frail and seriously ill patients are engaged as knowledge users in research. She is has served as a patient-partner on a number of research projects during a period of serious illness.

DS is Professor in the School of Nursing at the University of Ottawa and Senior Scientist at the Ottawa Hospital Research Institute, and currently holds a University Research Chair in Knowledge Translation to Patients. Her substantial research is focused on advancing the science of knowledge translation to patients and enhancing patient engagement in shared decision making.

JL is a Clinical Social Worker in Geriatric Psychiatry at the Royal Ottawa Mental Health Centre. Her practice is dedicated to working with the frail elderly population who have concurrent mental health issues. She is a strong advocate for inclusivity and equity of access to health and social care for vulnerable populations.

WG is Associate Professor at the University of Ottawa School of Nursing and Co-Director of the Centre for Research on Health and Nursing. Her program of research focuses on leadership and knowledge mobilization/translation to improve health care delivery and patient outcomes, and includes working with Indigenous communities in Canada.

IDG is Senior Scientist in the Clinical Epidemiology Program of the Ottawa Hospital Research Institute and Professor in the School of Epidemiology and Public Health and School of Nursing at University of Ottawa. His extensive research focuses on knowledge translation and studying research co-production/ integrated knowledge translation research.

CHAPTER 4: Embodiment, Representation, and Meaning: An Autoethnography of Patient Engagement in Research During Serious Illness

Author:

Claire Ludwig

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Abstract

Current commitment to patient engagement in research provides significant opportunities to advance our understanding and foster sensitivity and progress in the conduct of research. Yet, people with serious illness are typically excluded from many areas of research, and rarely given opportunity to act as co-researchers. Lack of inclusion limits opportunities for input into the relevance and appropriateness of the research and may reify existing inequities in health research. The vulnerability of seriously ill patients provides additional complexity to engagement processes, particularly regarding prolonged and more intensive involvement; hence their voices are seldom reflected in patient engagement literature. This dearth of evidence minimizes our capacity to investigate seriously ill patients' impact on the conduct of research and inhibits our ability to identify the best ways of involving patients 'meaningfully' in different activities.

Autoethnography as a method of qualitative inquiry enables a more reflective perspective from patients' standpoints, successfully disentangling patients' voices from those of caregivers, advocacy groups, and researchers. This paper provides an analytic autoethnographic account of the engagement of a seriously ill patient as a partner in research. The account is rendered and analyzed in the 'patient voice' as an attempt to complement (or counter) the existing narrative where others speak on behalf of patients. It addresses how engagement is embodied and situated at a time of serious illness and how the process of engagement is shaped within a broader discourse on representation. It further offers unique insight into the untapped power of embodied knowledge production in data analysis and demonstrates the importance of relationships in helping to reduce patient-partners' vulnerability. My hope in writing this autoethnography is to bring new visibilities and awareness related to ethical issues and power relations inherent in practice.

Keywords: Patient Engagement, PPI, Autoethnography, Research Co-production, Embodiment

4.1 Introduction

The drive to engage patients as partners in research has been inextricably linked to a proliferation in policy related to citizenship, democracy and rights [1]. The democratization of scientific knowledge continues to demand greater transparency in research and is predicated on the belief that whilst incorporating patients' voices in the research process satisfies an inherently democratic right, it also serves to enhance the relevancy of the knowledge produced by responding to the needs of those whose lives and bodies are most impacted by a disease or condition [2-4]. The concept of patient engagement has expanded patients' traditional roles as research participants to one where they are recognized as active collaborators in co-producing research knowledge [1, 5]. Over the past few decades, patient engagement in research has increased significantly and is now a prerequisite of major research funding bodies across the globe. In response to these imperatives, numerous models of consultation, collaboration and governance have been developed to support all stages of research; from prioritization of research questions, conduct of research, data analysis and dissemination of findings [6-8].

Today's practices of patient engagement in health research are deeply rooted in the legacy of citizen advocacy arising from disability, feminist and AIDs activism which all demanded increased transparency in the conduct of research, recognition of individual bodily rights, and reformation of the rules that regulated development and access to new therapies [9, 10]. Although significant advances have been made since this time, the journey has not been linear, nor without controversy. Claims of tokenism, inertia, questionable representation, inadequate attention to the ethics of engagement, and inadvertent harms to patients continue to dominate patient engagement literature [10-12]. In response to criticisms, and in an effort to address power differentials inherent in research practice, there is increasing momentum towards

adopting co-production and emancipatory research approaches, particularly in the areas of mental health and social care [13].

The goal of patient engagement serves to shift from a paradigm where the researcher is considered an expert to one where researchers and patients are both experts, bringing complementary knowledge and skills to the team [14]. Meaningful and productive engagement incorporates patients' lived experience of illness as an equally legitimate form of knowledge [2, 4, 10]. Experiential knowledge occurs through the conscious and unconscious conversion of experience into "personal insight" and ultimately culminates into a form of expertise [4; p.2576]. However, incorporating patients' experiential knowledge as an equally legitimate form of knowledge requires a significant epistemological shift within the biomedical and health research community before its full potential can be realized [10]. Many argue that this shift is happening, and if leveraged appropriately, has the potential to provide insight into patient populations who have typically been excluded, intentionally and unintentionally, from research co-production [10; p.3]. Yet, in spite of efforts to incorporate experiential knowledge within research teams, the concept of 'co-production' has received insufficient attention in terms of how it is incorporated into research processes or products [10]. Furthermore, people with serious illness remain excluded from many areas of research, and rarely given the opportunity to serve as research partners because of their perceived vulnerability [15]. Consequently, the voices of those who are seriously ill are seldom reflected in the patient engagement literature. This dearth of evidence minimizes our capacity to investigate the impact of seriously ill patients on research teams and inhibits the ability to identify ways of partnering 'meaningfully' with seriously ill patients on different research activities.

My own exposure to patient engagement in research started not as a patient but as a senior healthcare administrator engaged as a partner on a research team seeking to implement cancer symptom management practice guides into healthcare services. The team itself comprised many stakeholders: researchers, front-line clinicians, program managers, decision-makers, and a caregiver. The team worked together to understand the barriers and enablers of implementing the practice guides. I was so enamoured with this approach to research that I decided to pursue my PhD. However, months into my PhD, I became acutely ill and needed to take a prolonged leave of absence for treatment of a serious potentially life-limiting illness. It was during this time that I inadvertently stumbled into the role of patient on the research team. It was a role that afforded me with unique insight into what constitutes meaningful and ethical engagement. In writing this account, I aim to contribute to a broader understanding of meaningful engagement in research from the perspective of a patient engaged as a partner on the research team during a period of serious illness. More specifically, I examine how patient engagement is embodied and situated at a time of serious illness and describe how patient engagement is shaped within wider cultural meanings and social trends.

4.2 Methods

4.2.1 Study Design

An analytic autoethnographic approach [16] guided inquiry into my lived experience as a patient engaged as a partner in research during a period of serious illness. Utilising autoethnography moved my analysis beyond mere reflection towards a critical examination of how social, institutional, and political interests intersected with my own positionality [17]. The account is rendered and analyzed in my own voice as an attempt to complement (or counter) the existing narrative where others speak on behalf of patients. In providing narrative visibility of

(my)self, I have situated my experience across broader sources of data in the patient engagement literature to enable a more rigorous theoretical analysis [16]. This approach allowed for the 'writing-in' of tacit and subjugated knowledge inherent in the operationalization of patient engagement to reveal details often omitted or suppressed in formal accounts [18]. The goal of autoethnography is ultimately to write "texts [that] move others to ethical action" [19; p.70].

4.2.2 Autoethnographic Data

I used my personal experiences as primary data for this study. My experience—reactions, observations, biography, and emotions—*were* the data. I kept notes throughout my involvement as a patient-partner. My notes included reflections following meetings or presentations, during and after data analysis (including written and audio-taped transcripts of nurse-patient interactions), and other research activities. I would reflect on salient events/thoughts that occurred during my research engagement; which were often entwined with reflections on my health. I concurrently kept a diary during my illness and treatment, outlining how I was feeling physically and emotionally at any given time. Additional artifacts were comprised of random notes scribbled on scraps of paper and stuffed into my "treatment binder" (an amalgam of appointment reminders, nutrition guides, brochures for managing treatment side effects, list of who to call for assistance between treatments, etc.). I also documented my reflections on the personal communication with team members who reached out to check on my well-being. Finally, I further reflected back on my experiences associated with these data and expanded them to provide greater detail using hindsight to add richer detail. In this process of recall, I captured not only autobiographic data from the past, but was able to tap into my present thinking, attitudes, perceptions, and emotions consistent with an analytic autobiographical approach [20].

4.2.3 Data Analysis and Interpretation

Data analysis followed a non-linear process [17, 21]. Analysis of my illness diaries, reflective notes and other data sources was concurrent with documenting memory data to facilitate the "collection of more relevant and meaningful data" [17, p. 61]. I utilized an open-ended, inductive approach, reading and re-reading the data sources whilst capturing my immediate impressions [17]. Items were then coded and organized into broad descriptive themes [17]. During analysis and interpretation, my focus was to move beyond mere description to consider all components of autoethnography, i.e., the story (auto), the culture (ethno), and method (graphy) [17, 21, 22]. The intent of the analysis and interpretation was to "zoom out" of the data and capture the cultural/societal forces at play in the engagement of patients in research [17, 21]. Textual sources (i.e., literature and policy) served as important data sources to inform this component of the interpretation and allowed me to actively transform the data into culturally/socially relevant explanations of the findings from the narrative parts of my data.

4.2.4 Ethical Considerations

Although autoethnography features the self, the ethnographical component does not occur in a vacuum; there are always others represented in the narrative, either as active participants or characters on the periphery [17, 22]. Where others have been referenced as a result of a reflection or interaction, I have used broad composite role descriptors and gender neutral pronouns to protect privacy [17, 23]. Those in close academic circles who could potentially be identifiable, were aware of and actively encouraged this study. They were also provided with an opportunity to review this manuscript and provide feedback. Research Ethics Board approval was obtained through the University of Ottawa. From a personal standpoint, self-

disclosure carries risk due to lack of influence over readers' interpretation of the sensitive personal information which is coupled with inability to retract information post-publication [24].

4.2.5 Trustworthiness/Validity

In keeping with methodological standards of analytic autoethnography [25], I provide narrative visibility of myself, taking it beyond thick description of my personal experiences to provide sociocultural explanation of those experiences. The study was guided by "desired standards for health autoethnography" [25]: 1) use of reliable and trustworthy data from a variety of sources collected during a period of serious illness; 2) visibility of a reliable research process (detailed above and further addressed in the discussion); 3) adoption of ethical steps to protect the rights of self and others implicated in the autoethnography; 4) rigorous analysis and interpretation of the sociocultural meaning of my personal experiences; 5) contribution to the scholarly literature, particularly given the absence of the patient voice in patient engagement literature and implications for practice.

4.3 Findings

Findings have been organized into the main themes of embodiment and representation with a focus on meaningful engagement. Within the key themes, I grounded my findings within the broader literature to compare and contrast my own experience (auto) with the culture (ethno).

4.3.1 Embodied Temporality: Biographical Disruption

> *I look down at my desk. I stare at the post-it notes in front of me, reading the desperate scrawl "you can do this" written over and over again… it belies the way I am feeling, I am despondent… and oh, so very tired. Why do I feel this way? Why can't I push through this? I just want to lie on the floor of my office, curl up in a ball and sleep. I feel like I could sleep forever… until the relentless dry cough kicks in. Why won't this damn cough*

stop? The fevers? The night sweats? The dyspnea? Why won't my body cooperate… I just need to push through… I have papers due. I don't have time for another (pointless) trip to the doctor… another round of antibiotics. It all seems like too much effort… or maybe… just maybe, I'm afraid… I know something is terribly wrong (I'm a nurse, after all) (illness diary).

My life as I knew it was about to be interrupted. Cancer has been described a 'deep illness' which 'casts a shadow over the rest of a person's life' and leaves many 'feeling literally dislocated, no longer fully connected to the ground on which they stand' [26; p.185]. Life-altering illness, like cancer, presents a fundamental rupture in the fabric of everyday life, and results in a disruption of the narratives about the future that people use to understand themselves and trajectories of their lives [27]. My diagnosis of advanced cancer functioned as "a marker event" casting me apart from my "former self", interrupting everything I took for granted [28; p.30]. As described by Grinfelde (2018), illness serves to break down bodily certainty, whilst simultaneously breaking down a sense of self. The physical, emotional, and cognitive toll of cancer not only threatened my taken-for-granted everyday world but shed uncertainty on my future, leading to questions and fears about my own mortality; casting aspersion on my ontological certainty. Suddenly, illness and treatment impacts featured strongly in my 'biographical narrative' [30].

A serious diagnosis exposes an "embodied ontological frailty" to self and to others; necessitating reflexive revision and re-shaping of self-identity, whilst relatedly exposing the need to take new actions in a biographical path [31; p.118]. In the face of life-limiting illness, the search for reflexive revision and meaning becomes an imperative [32]. Staring down a potentially life-limiting illness, the task I faced was to determine how to integrate illness into my

pre-existing identity. My patient identity soon became inextricably intertwined with my professional and academic identities. Partnering as a patient in research, particularly during serious illness, allowed me to unify the roles of patient, nurse, and researcher into a meaningful and 'unified coherent sense of (my)self' [33].

4.3.2 Representation: Legitimacy

> *"Oh, we'd never have a patient like you on our team. You just aren't representative." I'm stunned by hearing these words from an academic well known for engaging patients on their studies... I seek clarification: "what do you mean?" I ask meekly. "Well, you just don't represent the general population…" it's like a slap, an affront to my experience, my suffering (I am still in treatment at this time and there are days when I can barely get out of bed). I laugh nervously, the words sting and I'm surprised how hurt I feel by this seemingly flippant comment. Do they mean that I'm not sick enough… that I'm too educated… that I'm not poor enough… that I am/am not… many other qualifiers run through my mind as I search to make sense of this? The comment throws me off. What does it mean? Does it mean that I don't belong here? That I'm a fraud? That my experience is somehow less valuable? That I am lesser? A charlatan masquerading in the midst of those who somehow know better. Those who know what a "real" patient is.* (conference).

Until this point, my identity and legitimacy as a patient had never been called into question; a reason no doubt for why this seemingly flippant comment 'stung' to the point where I questioned my own legitimacy. The notion of who a patient is, or how they should behave in relation to research team members and academics, has received long-standing attention in the literature [34]. Choosing the "right" patient-partner in health research is considered an

imperative to avoid the pitfalls of misrepresentation [35]. Some researchers have even spoken of the discomfort of knowing that they failed to be more selective in the recruitment of patient-partners on their studies [36]. The current discourse surrounding the desired traits of patient-partners is inextricably intertwined with complex ethical issues of representation [12, 36, 37]. Although representation in patient-partners is not necessarily equated with the statistical bench-marking required for empirical research (where patients are the object of study) many academics struggle with what representation means, how they operationalize it, and consequences of not doing it appropriately [35, 38].

I recognize the gravity of this exchange; what it means in the real world. I appreciate first-hand the importance of representation, or better yet inclusivity or recognition. I identify as a lesbian woman. I know the power of stigma and exclusion. Representation tells a story and reveals the voices of those who are seldom heard. I realise I am both present and absent in this exchange. I chose not to disclose my sexual orientation (I didn't feel safe). I am left questioning whether the disclosure of my identity as a lesbian woman would have altered perception and enhanced my credibility as a legitimate patient at the research table, in a way that my disease and condition could not. The voices of those identifying as LGBTQ+ remain under-represented in the patient engagement literature [12]; an irony that is not lost on me given the legacy and activism of the LGBTQ+ community in advancing a role for patients as partners in AIDs research [9]. Striving to meet the mandate for diverse representation without adequate thoughtful and ethical consideration about how to enact it, has led many to develop a poorly formulated and heuristic view of diversity as demographic characteristics [39]. As demonstrated in my decision not to disclose my sexual orientation, this seemingly reductionistic conceptualization of diversity held by others served to reproduce the very exclusionary spaces I have strived to avoid [39].

4.3.3 Representation: Contested Knowledge by Virtue of Multiple Roles

> *The words "you're not a typical patient, it's unusual to have someone with all your experience" make me pause. If I'm honest, I'm flattered; everyone wants to feel useful (or special) in some way but what does it mean to be a "typical" patient?* (Reflection post research meeting).

My patient identity and my role as a patient-partner in research is inextricably fused with my professional and academic identities. These identities present both opportunities and challenges. On the one hand, I possess intimate knowledge of the healthcare system, as well as the methods, process, and hierarchies inherent in research. On the other hand, I have lived experience of serious illness, aggressive treatment regimens, and the very real fear of recurrence (a constant companion, even in remission). Yet, for some, my identities as nurse, healthcare administrator, graduate student/novice researcher, and patient appeared to refute my legitimacy as a patient-partner in research. This tension has been described in the literature. Academic and survivor/mental health activist Sarah Carr, described how the dual roles she embodies "are indivisible (to her); but for some, one negates the other" [40; p.1142]. No one holds a singular identity [41], we are the sum of our parts; it is impossible to shed parts of ourselves in order to become a "pure" patient, or for that matter a "pure" researcher. Such constructions deny the reality of multiple intersecting identities, whereby individuals simultaneously inhabit and live in multiple social locations [42].

4.3.4 Embodied Illness: New Meaning

> *I had been a palliative care nurse. I thought I knew what fatigue was... I had no idea until now* [in the throes of chemo, immunotherapy, and anemia]. *I feel a rush of shame, memories of how, as an 'expert' clinician, I had counseled my patients on*

energy conservation, diet, hydration, self-care… I realise now how little I knew. Nothing could have prepared me for the sheer intensity of the physical and psychic pain of fatigue I am now feeling. This feeling of desperation, a body ravaged by disease, working so hard… every piece of me hurts… I am despondent… (illness diary).

Under normal circumstances, effort is required to engage subjectively with our bodies. The association between corporeality and its relationship to the world has long been a focus in social and medical sciences, including the notion of embodiment which is broadly defined as relating to the manner in which meanings, expectations, styles, and habits are articulated and experienced in the lived body [43]. We think, feel and process the world around us with our bodies. Yet, the body has also been referred to as an 'absent presence,' mostly taken for granted but simultaneously positioned to interpret and respond to the world around us [44]. Ordinarily, we do not acknowledge the primacy of our bodies in how we perceive and attend to others. A degree of mindfulness is required for us to channel our embodied knowledge and understanding [43, 45].

Like most people, before becoming ill, I took my body for granted. As described by Engman (2019), it took the trigger of serious illness to propel my 'normally absent body' into the foreground. With the unity of embodied experience disrupted, people with serious illness are forced to "integrate new bodily facts" when interpreting and reacting to the world around them [47; p.663]. From this perspective, embodied experience is not one that can be learned from a book [48]. As the physical symptoms of illness and treatment side effects ravaged through my body, I began to question old knowledge and integrate new ways of knowing and understanding. Illness has a profound impact on identity formation and can enhance an appreciation for the

suffering of others [47, 49]. I realised quickly that I needed to find a way to move through my limitations (physical and cognitive) and put aside parts of my identity (and associated roles) as I struggled to integrate new bodily facts into my identity. When I stumbled onto the role of a patient-partner in research, some pieces were cast fiercely aside (by virtue of the severity of my illness) and other pieces came together to meld a new identity. As I created meaning and purpose through my illness, I became astutely aware of the power of my body in making sense of the world around me.

Partnering as a patient in research offered me new forms of meaning in the face of a ruptured identity triggered by diagnosis of a serious and potentially life-limiting disease. Similar to other reports, serving as a patient-partner in research during a period of serious illness afforded me with a renewed sense of agency and purpose, particularly within a team where my role was not pre-defined and I was able to negotiate the terms of my involvement [50, 51]. As reported by others [52], partnering in research served as a major transformational function whilst coping with debilitating loss from cancer and treatments. And while my bodily experience became an engine through which I began to interpret my own illness, I began to acquire a deep awareness and appreciation of the suffering of others which I unconsciously incorporated into my role as a patient-partner.

4.3.5 Embodied Research: Making Meaning

> *This particular interaction has brought me to a familiar place. I'm immersed in her* [the patient] *experience. I can hear the struggle in her voice… her tiredness, her frustration, her fear. I wonder whether the nurse can hear it… part of me doubts it… the nurse has her own agenda. She has a job to do – get to the bottom of the issue, solve the problem, make the patient feel better before moving onto the next patient. It*

strikes me that this particular patient doesn't seem better as she hangs up the phone. I sense her disappointment at the perfect nursing assessment. I also wonder how much she actually absorbed during the nursing intervention… it seemed way too busy. At the same time, I am sensing the now all too familiar and all-encompassing nausea running through me. The patient's nausea becomes my nausea – persistent and unrelenting… sapping my energy, keeping me still… circling around me… ever decreasing circles… luring me into its grip… SNAP… But this isn't my nausea. I know I need to claw my way out of the space I am in… ever so gently… I need to come back… I need to reflect on the interaction… analyse the data. I've ticked the boxes, captured the conversation, checked the notes. An assessment well-done - checked, medications – checked, self-care - checked, follow-up - checked. Picture perfect and yet I'm left wondering about the patient, her experience. What did she remember from talking to the nurse? Did she try the medication? Did she remember to eat small bites but frequently… avoid spicy food and strong smells? Did she remember anything? But most of all, I wonder how she is now (reflections from data analysis of recorded nurse/patient interactions).

In reflecting on this experience of data analysis as a patient-partner, I am struck by the words of Merleau-Ponty: 'It is as if the other person's intention inhabited my body'[53; p.185]. Hearing the words of the suffering patient, enacted a bodily response through which I was able to interpret the interaction, specifically from the perspective of the patient. Our bodies have been described as "the tool of tools," an "indispensable instrument for perception, action and thought," expressing our double status in the world as subject and object [54; p.2]. A body is both active and acted-upon [44]. Listening and analyzing the content of this interview (and others) forced

recognition not only of my own bodily experiences but those of the patient during their interaction with the nurse. After comparing my analysis to the second analyst (a nurse), the research team provided feedback that validated my experience and spoke to the fundamental difference and value provided by having a patient-partner involved in data analysis who was actively experiencing the same symptoms reported by patients in the study. Input from data analysis based on my embodied knowledge led to refinement of a quality appraisal instrument for the project and development of a teaching aid. Looking back, I realise this type of embodied and emotive interaction with the data formed the basis of my ongoing contribution as a patient-partner during a time when I was highly symptomatic from both my disease and treatment side effects. Being afforded the latitude to define the scope of my role as well as the way I enacted my role as a patient-partner not only brought depth of meaning to my illness experience but enriched the research itself.

4.3.6 Embodied Vulnerability

> *It has been difficult on so many levels listening to these calls (audio-transcripts); hearing the tiredness, the fatigue, the worry, the anxiety, and at times the frustration in the voices of patients calling into the line. Caregivers seem to be calling in for those who are too sick to call-in themselves. I can't help but sense the fear in some of their voices… maybe anger too for a system that doesn't seem to be responding quickly enough or one that can't see what they're going through. The nurses also sometimes seem to be out of their depth. Conversations [assessments] go into some weird spaces at times… symptoms and their impacts minimized, or perhaps not heard… (in the way that I am hearing them)* (reflections from data analysis of recorded nurse/patient interactions).

Embodied sensemaking cuts both ways – although largely positive, it opened me up to extremes of vulnerability, particularly during times I was struggling with my own suffering and mortality. My experience was similar to other seriously ill patient-partners' reports of distress when reliving painful illness experiences or experiencing the suffering of others [11, 55]. Illness represents a moment of profound bodily vulnerability [56] and necessitates a great deal of consideration in research partnerships, particularly when considering unpredictable illness trajectories inherent during serious illness.

As reported in other studies of patient engagement [e.g., 57], my embodied reactions as a patient-partner also encompassed conflictual and negative emotions, such as insecurity, inadequacy, and fear, when interacting with the broader research community. Guilt and stress wracked through me when deadlines were missed because of what I perceived as my "failing body and worse yet, my brain." The impact of "chemo-brain" described as a complex interaction of chemotherapy, fatigue, and depression [58] further stoked my feelings of inadequacy and insecurity despite reassurances of a supportive principal investigator on the team. Additionally, in dissemination activities, I found that exposing myself and my story to unreceptive academic audiences served to negate many of the positive benefits I gleaned from patient engagement and perhaps spoke to the continued resistance of some in the scientific community to acknowledge experiential knowledge as an equally legitimate form of knowledge.

As I entered remission, feelings of vulnerability also encompassed fear and trepidation, particularly around the unintended harms of disclosure of my illness in public spaces. Ironically, the more my health improved, the more pronounced were concerns of stigmatization and the potential impacts disclosure could have on my career in an unstable employment market. These fears were compounded in environments where there was unwitting pressure to reveal intimate

details about my health. The disclosure of my illness became ever more personal, highlighting that issues surrounding disclosure are complex and heavily dependent on other factors such as the nature of an illness or condition, a person's cultural traditions, social values and norms, and what the illness means to the person experiencing it [59]. Acknowledging having an illness also means affirming its continuity in one's life and perhaps its immediate or looming presence [59]. Disclosing my illness raised serious dilemmas for me. Sociologist Irving Goffman spoke of a "spoiled identity" whereby one is stigmatized and forced to carry a mark of difference, dishonor or disgrace [60]. In a society that values health, I became increasingly aware of the tacit implications of disclosing my illness to present and future colleagues or employers.

4.3.7 Embodied Relationality

> *I'm sitting at my computer with tears streaming down my face. I am profoundly touched by the email from one of the research team members (not someone I know well). The kind words of encouragement are compounded by an (attached) article written by a psychologist providing reassurance and tips on how to best deal with the emotional impacts of cancer and recovery. It captures perfectly what I am feeling - how frightened I am and how dark my worldview is now. How did they know? What did they pick up during the meeting earlier today? I thought I had hidden my distress well… particularly this deep depression that I can't seem to shake* (reflections post research meeting).

My vulnerability heightened awareness of my interconnectedness with others. As described by Merleau-Ponty (1947/2012) embodied behaviors serve as a mechanism to communicate (consciously and unconsciously) with those around us. My illness became a mediator in my relationships with the research team, some of whom sensing my bodily vulnerability, expressed concern for my welfare throughout the research projects (and beyond).

These connections ultimately gave me permission in a safe space to open up and describe my insecurity as I struggled with "chemo-brain", depression and fear of my own mortality. The emotional support provided by research team members, especially validation of patient-partners' illness experience has been described as a key motivator for patients to continue their contributions, even when they are struggling with disease and treatment side effects [52, 62]. Such support also can engender trust, inclusivity and connection in this relational space, particularly when research relationships are more intensive and prolonged [37, 63].

4.4 Discussion

This study sought to outline patient engagement during a period of serious illness through the embodied experience of a patient. It adds to the burgeoning literature on patient engagement, acknowledging the complexities inherent in the current discourse on representation with a need to refocus attention on the relational space between patient-partners and research team members. The study also speaks to a need when partnering with patients in research to harness the power of patients' embodied experience in shaping how research studies are developed and conducted.

Embodied knowledge production has the potential to contribute to the critically important discourse on representation. Adequate representation in patient research partners – not as statistical representation but as a "regulative ideal" can only be achieved when a variety of voices are heard [35], including those who are seriously ill. But whilst there is concern about lack of representation of marginalised and seldom heard groups, there is surprisingly little discussion about how to address these concerns [12]. Without this guidance, researchers are driven to guidelines posed by funding agencies and have enacted patient engagement in research "to respond to and impress the funder's gaze" to secure research funds [64; p.78]. Unsurprisingly, this has resulted in a poorly defined and executed vision of diversity as

demographic statistics, which unwittingly has the potential to overburden marginalized groups or subject them to practices that instrumentalize their experience [39]. It may also serve to further marginalize or exclude those who choose not to disclose their "difference", e.g., socio-economic status, gender identification, or sexual orientation. Not taking time to understand patient-partners' backgrounds, or refusing to value and nurture those contributing is unlikely to encourage others to these roles [38; p.67]. To enact inclusivity, the research community must take the time to critically reflect on "current tokenistic expectations for diversity" to ensure the needs are met of those suffering the worst health outcomes [39; p.11].

Illness and the body are largely absent from the literature on patient engagement, and it was therefore important for me in the writing of this autoethnographic account, to give primacy to the writing-in of my (sick) body. In doing so, I hoped to offset current disembodied reports of patient engagement. Embodied accounts become particularly important in a research culture of epistemic dissonance where the lived experience and inherent emotional response to illness continues to be regarded as a lesser form of knowledge than scientific knowledge [65]. Reproducing disembodied knowledge production reifies current research methodology and continues to limit our full appreciation of the depth and breadth of the experiential knowledge that patient-partners have to offer. Yet, significant epistemic and ontological shifts are required to reverse current practices which encourage patients to deny their individual experience (for the sake of representation) and provide "objective" and disembodied accounts of illness [66]. Paradoxically, by denying patient-partners the opportunity to enact embodied knowledge production, they are actually rendered less representative of the patient population under study.

Leveraging embodied knowledge not only facilitates new understanding but it may also create novel approaches to how we conduct research in partnership with those who are more

vulnerable. Harnessing the embodied knowledge of patient-partners may provide much richer insight and interpretation of study data, particularly when dealing with the same condition or symptoms as the study participants [36]. Embodied relationality may also help research participants share more candid responses when interviewed by those they more readily identify with [67]. As patient engagement in research progresses to approaches more akin to co-production, it would appear that embodied research can be taken to new heights with the potential for patient-partners to channel their bodily experience and bring data analyses to another level through a reflection on their own experience in order to better understand a lived reality of others. Foregrounding of my body-self allowed me to turn a critical gaze towards my embodied knowledge rather than my professional or academic self. I am aware that my insights today (writing when I am well) would be vastly different than during the acute phases of illness and treatment.

It is the meaningful actions of "local actors" that promotes inclusion on a team [68]. This study highlights the importance of emotional inclusion and recognition, whereby my "feelings" of belonging were reinforced by the "practices" of belonging [63; p.245]. As such, attention should be consciously directed to the ways in which power and positionality are enacted throughout the research process (including during dissemination activities). Competing views and the hierarchy of disciplines within a project team can make this a challenging endeavor given the differing epistemological and ontological paradigms inherent in multi-disciplinary team composition [68]. Asymmetries of power and knowledge where identities and values are in competition require different ways of interacting, particularly in research partnerships with those who are vulnerable and seriously ill [66]. Some team members may be familiar with the epistemological and theoretical underpinnings of patient-engaged research whilst others may be

more interested in maintaining current hierarchies of knowledge production. As such, strategies need to be implemented to reduce the impact for patients and promote their inclusion as an equal partner on the team [68]. Yet, these shifts may only be realized through increased reflexivity and a willingness on the part of researchers to turn their gaze inwards and embrace their own vulnerabilities and biases in the production of knowledge with patients. The notion of humility is an underexplored concept in the patient engagement literature but the enactment of humility in research partnerships offers a path towards building authentic, meaningful and trusting relationships between the research community and patients [69].

Postmodern research methods make it possible to gain and share knowledge in diverse ways [70; p.203]. As I was writing this autoethnography, I was struck by the fact that autoethnography encompasses and privileges the very same approaches championed by proponents of patient engagement. Both eschew rigid definitions of what constitutes meaningful and useful research, and both incorporate subjectivity by giving voice to personal experience in order to shape how research is produced [21, 71]. In illness autoethnographies "the story is particularly intimate and the telling of it can render the writer vulnerable" [72, p. 1718]. Writing and speaking about illness has the potential to amplify any residual suffering following diagnosis [72]. Similar to the dilemma I faced with disclosure during patient engagement activities, I realise that autoethnography is like an "inked tattoo" and cannot be retracted once published [24, p.1605]. In the same way that autoethnography demands narrative visibility of the researcher's self, so do patients' stories. Self-disclosure in both instances may expose autoethnographers and patients alike to inadvertent harms, unable to retract their narrative whilst having little control over how their audience perceives the sensitive biographical information they are sharing. And

yet, conversely both autoethnography and patient engagement offer enormous emancipatory potential [23, 73].

4.4.1 Limitations

Writing an autoethnography is not without its challenges. Fears of self-disclosure, coupled with the discomfort of communicating deeply personal details about my physical and emotional health led me to question the degree to which I should censor my story. Although some details have been omitted in order to protect myself, the account I have presented remains true to my experience and has not altered the fidelity of the study. Moreover, I am writing this account when I am well and not immersed in the bodily experience of disease and suffering. Yet, this lapse of time has afforded me the space (physical and cognitive) to gather the momentum to re-submerge myself in data, write, and work to actively capture what was germane to my experience at the time. In many ways it also reinforced my awareness that the experiential knowledge that I contribute to studies today is qualitatively different than in the throes of active symptomatic disease.

4.4.2 Implications for Practice

My hope in writing this autoethnography is to bring new visibilities and awareness related to ethical issues and power relations inherent in practice [74]; and to honour my ethical obligation "to give something important back to the community" I have studied and written about [75; p.56]. Researchers have a major role to play in creating a more inviting and supportive space to foster inclusive practice and take concrete measures to mediate or ameliorate vulnerability in a way that takes into consideration patient-partners' rights to autonomy [37, 57, 76]. It is with this intention in mind that I extend the following considerations to researchers and

seriously ill patients who are partnering in research at a time when patients may be at their most vulnerable (see Table 4.1).

4.4.3 Conclusion

In this analytic autoethnography, I outlined my experience as a patient-partner engaged in research during a period of serious illness. The study highlights the need when partnering with patients in research to harness the power of patients' embodied experience in shaping how research studies are developed and conducted.

Table 4.1 Considerations for Patient-Partnership in Research During Patients' Serious Illness

	Patient-Partner Considerations	**Researcher Considerations**
Representation	• Be prepared to respond to questions/comments regarding the extent to which you represent or do not represent the patient population under study &/or the general population. • When/if your representativeness is called into question, recognize that your emotional response may be commensurate to how vulnerable you are feeling (for me it "stung" and rendered me silent). • Enlist support from a team member to help address concerns about legitimacy & representation • Reflect on what you contribute – it likely encompasses much more than your condition/ disease. • Acknowledge that there may be times where your condition/demographics don't meet the needs of the project – have an open dialogue with the PI/team.	• Take time before initiation of the project to seriously consider what representation and diversity means so that it doesn't risk being perceived as a tokenistic gesture or response. • Develop networks through the communities you are seeking to engage – ensure that relevant ethical guidelines/practices are followed. • Focus on authentic and prolonged engagement. • Remember that words have power and can be offensive, more so when patient-partners are feeling vulnerable. • Recognize the offence that is caused when calling a patient's legitimacy into question – they are unlikely to sustain their input and may deter others if their experience is negative. • Take time to get to know the patient-partners on your team – the other roles they hold may bring new skills to the team.
Embodiment: Finding & Making Meaning	• Although many patient-partners defer partnership with research teams during acute or serious illness, consider that you bring a very different perspective to the table than during times when you are more well or in survivorship. • Reflect on whether you have something more to contribute to the research - appreciate that research participants may more readily identify with you.	• Don't rule out partnering with patients who are acutely or seriously ill – they will likely bring a very different perspective than when they are well. • Understand where your patient-partners' are in terms of their disease/illness trajectory. Acknowledge their illness or condition (whilst checking-in on their comfort level to share) • Ask your patient-partner about what type of role they would like to take on – consider whether they would be interested in a role such

		as data collection (e.g., interviews) or data analysis and provide relevant teaching and support.
Embodied Vulnerability & Relationality	• Recognize that you may be more in tune with suffering of others but ensure that you are able to reflect on this and have the support of the team to mitigate potential harms. • Be aware of your own emotional, cognitive, physical capacity and know that you can withdraw at any time. • Acknowledge the actions of the team in providing support. • Address words or actions that increase your feelings of vulnerability. Ensure you have a forum to express how you're feeling.	• Be aware of the potential ramifications of asking patient-partners to recount or relay sensitive biographical or health information – actively ascertain what they are comfortable sharing. • Check-in with your patient-partner before and after each meeting/activity regarding research – leverage as a 'pulse-check' on how they are feeling. • Recognize when patient-partners might be feeling vulnerable and take the time to address it. • Observe team dynamics – address the skeptics in the room and have an open dialogue. • Non-verbal communication can be more powerful than verbal communication in silencing others – be aware of non-verbal cues (e.g., foot tapping, doing email). • Practice humility – know your own strengths & weakness & be open to others.

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CHAPTER 5: Integrated Discussion

This purpose of this chapter is to integrate and discuss the findings from the three dissertation studies and place them within the broader literature. First, I will briefly summarize each manuscript. Second, I will discuss the contributions this dissertation makes to the evolving literature on patient engagement in nursing and health care research with specific reference to: meaningful engagement, power, and representation. Third, I will conclude with implications for nursing education and research.

5.1. Summary of Studies

My dissertation explored the factors associated with engaging frail and seriously ill patients as partners in health care research. In my systematic review of the literature (Chapter 2), I identified 30 studies where frail and seriously ill patients had been engaged as research partners across the research cycle. Findings highlighted an upward trend over the past decade towards engaging frail and seriously ill patients as partners in research. There was evidence of collaboration with frail and seriously ill patient-partners at different stages across the research cycle, in activities related to: setting priorities, selecting outcomes considered important to patients, grant review, tool development, research conduct, and dissemination of findings. Only 4/30 studies demonstrated collaboration with frail and seriously patients across all stages of the research trajectory; specific activities encompassed: delineation of the scope of the partnership, contribution to study design, co-leadership on working groups during study execution, data analysis, dissemination activities, and adoption of decision-making roles on research steering/advisory committees.

Included studies identified researchers' perceived barriers to engaging frail and seriously ill patients as partners such as lack of time and resources, fear of discontinuity in the contribution of patient-partners due to illness, increasing frailty or death, and researchers' concerns for the

well-being of patient-partners. Studies also reported researchers and patients perceived that engaging frail and seriously ill patients as partners was facilitated by trust and mutual respect between researchers and patient-partners, accessibility and flexibility in how patients were engaged, and researchers' attention to the care and comfort of their patient-partners. Studies reported that perceived impacts on patients partnering in research included patients' experience of a renewed sense of personal agency in the face of debilitating disease and the positive benefits gleaned from the emotional support provided by academics and other patients on the research team. Impacts on researchers included exposure and sensitization to the lived experience of serious illness and frailty and an increased appreciation of the benefits of partnering with patients in research. Researchers reported benefits of patient-partnerships in relation to research design, conduct and outputs. Researchers also reported that research developed in partnership with patients was deemed more relevant and reflective of patients' priorities. Concerns for the well-being of frail and seriously ill patients are warranted but given significant positive impacts of partnering with this population, researchers need to work with patients to overcome barriers to their engagement. Research partnerships with patients who are frail and seriously ill should be done thoughtfully, ethically and with intention throughout all stages of the research cycle.

I conducted a sub-analysis with 25 of 30 studies included in the systematic review that made reference to ethical considerations related to engaging frail and seriously ill patients in research (Chapter 3). I analyzed the included studies utilizing Beauchamp and Childress' framework of a universalizable set of four bioethical principles (respect for autonomy, non-maleficence, beneficence, and justice) [1]. Common ethical considerations related to *respect for autonomy* reported in 24/25 of the studies included: accommodate patients' desired level of involvement, address issues related to relational and intellectual power, promote patients'

knowledge and understanding of research, ensure the engagement has a defined purpose, guard against unnecessary/uninformed disclosure of health and other personal information, and recognize and respond to impaired or diminished responsibility of patient-partners. In terms of *non-maleficence*, 20/25 studies reported on efforts required to: protect patients from financial burden, physical and emotional suffering. With regard to the principle of *beneficence*, 14/25 studies described patients' desire to add value to research and put things right for others. *Justice*-based considerations reported in 20/25 studies included the need to: ensure appropriate representation, acknowledge mutual respect for contributions, and consider an equal distribution of risks and benefits during the partnership. Findings highlighted research teams need to establish shared values and ensure processes are in place to identify and address ethical issues when partnering with frail and seriously ill patients. Furthermore, researchers and patients should work together to clarify the intent and outcomes of the partnership, actively address power differentials, recognize and minimize the potential for unintended harm, and strive to maximize the benefits of partnership.

The analytic autoethnographic study (Chapter 4) provided a first-person account of my experience of partnering in research as a patient during a period of serious illness. Grounded within relevant theoretical frameworks and situated within the current literature on patient engagement, employing analytic autoethnography as a method of inquiry allowed me to move beyond a purely narrative account of my experience. Throughout this embodied autoethnographic account, primacy was given to the writing-in of my (sick) body, thereby countering current reports of patient engagement in research in which the body itself is largely absent. Serious illness represents a time of extreme bodily and emotional vulnerability, which rightfully engenders concerns for patient's well-being. Yet, when embodied vulnerability is

acknowledged and heard, the body itself becomes a site for agency and interpretation. Embodied knowledge production can serve as a powerful tool through which to understand the illness experience of self and others and to date has been underutilized in patient engaged research. It also illustrated the potential to harness patients' embodied knowledge particularly during the data analysis phase of a research study. Serious illness can undoubtedly represent a time of extreme bodily vulnerability but it also can serve as a way to interpret and understand a phenomenon under study as well as provide a time for a renewed sense of self and purpose. The study further illustrates the potential for patients who are going through life-altering events to find meaning through research partnerships. The flexibility, respect and trust of the research team members in this study was instrumental in my ability to both make and find meaning in the process of patient engagement.

Collectively, my dissertation findings suggest that there are many diverse factors related to partnering with frail and seriously ill patients in research. In spite of an upward trend towards the safe and ethical inclusion of frail and seriously ill patients throughout the research life cycle, researchers continue to struggle with how to operationalize the concept into practice. The findings from this dissertation lead to three broader discussion points: meaningful engagement, relational and intellectual power, and representation.

5.2 Meaningful Engagement

Making meaning is linked to the creation of something new [2]. Meaningful engagement during research partnerships for those who are frail and seriously ill featured strongly in the findings in this dissertation. For patient-partners, the creation of meaning appeared to involve two distinct, and potentially synergistic, processes that allowed patients to 'make meaning' during life-changing events like frailty and illness and 'find meaning' in events that inspired

satisfaction, joy, or making things right with the world [2]. Findings from the systematic review (Chapter 2) described how patients coping with frailty and serious illness both found and made meaning through their research partnerships. Partnering in research allowed patient-partners to make sense of illness through reconfiguration of their identities; thereby allowing them to make meaning by providing opportunity for a renewed sense of self in the face of debilitating and life-limiting illness. Patient-partners in these studies described their contributions to research in altruistic terms; finding meaning through a conviction that they were putting things right for others and hopeful that their contribution to the knowledge produced would change the illness trajectory of future generations (particularly in diseases with genetic or familial links). The sub-analysis (Chapter 3) further emphasized the ethical principle of beneficence and a positive obligation for the research partnership to produce tangible benefits for patient-partners. This study highlighted the need for research mechanisms to ensure that patient-partners' are able to visibly discern the results of their input, to know that their voices mattered, and to feel that their work had contributed in a meaningful way. Study three (Chapter 4) provided an autoethnographic account of making and finding meaning during serious illness whereby partnering in research served as a major transformational function whilst coping with debilitating loss from cancer and related treatments. The studies in this dissertation illustrate, when patient engagement is done well (i.e., in an authentic and purposeful manner), patient-partners have an active role in the co-creation of meaning.

Paradoxically, whilst meaning is defined at the level of self, it is simultaneously created in the space between self and others [3]. The construction of a meaningful research partnership is not done in isolation; it is a dynamic process. Within a relational ethic, the relationship between people is of primary consideration, where the space between us allows for a realization of an

interconnectedness [4]. Inter-personal connections are of paramount importance in creating meaningful research partnerships; more so when patients are experiencing vulnerability. As demonstrated in the autoethnographic study (Chapter 4), and consistent with other studies [5], embodied vulnerability further accentuates the risk for patients to experience negative emotions such as fear, guilt or inadequacy. Negative experiences are further defined as meaning being absent – neither made or found [2]. The absence of personal connection denies patient-partners the opportunity to reap the psychosocial and intellectual benefits of the partnership [6].

Relationships are the mediator to a meaningful experience for both patient-partners and researchers. Longevity and the depth of the relationship and engagement is important in engendering trust [7]. Trust is important; it is also bi-directional. The findings in this dissertation (Chapters 2-4) further demonstrate that research partnerships provide researchers with the opportunity to develop new understanding and meaning through exposure to patient-partners' lived experience of illness and frailty, but patient-partners' sharing is heavily dependent on the quality of that relationship. The autoethnography (Chapter 4) offered unique insight into how patient-partners have the power to generate and bring new meaning to research findings through a process of embodied reflexivity, particularly when they carry similar and concurrent physical or emotional burden to the patient population under study.

Meaningful engagement in research has largely been defined as a riposte against tokenism. To date there has been scant critical analysis of what actually constitutes meaning, particularly with regard to how patient engagement fits into the broader context of patient-partners' lives [8]. The majority of studies evaluating meaningful patient engagement have taken a research-centric approach, evaluating impact or effect as a proxy for meaningful [8]. This predetermined notion of what is "meaningful" is problematic. Team structure and the

epistemological and ontological underpinnings that govern team dynamics make it complex to evaluate meaningful research partnerships with patients [9]. What brings meaning to patients is qualitatively different from what researchers consider to be meaningful [10]. The evaluation of meaningful engagement will continue to be problematic until such time as teams invest the time and effort prior to embarking on the research study to define what is meaningful to them as individuals, as a team, and for research endeavor itself.

5.3. Power

The findings generated in this dissertation add to the mounting discourse on the ways in which power is enacted and negotiated in the context of patient engagement and research partnerships [11, 12]. The justification for patient engagement in research is largely divided into two divergent approaches, one of which is conceptualized as meeting consumerist or technocratic needs, and the other as satisfying democratic rights [11, 13].The 'consumerist' approach to patient engagement is based on less intensive levels of engagement such as consultation and information gathering without any commitment to power sharing [11]. In contrast, the democratic approach to patient engagement in research is focused on a more equitable distribution of power in order to effect positive change (individually and collectively), and is facilitated through inclusion, autonomy, and independence [11].

Although the studies included in the systematic review and sub-analysis (Chapters 2 and 3) appear to be predicated on the democratic approach to patient engagement (i.e., focus on partnership), they illustrate significant barriers to the sharing of power at both individual and structural levels. Researchers cited structural barriers in their efforts to implement more intensive and prolonged research partnerships. Structural or contextual barriers such as lack of policy, paucity of research funding, and lack of compensation for patient engagement activities served to

limit partnership with patients to activities earlier in the research trajectory, which subsequently constrained the potential for more equitable distribution of power throughout the study. At the team level, asymmetry of power relations and the inherent vulnerability of frail and seriously ill patient-partners present significant issues for patient-partners' autonomy. Furthermore, patients who are frail and seriously ill are often excluded from the opportunity to partner because of researchers' concern for their wellbeing and fears around discontinuity of their contribution; this not only suppresses input from these patient populations but reifies the soft paternalism inherent in biomedicine. Elsewhere in the literature, the role of academia itself has been highlighted in demonstrating how power is enacted in a publish or perish culture, that operates with time-limited funding and in an environment that is increasingly dependent on fixed short-term contracts [14, 15]. Such restraints again limit the capacity of researchers who are committed to authentic and more equitable research partnerships with patients, whilst paradoxically providing those who are sceptical of power sharing with patient-partners a seemingly legitimized justification for tokenistic practices or zero engagement.

The concept of symbolic capital in the enactment and negotiation of power in research relationships between patients and researchers is a relatively new area of investigation [12]. In this context, the possession and display of prestige, status and authority may be derived from a patient-partners' illness experience [12]. The autoethnographic study (Chapter 4) in this dissertation demonstrates the significant potential of the symbolic capital that frail and seriously ill patient-partners' bring to the table through embodied and experiential knowledge. Yet, as also demonstrated in my autoethnographic account, there remain those in the research community who are distrustful of patient-partners' motivations for sharing this knowledge, and potentially regard it as a lesser form of knowledge. De-valuing experiential knowledge & patient-partners'

contributions can be seen as scholarly domination [16] and serve as a stark reminder of the asymmetries of power inherent in many researcher-patient partnerships [16]. Further complicating matters is that patients' symbolic capital is not static and may weaken over time [12] which has serious implications for frail and seriously ill patient-partners whose illness trajectories are subject to change.

The spheres of authority in the positivist paradigm of biomedical and applied health research replicate a strict hierarchy of knowledge production, privileging characteristically scientific ways of thinking and rendering the inclusion of experiential knowledge problematic [17]. Relationships governing knowledge production are fraught with tension even when that knowledge is developed with other academics, each of whom bring their own symbolic and social capital through professional codes of conduct, training, and codified knowledge [18]. Intra-team tension may be further heightened with the introduction of others who lay claim to expert knowledge by experience [19]. Careful consideration must be afforded to frail and seriously ill patient-partners who may be particularly vulnerable to receiving the negative or sceptical views of others who perceive their input as a lesser form of knowledge [20].

The sharing of power in research relationships is fraught with complexity. Partnering with patients in research has challenged the status quo at both a micro and a macro level [12] As demonstrated in my autoethnography study (Chapter 4), many researchers and institutions have actively embraced patient-partners' experiential knowledge as a legitimate and much needed form of expertise. At a personal and team level, promotion of patient-partners' autonomy in research relationships requires an openness to dissenting opinions and a willingness to embrace the requisite emotional labor associated with navigating difficult conversations and conceding power where appropriate [14]. At the macro level, significant advocacy and action is required to

redress long-standing structural and institutional barriers to power sharing, e.g., university and clinical hierarchies, pressure from funders, and a paucity of financial and human resources for research partnerships [12]. Resetting the power equilibrium also falls to patient-partners who have a responsibility to harness their individual and collective agency to ensure they are partnering on their own terms and in a way that meets the objectives of the research endeavor, whilst also serving the needs of the broader patient population under study.

5.4. Representation

Representation and inclusivity function as central tenets of patient engagement in research and are increasingly built into standards to guide the practice [21]. Yet, certain groups, including those who are frail and seriously ill, appear to be extended less opportunity to partner in research. This dissertation provides a timely contribution to our knowledge of the extent to which frail and seriously ill patients serve as partners in research and speaks to the practical, attitudinal and systemic barriers to their involvement. Somewhat encouraging are the findings generated through the systematic review (Chapter 2) which revealed evidence over the last decade of the increasing propensity for research teams to partner with patients who are frail and seriously ill. The systematic review (Chapter 2) emphasized concerns related to a lack of detailed reporting of patient characteristics, which in turn confounds the issue of under-representation of research partnerships with frail or seriously ill patients in the literature. This oversight makes it difficult to gauge the inclusion of individuals from diverse patient populations throughout the stages of the research process. Concerns about under-reporting have been highlighted elsewhere in the literature [22-25]. In fact, surprisingly little is known about who is engaged and at what level of intensity; and conversely, who is not engaged and the impacts of their exclusion [26].

The systematic review and related sub-analysis (Chapters 2 and 3) highlighted the ethical and practical challenges posed by the conflation of frail and seriously ill patient-partners with other stakeholders (e.g., caregivers, those experiencing chronic disease, or those in remission/survivors, advocacy group members). This practice presents further limitations to our understanding of the data surrounding engagement of frail and seriously ill patients as partners in research. Caregivers and patient advocacy groups are often called upon as a proxy, but caution is required as they may not be representative of the patient experience, particularly in circumstances towards end of life or during acute serious illness [27]. A patient's lived experience is vastly different depending where they are situated along the trajectory of their illness/condition. Patients' experiential knowledge shifts as their health changes; as they move through diagnosis, to treatment, to after treatment (which is markedly dependent on whether their disease/condition is cured, persists as a chronic condition, or relapses) [28]. In treating patients as a homogeneous group, it fails to capture essential characteristics of their needs and experiences over time. Furthermore, it deprives caregivers, those experiencing chronic disease, or those in remission/survivors of the opportunity to speak to their own distinct lived experience.

The autoethnographic study (Chapter 4) offered unique perspectives of both the positive and negative aspects of representation. Experiential knowledge helps us to tap into knowledge that is under-developed [16]. In this study, I provided a crucial and novel contribution to the role of embodied knowledge production in the discourse on representation in patient engagement. I was also able to demonstrate the importance of giving primacy to my patient-partner voice/experience during serious illness. Patients are situated within the context and temporality of illness experience [29]. It is therefore imperative that patients experiencing frailty or dealing

with serious illness be extended the opportunity to partner in research. Others may describe what they see but they will never be able to relay the depth of that experience.

Both the sub-analysis and the autoethnography (Chapters 3 and 4) highlighted the ethical imperative and the challenges faced by researchers in attempting to meet the mandate for recognition, diversity, inclusion and more equitable representation in the patients with whom they are partnering. The focus on diversity and representation is increasingly tied to the (visual) demographic characteristics of patient-partners [26]. But whilst there is concern about the lack of representation of marginalised and seldom heard groups, there is surprisingly little discussion about how to address these concerns [30]. This has left many academics struggling with how they operationalize it, and the consequences of not doing it appropriately [31, 32]. As illustrated in my autoethnography study (Chapter 4), I discuss the problem of discounting experiential knowledge and focusing solely on visible characteristics, that may lead researchers to run the risk of inflicting unintended harms and causing unnecessary offence to patient-partners. Paradoxically, in striving to meet the mandate for diverse representation in patient-partners, surprisingly little attention is directed towards the diversity and characteristics of the researcher members of the team.

5.5. Implications for Nursing

This doctoral dissertation makes a substantive methodological, theoretical and ethical contribution to partnering with frail and seriously ill patients in nursing research. The findings from these studies have implications for education and research (including research conduct and future direction) in nursing and for other academic researchers as well.

5.5.1. Nursing Education

Based on the contribution of this dissertation and the broader literature, gaps in nursing education have been identified in relation to the epistemology, praxis, and impacts of partnering with patients in research. Furthermore, early career researchers report feeling inadequately prepared to deal with the practical and ethical implications of partnering with patients in research – even at lower levels of engagement with patients whose conditions are more stable [33]. As a result of this deficit, early and mid-career researchers have identified key priorities for nursing education, including the incorporation of education and training on patient engaged research into all graduate nursing programs (masters, doctoral, and nurse practitioner). Embedding patient engaged research into doctoral training has served to enable patient-partnerships in doctoral research, including partnership with patients with serious illness [34, 35]. However, given the additional time, effort and resources required to enact meaningful patient-partnerships, especially with more vulnerable patients, it is imperative that doctoral students engaged in this endeavor are provided with the necessary academic, financial and supervisory support to sustain the relationship whilst enhancing their skills [35].

To promote meaningful and more intensive research partnerships with frail and seriously ill patients, supplementary education is required to enhance interpersonal skills [7]. Training programs on cultural humility, team-science, patient safety, conflict resolution, and communication skills are also warranted due to the complex, multi-faceted nature of communication required for successful research partnerships with patients [36]**.** In palliative care and cancer research, it is especially important for novice researchers who are partnering with patients to be equipped to deal with distress (their own distress due to exposure to sensitive issues and the suffering of others and the potential distress displayed by patient-partners); it is

therefore imperative they have the appropriate resources and processes in place to support them [35].

In addition to graduate student education, training and support should be extended to early career researchers, with ongoing mentorship provided by more experienced academic researchers who have patient engagement practices firmly embedded into their research programs. Innovative programs, such as those co-created, co-taught, and delivered to patients, researchers and other stakeholders within the same classroom promote an inclusive learning environment; moreover, this approach has demonstrated efficacy in building capacity for patient engaged research [37]. Direct interaction with patient-partners in an innovative learning environment such as this may also be instrumental in shifting recognition and respect for multiple frames of knowledge and heighten appreciation for patients' lived experience.

5.5.2. Nursing Research

This dissertation demonstrates the need for nursing researchers to embrace research partnerships with patients, whilst also promoting the value of safe ethical practices as a foundation to the partnership. Nurse scientists need to share and publish work that contributes to a deeper understanding of what constitutes meaningful research partnerships with patients. Nurses are ideally positioned to champion inclusive and supportive research partnerships with frail and seriously ill patients. As patient care shifts from paternalism to a more holistic and collaborative approach, so too should our research partnerships [38, 39]. In order to facilitate safe and ethical practice, it is imperative that team dynamics and structural factors are proactively addressed at the initiation of a project and revisited throughout the research life cycle.

Preparedness and the positionality of researchers and patient-partners should be addressed before they enter into research partnerships [40]. The importance of self-reflection and de-briefing should not be underestimated; nursing researchers need to be aware of their own strengths and weaknesses and value the contribution of their patient-partners [38]. As demonstrated throughout this dissertation, relationships are the foundation to the creation of meaning and the sharing of power in partnerships with patients. Nursing researchers should pay attention to the intersubjective spaces between themselves and patient-partners; this relational and ethical practice is fundamental to facilitating an inclusive and safe participatory space for research partnerships across the entire research trajectory of the project. Additional attention is required to establish what diverse representation means and how representation is enacted to ensure exclusionary practices are not unintentionally reified. Respect for person acknowledges the vulnerability and agency bound within the illness identities of patient-partners whilst also incorporating the knowledge associated with their non-illness identities.

5.5.3. Implications for Future Research

This dissertation has highlighted a number of areas of focus for future nursing research with frail and seriously ill patient-partners. In spite of continued commentary on meaningful research partnerships, additional inquiry is needed to examine how all team members co-construct meaningful partnerships. Nursing researchers also need to understand how a focus on meaningful engagement serves to shift practice and promote better research outcomes [41]. The ontological component of the ways in which patients experience partnering in research during serious illness and frailty have been relatively unexplored. As demonstrated in the autoethnographic study (Chapter 4) the current methodological imperative of patient engaged research does not fully capture the deeply personal ways in which patient-partners' create

meaning and navigate sensitive relational issues, thereby necessitating novel approaches to inquiry. Autoethnography emanates from the social sciences and education, but analytic autoethnography in particular is now gaining traction as a viable and effective research methodology in nursing and health science research [42, 43]. Moreover, embodied autoethnographic accounts in health research can be a powerful tool in ascertaining the impact of power relations within research partnerships with patients. Similarly, collaborative autoethnography offers research teams the opportunity to turn their interrogative tools on themselves in order to generate and utilize data to better understand and evaluate research partnerships [44]. Further inquiry is required to determine how power is enacted and negotiated in research partnerships [41], particularly in situations where patient-partners may be more vulnerable, e.g., those who are dealing with frailty and serious illness.

The negative impacts and the unintended harms of research partnerships remain largely under-reported in the literature [41]. The continued lapse in detailed reporting makes it difficult to evaluate where changes in policy and practice should be directed. There is a paucity of investigation into the qualities, skills and values required for both patients and researchers in enabling and establishing successful research partnerships. The emerging discourse of the role of humility in negotiating research partnerships offers some promise, but to date the concept of humility remains relatively underexplored in the patient engagement literature [39]. The clinical literature has focused on humility in physician-patient relations; however, nurses and physicians are trained differently and exhibit differences in communication styles [36]. This distinction raises the question about whether there are significant disciplinary differences in the enactment of research partnerships with patients and whether humility plays a mediating role in promoting meaningful and more equitable relationships.

5.6. Conclusion

The findings generated from this dissertation clearly signal the need for more inclusionary practices by researchers when partnering with patients in research. Given the significant benefits of research partnerships with those who are frail and seriously ill, researchers and patients need to work together to harness the full potential of patients' experiential knowledge during periods of serious illness and frailty. Embodied knowledge production is instrumental to a deeper understanding of patients' lived experience; empowering patients and generating research that is more relevant and meaningful to the patient population under study. The findings in this dissertation are offered as a call to action for nursing researchers to not only embrace patient-partnerships in research but to ensure that frail and seriously ill patients have the opportunity to partner across the research trajectory using an inclusive approach with a balanced distribution of power to achieve meaningful engagement.

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Appendices

Appendix 1 – Certificate of Ethics Approval

20/05/2022

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CERTIFICAT D'APPROBATION ÉTHIQUE | CERTIFICATE OF ETHICS APPROVAL

Numéro du dossier / Ethics File Number	H-04-22-7997
Titre du projet / Project Title	An Autoethnography of Patient Engagement in Research During Serious Illness
Type de projet / Project Type	Thèse de doctorat / Doctoral thesis
Statut du projet / Project Status	Approuvé / Approved
Date d'approbation (jj/mm/aaaa) / Approval Date (dd/mm/yyyy)	20/05/2022
Date d'expiration (jj/mm/aaaa) / Expiry Date (dd/mm/yyyy)	19/05/2023

Équipe de recherche / Research Team

Chercheur / Researcher	Affiliation	Role
Claire LUDWIG	École des sciences infirmières / School of Nursing	Chercheur Principal / Principal Investigator
Dawn STACEY	École des sciences infirmières / School of Nursing	Superviseur / Supervisor
Ian GRAHAM	Département d'épidémiologie et santé publique / Department of Epidemiology and Public Health	Autre / Other
Wendy GIFFORD	École des sciences infirmières / School of Nursing	Autre / Other

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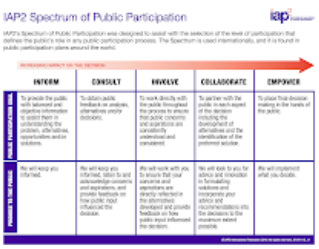

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Appendix 3 – Chapter 2 Supplementary File 1: International Association of Public Participation (IAP2) Spectrum of Public Participation

IAP2 Spectrum of Public Participation

IAP2's Spectrum of Public Participation was designed to assist with the selection of the level of participation that defines the public's role in any public participation process. The Spectrum is used internationally, and it is found in public participation plans around the world.

INCREASING IMPACT ON THE DECISION

	INFORM	CONSULT	INVOLVE	COLLABORATE	EMPOWER
PUBLIC PARTICIPATION GOAL	To provide the public with balanced and objective information to assist them in understanding the problem, alternatives, opportunities and/or solutions.	To obtain public feedback on analysis, alternatives and/or decisions.	To work directly with the public throughout the process to ensure that public concerns and aspirations are consistently understood and considered.	To partner with the public in each aspect of the decision including the development of alternatives and the identification of the preferred solution.	To place final decision making in the hands of the public.
PROMISE TO THE PUBLIC	We will keep you informed.	We will keep you informed, listen to and acknowledge concerns and aspirations, and provide feedback on how public input influenced the decision.	We will work with you to ensure that your concerns and aspirations are directly reflected in the alternatives developed and provide feedback on how public input influenced the decision.	We will look to you for advice and innovation in formulating solutions and incorporate your advice and recommendations into the decisions to the maximum extent possible.	We will implement what you decide.

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Appendix 4 – Chapter 2 Supplementary File 2: Medline Search Terms

Steps	Query
#1	Patient Participation/
#2	(patient* adj2 participat*).tw.
#3	(patient* adj2 engag*).tw.
#4	(patient* adj2 research*).tw.
#5	(patient* adj2 empower*).tw.
#6	(patient* adj2 involv*).tw.
#7	(patient* adj2 collabor*).tw.
#8	(patient* adj2 partner*).tw.
#9	(patient* adj2 consult*).tw.
#10	(consumer* adj2 participat*).tw.
#11	(consumer* adj2 engag*).tw.
#12	(consumer* adj2 research*).tw.
#13	(consumer* adj2 empower*).tw.
#14	(consumer* adj2 involv*).tw.
#15	(consumer* adj2 collabor*).tw.
#16	(consumer* adj2 partner*).tw.
#17	(consumer* adj2 consult*).tw.
#18	(user* adj2 participat*).tw.
#19	(user* adj2 engag*).tw.
#20	(user* adj2 research*).tw.
#21	(user* adj2 empower*).tw.
#22	(user* adj2 involv*).tw.
#23	(user* adj2 collabor*).tw.
#24	(user* adj2 partner*).tw.
#25	(user* adj2 consult*).tw.
#26	(stakeholder* adj2 participat*).tw.
#27	(stakeholder* adj2 engag*).tw.
#28	(stakeholder* adj2 research*).tw.
#29	(stakeholder* adj2 empower*).tw.
#30	(stakeholder* adj2 involv*).tw.
#31	(stakeholder* adj2 collabor*).tw.
#32	(stakeholder* adj2 partner*).tw.
#33	(stakeholder* adj2 consult*).tw.
#34	(citizen* adj2 participat*).tw.
#35	(citizen* adj2 engag*).tw.
#36	(citizen* adj2 research*).tw.
#37	(citizen* adj2 empower*).tw.
#38	(citizen* adj2 involv*).tw.
#39	(citizen* adj2 collabor*).tw.
#40	(citizen* adj2 partner*).tw.
#41	(citizen* adj2 consult*).tw.
#42	(lay* adj2 participat*).tw.
#43	(lay* adj2 engag*).tw
#44	(lay* adj2 research*).tw.
#45	(lay* adj2 empower*).tw.
#46	(lay* adj2 involv*).tw.

#47	(lay* adj2 collabor*).tw.
#48	(lay* adj2 partner*).tw.
#49	(lay* adj2 consult*).tw.
#50	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49
#51	(translational adj3 research*).tw.
#52	(shared adj3 learn*).tw.
#53	exp Evidence-Based Practice/
#54	evidence-based practice.tw.
#55	Biomedical research/
#56	Health Services Research/
#57	Clinical Trial/
#58	delphi*.tw.
#59	(research adj utilization).tw.
#60	(research adj develop*).tw.
#61	(research adj implement*).tw.
#62	(research adj translat*).tw.
#63	(guideline* adj implement*).tw.
#64	(guideline* adj develop*).tw.
#65	(knowledge adj2 exchange).tw.
#66	(knowledge adj2 translation).tw.
#67	51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66
#68	**50 and 67**
#69	Limit 68 to humans

Appendix 5 – Chapter 2 Supplementary File 3: PRISMA 2009 Checklist for systematic review

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5-7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	8
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	8
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	10-11
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	9-10
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	10-11
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	11-12
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	12
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	12-13
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	12
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Not applicable

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Not applicable
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	13, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	13-15, Tables 3-5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	21, Table 6
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Not applicable
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Not applicable
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Not applicable
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not applicable
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	22-26
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	26-27
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	27-28
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	29

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