HS&DR Project: NIHR131800 – Integrating Palliative Care and Heart Failure: a Realist Synthesis (PalliatHeartSynthesis)

PROTOCOL: Version 1.1.

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0.1	August 2020	Applicant team	Detailed Project Description submitted with the funding application.
0.2	November 2020	Applicant team	Detailed Project Description updated in response to the Board’s feedback.
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1.1	March 2021	Investigator team	Final Detailed Project Description document (V0.2) with personal details removed for sharing via the HS&DR website.

1. Integrating Palliative Care and Heart Failure: a Realist Synthesis (PalliatHeartSynthesis)

2. SUMMARY OF RESEARCH

Background
Heart Failure is referred to internationally as a modern-day epidemic, with prevalence rates similar to the leading forms of cancer. At least 5% of those with advanced heart failure (defined as New York Heart Association (NYHA) class III and IV) in the United Kingdom (UK) are over 75 years old, rising to 22% in those ≥ 85 years, with highly complex healthcare needs. This puts considerable burden on already overstretched health service resources, with an estimated 1–2% of the NHS budget spent on heart failure. Up to 70% of advanced heart failure costs relate to hospitalisation, with 80% of those hospitalised aged ≥ 65 years. Patient burden is also considerable, involving debilitating emotional and physical symptoms which severely impact on quality of life (QoL) for patients and caregivers.

Emerging evidence demonstrates improved QoL, reduced symptom burden, and health service costs when Integrated palliative care and heart failure interventions are implemented. Integrated palliative care aims to achieve continuity of care by integrating administrative, organizational, and clinical services that make up the patients care network. However, integrated palliative care for advanced heart failure is not common practice. It is over a decade since the first national strategy for end of life care in England, 2008, closely followed by other nation specific strategies for Scotland, 2008, Northern Ireland, 2010 and Wales, 2013 emphasising equity of palliative care irrespective of diagnosis. However, only 7% of people with advanced heart failure are placed on the primary care palliative register in the UK compared to 48% of those with advanced cancer.

Aim
To understand how integrated palliative care and heart failure interventions may work in different healthcare settings (inpatient/outpatient), and for which groups of people (symptomatic and/or advanced heart failure), so we can recommend strategies to maximise the potential for widespread implementation, reduced healthcare costs, and improved QoL for patients and families.

Objectives
1. Conduct a realist synthesis to develop a programme theory of why, for whom and in what contexts desired outcomes occur
2 Use the programme theory to co-produce, with stakeholders (e.g. patient/carers, local, national, international content experts and multidisciplinary practitioners), recommendations to inform implementation of best practice and guide future research

Methods
A realist synthesis is the best approach to synthesising the evidence as successful implementation of integrated palliative care and heart failure is complex, depending on the context and people involved. Our synthesis of the literature will follow Pawson's five iterative stages: 1) locating existing theories; 2) searching for evidence; 3) article selection; 4) extracting and organising data; 5) synthesising the evidence and drawing conclusions. We will recruit a UK wide stakeholder group, including NHS Management, and healthcare professionals (HCPs) involved in the delivery of palliative care and heart failure management, Public Health Agency Northern Ireland, Palliative Care Policy Groups, Community Groups, plus members of the public and patients, to advise and give us feedback throughout the project. We will also follow RAMESES quality standards for conducting a realist synthesis, developed by one of the research team.

Outputs and dissemination

We will collaborate closely with our stakeholder group to ensure our findings are developed into user friendly guides tailored to the needs of key audiences. Marie Curie, the British Heart Foundation, and NIHR will also help us disseminate through their well-established channels. Findings will also help inform further research in the field of palliative care and heart failure. Additional funding will be sought for such research once this synthesis is completed.

3. BACKGROUND AND RATIONALE

Cardiovascular disease is the most common cause of death worldwide (1). Heart failure characterises the final phenotype of many cardiovascular diseases, with a prevalence of approximately 1–2% in the general population, increasing to >10% in those aged ≥70years (2). A population-based study of 4 million individuals in the United Kingdom (UK) showed an increase in the prevalence of heart failure to that similar of the four most common forms of cancer (lung, breast, prostate and bowel) combined (3). Symptom burden in advanced heart failure cases is also comparable to advanced cancer, with research showing high prevalence of fatigue (69-92%), dyspnoea (60-88%), pain (44-77%) and depression (50%) (4).However, compared to patients with cancer, those with heart failure understand less about the terminal nature of their illness. In addition, many of these patients have limited access to palliative care, despite symptoms, frequently die in hospital while receiving invasive and intensive medical interventions, lacking opportunities to discuss options focused on improving quality of life (QOL) and end-of-life care (5).

Advanced heart failure or patients with NYHA III or IV symptoms, account for over 150,000 hospitalisations per year in the UK (6). Healthcare costs attributable to heart failure increase sharply in advanced stages of the illness and are dominated by hospital care. An estimated 1–2% of the NHS budget is spent on heart failure, of which 60–70% relates to costs of hospitalisation, with 80% of those hospitalised aged ≥ 65 years old (7). There is potential to save the NHS money through evaluation and implementation of interventions that demonstrate reductions in healthcare costs and hospitalisations for advanced heart failure (8). Palliative care has been shown to significantly reduce healthcare costs overall compared to usual care and reduce hospital costs by up to £4955 per patient compared to usual care (9). The National Audit Office review of end of life care recommended palliative care for patients with heart failure due to likely cost savings in reducing utilisation of acute services (10).

Although palliative care was initially established for patients with advanced cancer in recognition of poor QoL and high symptom burden, its benefits are increasingly being recognised and expanded to other chronic life limiting illnesses, such as heart failure (11). It seems evident that people with advanced heart failure should have access to palliative care which aims to *“improve the quality of life of patients and their families facing the problem associated with life threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial, and spiritual”* (12, para 2). However, only a small proportion of people with advanced heart failure are placed on the primary care palliative register in the UK compared to those with advanced cancer (7% vs 48%) (13). Despite national policy directives (14), we still have stark evidence of inequities of palliative care provision for patients with advanced heart failure. Although a recent All Party Parliamentary Group on heart failure noted some progress towards integrated palliative care and heart failure, this has been slow and inconsistent across the UK (15). Indeed, a recent study in the UK involving 499 palliative care consultants, non-consultant doctors, specialist nurse practitioners and other nurses working in palliative care found that, although there was palliative care provision in the hospice (59%), hospital (46%), and community setting (47%), palliative care practitioners received less than 10 or no referrals for patients with heart failure per year (16). This low number of referrals is startling given the high prevalence of heart failure, estimated at over half a million people in the UK (6). A more recent review of acute heart failure deaths in hospital found that only half of hospitals across the UK had specific palliative care consultant ward rounds (85/169; 50.3%), and only 29.4% of hospitals had a palliative care clinician as part of the multidisciplinary heart failure team (17).

Overview of the existing evidence

Integrated palliative care aims to achieve continuity of care by integrating administrative, organizational, and clinical services that make up the patients care network (18). Examples of integrated palliative care and heart failure Interventions include collaborations and shared goal setting between palliative care and clinical cardiology teams to ameliorate symptoms with palliative care goals. alongside heart failure management (19), and social work led palliative care services alongside heart failure management (20); all aimed at improving physical, psychological, social, spiritual, and end of life outcomes.

Although two decades have passed since the first publication on the benefits of palliative care for patients with advanced heart failure (21) many patients remain less likely to receive palliative care compared to patients with advanced cancer (13,22). The poor integration of palliative care into advanced heart failure management can be explained by a number of factors, including uncertainty around the heart failure disease trajectory and complexities of communicating this uncertainty to patient and family members. Heart failure is an unpredictable illness, with periods of stability of symptoms, interjected with numerous exacerbations, of which many can lead to a temporary improvement in health status; others can lead to a progressive decline towards death. Many patients with advanced heart failure overestimate survival by up to 40%, further adding to cardiology providers reluctance to initiate difficult conversations around prognosis. This difficulty is further compounded by lack of patient and practitioner knowledge around what palliative care is; misunderstanding that palliative care equals end-of-life care only. The fragmentation of inpatient and outpatient services also creates a barrier to the holistic need's assessment required for an integrated palliative care approach (11).

Until recently, the lack of evidence from clinical trials demonstrating benefits of palliative care for people with advanced heart failure posed an additional barrier. However, research in this area has shown an exponential increase since the turn of the century, increasing from 10 publications on average in 2000 until over 100 publications per year in 2017 (23). McIlvennan and Allen (11) published a literature review summarising the evolving role of palliative care for patients with heart failure, along with the barriers and opportunities for its integration into routine practice. The review included a search of PubMed and clinicaltrials.gov registry between January 2010 to September 2015, with an additional search for publications prior to 2010 which were only included if they demonstrated impact on the current state of evidence. Findings from the review highlighted the need for evidence on how best to integrate palliative care and heart failure given the cultural and environmental differences in how palliative care services are delivered.

A forward citation search of McIlvennan and Allen's (11) review, along with a PubMed search using the same search terms "heart failure", "palliative care", "quality of life", "symptom burden", and "end of life" identified three subsequent systematic reviews (24-26).

Diop et al.'s (24) Systematic Review and Meta-Analysis of Palliative Care Interventions for Patients with Heart Failure included fifteen studies, all of which varied in terms of methods, patient populations, interventions, settings, measurement tools, and outcomes. Although the authors suggest that findings support the use of home and team-based palliative care interventions for improving patient-centred outcomes, documentation of preferences and healthcare utilisation, these claims must be interpreted with caution as the authors did not conduct a quality appraisal of included studies. Given the heterogeneity of the included studies it was not possible to determine the most effective palliative care approach for the management of patients with advanced heart failure.

Two years later, Datla et al (25), published a more robust systematic review and narrative synthesis of patients with symptomatic heart failure, including a more comprehensive search of five electronic databases and grey literature. Twenty-three studies were included. Evaluation phase studies provided evidence for the effectiveness of multi-component, multi-disciplinary palliative care interventions for improving patient-centred outcomes (symptom burden, depression, quality of life, functional status) and reducing healthcare resource utilisation and costs of care, with no impact on survival. The most recent systematic review of randomised controlled trials (n=9) conducted by Sahlollbey et al. in 2020 showed that compared to usual care (heart failure management only), the integration of multidisciplinary palliative care improved both symptom burden and QoL, substantially reduced hospitalizations and had no adverse effects on survival (26).

A recent editorial (22) exploring the phenomenon of inconsistent implementation of integrated palliative care and heart failure interventions proposed a realist approach (focusing on what works, for whom, and in what circumstances) could provide a sound theoretical understanding of the barriers and facilitators to routine implementation. The research to date has focused on “trying to evidence effectiveness through a linear cause and effect approach, which fails to ignore the messy, non-linear world of real-life practice” (22, p.1). This is further compounded by the heterogeneity of the research to date. Neither Diop et al. (24) or Datla et al. (25) were able to conduct a meta-analysis due to the large variation in integrated palliative care and heart failure interventions worldwide. Overall, Datla et al. (25) concluded that there is no clear consensus around: 1) the core components of integrated palliative care and heart failure interventions, 2) the ideal configuration for the multi-disciplinary team, and 3) the most effective service provision model to ensure that generalist and/or specialist palliative care is tailored to patient needs.

The issue of heterogeneity was further highlighted in a narrative literature review aimed at identifying the key characteristics of integrated palliative care and heart failure interventions (27). Of the nine studies included, all integrated palliative care and heart failure interventions were implemented in different countries with different models of health service provision for citizens (USA, Sweden, Hong Kong), different settings (inpatient, outpatient and home-based), delivered by a heterogenous mix of multidisciplinary teams (cardiologists, heart failure-nurses, General Practitioners, community nurses, occupational therapists), using different modes of delivery (face-to-face, telemedicine), and involving different intervention components (symptom management, advance care planning). Therefore, we still do not know which intervention produces the best outcomes for patients and their families (what works: specialist vs primary care etc.?), when best to initiate palliative care (for whom; at what stage in the disease trajectory?), or the optimal delivery method (in what circumstances; required infrastructure, staff competencies etc.?).

Capacity to generate new knowledge

A realist approach can address the heterogeneity of existing research by identifying common mechanisms, contextual features and outcomes. Therefore, the proposed research will make an empirical contribution to the existing body of knowledge with reference to current health and social care policy and practice as follows:

1. by developing a programme theory of how integrated palliative care and heart failure is supposed to work, for whom and in what contexts, we can develop recommendations to guide best practice and future research for older patients with advanced heart failure. This is in line with current NHS ambitions to identify and support implementation of best practice interventions for older people with complex

health needs. Given that heart failure often dominates older people's health, medical, psychological and social needs overall (11), and integration of palliative care has been shown to be effective for alleviating psychological and physical symptoms – determining what works, for whom, and in what circumstances will help address current gaps in the knowledge base to improve patient, carer and health service outcomes.

2. by focusing on the integration of a palliative care approach to heart failure management, we can use the findings from the realist synthesis to promote tailored and personalised care planning which documents peoples' preferences and supports choices about key aspects of care towards the end of life for older people [NHS Improving care for older people https://www.england.nhs.uk/ourwork/clinical-policy/older-people/improving-care-for-older-people/]

Realist Synthesis is a theory-driven approach for understanding existing diverse multiple sources of evidence relating to complex interventions. It is theory driven because it uses evidence to iteratively develop and test structurally coherent explanations (i.e. theories) of complex interventions. The realist approach aims to understand "What works for whom, in what circumstances, how and why?". This approach optimally explores how and why a complex social programme involving human actions and decisions, such as integrating palliative care and heart failure management, may or may not work (28).

Although there are a number of systematic reviews (24-26) and pragmatic studies of the practicalities and challenges of introducing integrated palliative care and heart failure (29), such studies are largely atheoretical and do not 'explain' what works, for whom, and in what circumstances when trying to: 1) implement an intervention into a different setting; 2) develop an optimal implementation strategy; and 3) inform clinical guidelines and policy decision making around what needs to be in place to facilitate their use in routine practice.

Emphasis is put on the importance of theory when developing and evaluating complex (i.e., multi-component) interventions, as evidence suggests that theoretically informed interventions lead to better outcomes (30). Theories help us to make sense of complex phenomena by providing tentative explanations for why and under what circumstances behaviours occur, or as importantly do not occur. Theory informed interventions can then be designed or modified to address these myriad of influences (31).

3a. EVIDENCE EXPLAINING WHY THIS RESEARCH IS NEEDED NOW

The UK population is living longer than ever before. There are currently more than three million people aged ≥ 80. Projections estimate that this figure will almost double by 2030 and reach eight million by 2050 (32). Although we can celebrate this achievement in life expectancy, it comes with significant challenges for the NHS now and in the future. Older people have complex health needs, with on average 4.5 comorbidities. Heart failure often dominates their physical and psychological needs overall (11), along with being the costliest aspect of their care due to high rates of hospitalisation and futile treatment as their heart failure progresses (7). Older people with advanced heart failure have undeniably had their needs overlooked, with calls for more attention to, and research for this vulnerable group to ensure they receive appropriate, effective treatment and care (11,33). As outlined previously, palliative care can mitigate both the human and health service costs by reducing symptom burden and health service costs (7,9-10). Yet, almost two decades after the first publication on the benefits of palliative care for patients with heart failure (21) when compared to patients with cancer, heart failure patients are more likely to receive palliative care too late, or not at all (13,22). Therefore, in many parts of the UK routine implementation of palliative care integrated with active heart failure management is still an ideal rather than a reality.

Although we have some promising examples of integrated palliative care and heart failure interventions (19-20), many have been developed in different countries, in a number of different settings, delivered by a heterogenous mix of multidisciplinary teams, using different modes of delivery and involving different intervention components (28). Hence, it is unknown which model works best, for whom, or in what circumstances. Over recent months, as a consequence of the global Covid-19 pandemic, the concept and delivery of palliative care has been redefined. Escalating mortality rates with restrictions on family involvement and altered modes of communication have renewed professional’s recognition of the importance of collaborative working across specialities and geographical boundaries (34). Findings from this review will recognise that the evidence during the pandemic can illustrate the ongoing rapid changes and uncertainties facing the NHS now and in the future. It is by combining and analysing this evidence that we seek to answer the vital questions set out below.

4. AIMS AND OBJECTIVES

Aim
To understand how integrated palliative care and heart failure interventions may work in different healthcare settings (e.g. inpatient/outpatient), and for which groups of people (e.g. Symptomatic and/or advanced heart failure), so we can recommend strategies to maximise the potential for widespread implementation, reduced healthcare costs, and improved QoL for patients and families.

Objectives
1. Conduct a realist synthesis to develop a programme theory of why, for whom and in what contexts desired outcomes occur
2 Use the programme theory to co-produce, with stakeholders (e.g. patient/carers, local, national, international content experts and multidisciplinary practitioners), recommendations to inform implementation of best practice and guide future research

Review Questions

1. What are the mechanisms by which integrated palliative care and heart failure interventions work in order to produce their intended outcomes?
2. What are the contexts, which determine whether integrated palliative care and heart failure interventions produce their intended or unintended outcomes?
3. In what settings are integrated palliative care and heart failure interventions likely to be effective?

5. RESEARCH PLANS

Objective 1: Conduct a realist synthesis to develop a programme theory of why, for whom and in what contexts desired outcomes occur

5.1 Methodology – Realist synthesis
The proposed study is a realist synthesis of literature on integrated palliative care and heart failure interventions. Realist synthesis is a practical methodological approach designed to inform policy and practice. The realist synthesis method is distinct from other types of literature reviews as it is based on an interpretive and theory driven approach, synthesising evidence from qualitative, quantitative and mixed-methods research. The unique contribution of this approach is that it yields transferable findings that explain how and why context can

affect outcomes. It does so by developing realist programme theories that explain how, why, in what contexts, for whom and to what extent interventions 'work' (28).

Realist syntheses are particularly suited to research on integrated palliative care and heart failure as they focus on making sense of the contextual factors that determine the outcomes of an intervention. Like other interventions that seek to propagate behavioural change, implementation of integrated palliative care and heart failure is highly context dependent, i.e. implementation of the same intervention will vary in its success depending, for example, on who delivers it and how it is delivered, the characteristics of the health care professionals, the circumstances surrounding it, and the tools and techniques used. Research designs that seek to "strip away" these contexts limit our understanding of "how, when and for whom" the intervention will be effective (28). A realist synthesis takes context as central to any explanation by exploring how an intervention manipulates context to trigger mechanisms that cause behavioural change.

The explanation building will ultimately start with the development of an initial programme theory of "how integrated palliative care and heart failure interventions produce desired outcomes (or not)". To achieve this, our initial realist programme theory will set out the necessary steps needed to accomplish the final intended outcome(s) from implementation of integrated palliative care and heart failure. As the synthesis progresses, how and why each step (or intermediate outcome) can then be 'made' to happen will be explained using a realist logic of analysis - i.e. what relationship between context and mechanism(s) might lead to that outcome (28). This initial programme theory is then challenged and shaped through an iterative process of testing - i.e. parts of it are confirmed, refuted or refined against a range of relevant data from existing literature.

5.2 Plan of investigation

The plan of investigation will follow a detailed realist synthesis protocol, which will be developed by the research team. We have extensive experience in conducting both realist syntheses and systematic reviews. The protocol will be designed based on Pawson's (2005) five iterative steps in conducting realist synthesis. It will also be informed by the quality and publication standards and training materials for realist synthesis developed by one of the research team members (35) (see www.ramesesproject.org). The protocol will be registered with PROSPERO which is a prospective register of systematic reviews.

Step 1: Locate existing theories

The purpose of this step is to locate existing theories that explain why, how, in what contexts, for whom and to what extent does integrated palliative care and heart failure work. This involves identifying the theories that explain how integrated palliative care and heart failure is supposed to work to bring about improved outcomes for advanced heart failure patients and their family/carers. While we have already established there is limited theory underlying integrated palliative care and heart failure interventions, the realist synthesis approach allows for the literature net to be cast wider to include literature from other fields and other professions where potentially shared mechanisms may be in operation.

To identify these theories, we shall iteratively: a) consult with key content experts in our stakeholder group (see Table 1 below), and b) informally search the literature to identify existing theories. The informal searches conducted in step 1 differ from the more formal searching that will be carried in step 2 as their purpose is to quickly identify the kinds of theory that may be relevant; thus exploratory and informal search methods including, citation tracking and snow-balling based on known existing studies will be used. Once the theories have been identified, we shall build an initial programme theory to test in the synthesis. Programme theory development will necessitate iterative discussions within the research team to bring together the different theories into an initial programme theory.

Table 1: Stakeholder group members

	Group	Members
1	NHS Management and Leadership	- Dr Lana Dixon - Clinical heart failure lead in Belfast Health and Social Care Trust (BHSCT), Northern Ireland (NI) - Representative - Clinical service manager (BHSCT), NI - Dr Karen Hogg - Cardiology Consultant and Clinical Lead for Cardiac Palliative Care at NHS National Services Scotland,
2	Health care professionals involved in the delivery of palliative care and heart failure management	- Representative - Heart Failure Nurse BHSCT, NI - Dr Carol Stone – Consultant in Palliative Medicine Marie Curie Hospice Belfast and BHSCT, NI - GP NHS England - Dr Grainne Doran, Principal GP Bangor Health Centre Northern Ireland, Former Chair of the Royal College of General Practitioners in NI
3	PPI Partners: BHF London heart failure group members	- Bob Jones - John Burden - Robert Ruane
4	National and International Research Clinicians in palliative care and heart failure	- Prof Miriam Johnson - Professor of Palliative Medicine at Hull York Medical School England, leading academic and clinician in the field of palliative care services for people with heart failure - Dr Clea Atkinson - Palliative Care Consultant and Clinical Lead for the Heart Failure Supportive Care pathway at NHS Wales - Prof.Akshay Desai - Medical Director, Cardiomyopathy and Heart Failure Program, Advanced Heart Disease Section - Harvard Medical School and Brigham and Women’s Hospital, USA, led on social work assisted integrated palliative care and heart failure pilot RCT - Prof Joseph G. Rogers - Chief Medical Officer Cardiology, Duke University Health System, USA, led on large RCT evaluating palliative care for heart failure
5	Policy and Community Groups	- Richard Meade, Head of Policy and Public Affairs for Marie Curie Scotland, actively involved in drafting BHF new heart failure strategy - Karen McCammon - Health Services Engagement Lead BHF NI. Works closely with colleagues across UK and will ensure findings have national relevance

Named individuals have kindly confirmed their involvement

Step 2: Search strategy

Formal search

The goal of Step 2 is to find a body of relevant literature in order to further develop and refine the initial programme theory developed in Step 1. The searches will be designed, piloted and carried out by an experienced information specialist with experience of carrying out iterative searches for realist synthesis (CD). The following databases will be searched as required CINAHL, PsycINFO, PubMed, MEDLINE, AMED and EMBASE. A search for grey literature will also be carried out in Google, OpenGrey, NICE, and Health Management Information Consortium (HMIC). Citation searching will also be undertaken including 'cited by' searches and searches of citations in the reference lists of relevant documents. We shall also ask the research team and steering group to identify any literature they may think is relevant. The databases will be searched using free text keywords and controlled vocabulary where appropriate, using terms such as advanced heart failure AND palliative care. The strategy will be informed by our informal scoping searches, search strategies employed in existing reviews and knowledge of the project team. Any literature that is likely to provide conceptually rich data, including grey literature, will be considered for inclusion in the synthesis. Three existing reviews (including 43 individual studies) and results of a scoping search in MEDLINE conducted by CD indicate that we will have sufficient material to develop the programme theory.

Screening
When screening the identified literature, the inclusion and exclusion criteria will be deliberately broad as we seek to identify quantitative, qualitative, mixed-methods and non-empirical documents. The following inclusion criteria will be applied:

- All documents focused on palliative care for advanced heart failure patients.
- Study design – all study designs
- Non-empirical data (e.g. from opinion/commentary pieces) which help direct/shape theory development
- Types of settings – all documents about inpatient or outpatient or home-based care settings
- Types of participant – all adult patients (18 years and over). The majority of research has involved patients with advanced heart failure (defined as NYHA class III and IV)
- Types of intervention – any combination of palliative care strategies for the management of patients with advanced heart failure
- Outcome measures – all integrated palliative care and heart failure related outcome measures

The screening process will be piloted with small samples of documents until agreement on the application of the inclusion criteria is reached within the research team. Two review authors will then independently screen the titles and abstracts of all retrieved articles to identify documents that meet the inclusion criteria (TM, RF). If there are disagreements these will be resolved through discussion between members of the research team. In the event of disagreements remaining, these will be discussed and resolved by majority vote amongst the academic stakeholder group. Documents included after title and abstract screening will then be screened again against inclusion criteria based on the full text. The same quality assurance process as described above will be used.

Additional searching
A vital part of conducting a realist synthesis involves searching for additional data to explain particular parts of the programme theory. Therefore, more searches will be conducted if we need more data to develop and test specific areas of the programme theory. Based on our understanding of integrated palliative care and heart failure to date, these could include areas like clinician/patient/informal carers attitude towards and understanding of palliative care, non-specialist palliative care education and training, having difficult conversations. These additional topics will increase the quantity of relevant data available for us to test the programme theory. The searches will be developed, piloted and refined by the research team with the help of the Information Specialist (CD). These searches will differ from the

‘formal searches’ outlined above through being more exploratory and purposive, and from a range of different disciplines. Each additional search instigated, along with the inclusion and exclusion criteria, will be discussed by the research team to ensure alignment with objectives.

Step 3: Article selection

We are aware that there will be evidence that is of variable quality. However, it is because of this potential challenge that we have chosen to use a realist review approach. Within realist reviews even 'low quality' evidence can provide important insights, but to ensure that our explanatory programme theory is sufficiently plausible and trustworthy, we will follow RAMESES quality standards for realist syntheses. For example, full text documents will be selected based on relevance (whether data can contribute to theory building and/or testing) and rigour (whether methods used to generate the relevant data are credible and trustworthy). Assessments will also be made of the plausibility and rigour at the level of the programme theory (28). The Research Fellow (RF) will read the full text of all the included papers and include all documents or studies that they judge to contain data that is relevant and will aid development of some part of the programme theory.

To ensure consistency TM and the RF will independently assess included papers for relevance. In the event of any uncertainty, the review team will discuss the relevance or rigour of the articles and any disagreements will be resolved through research team member discussions. A majority vote among the academic stakeholder group will be used to resolve any remaining disagreements.

Step 4: Extracting and organising data

The realist synthesis approach synthesises information through notetaking and annotation. Full texts of the included articles will be imported into NVivo. NVivo is a data management system that has been successfully used by the research team in previous syntheses. The RF will carry out data extraction. If required, NVivo training will be provided for the RF via the Staff Learning and Development Programme at Queen’s University Belfast. Relevant sections of texts relating to one or more part of the programme theory will be coded in NVivo firstly by conceptual ‘themes’ and then as the synthesis progresses these will be developed into context-mechanism-outcome (CMO) configurations (see Step 5 below), the appropriateness of which is outlined in the literature (28). Data on the characteristics of the documents will be extracted separately into an Excel spreadsheet. As a quality assurance process, a random 10% of the coding will be independently checked by a member of the research team (JR), with any disagreement resolved by discussion within the team.

Step 5: Synthesising evidence and drawing conclusions

A realist logic of analysis will be used to analyse the data from included documents. Interpretive cross-case comparison will be used to understand and explain how and why actual outcomes have happened e.g. by comparing integrated palliative care and heart failure interventions that have been successful against those which have not, in order to understand how context has influenced reported findings (28). The following reasoning processes are typically used in synthesising evidence in realist synthesis:

a) Juxtaposition of sources of evidence e.g. where evidence about behaviour change in one source allows insights into evidence about outcomes in another source
b) Reconciling of sources of evidence – where results differ in similar situations, these will be further examined to find explanations for these differences
c) Adjudication of sources of evidence – centred on methodological strengths or weaknesses

d) Consolidation of sources of evidence – where different outcomes occur in similar contexts, a reason can be developed as to how and why these outcomes happen differently.

Throughout the synthesis, we shall move iteratively between the analysis of examples, refinement of programme theory, and further iterative searching for data (where needed) to test specific parts of the programme theory. The final realist programme theory will be presented in a diagram and through a narrative description of CMO configurations. In all realist reviews there is always a risk that the review team will be swamped by the sheer breadth and detail they could cover. As is usual and expected practice in realist reviews (as seen in Item 3 of the RAMESES quality standards for realist syntheses: https://www.ramesesproject.org/media/RS_qual_standards_researchers.pdf), we will progressively focus the review.

For previous projects we have worked on, progressive focussing has been undertaken to prioritise those aspects of the programme theory and/or CMOCs that are most important to stakeholders and/or provide the most useful findings that can be more readily actioned in the NHS. We have done so in the past by bringing such issues to stakeholder group meetings and combining the feedback and advice we get with the content and methodological expertise of the project team.

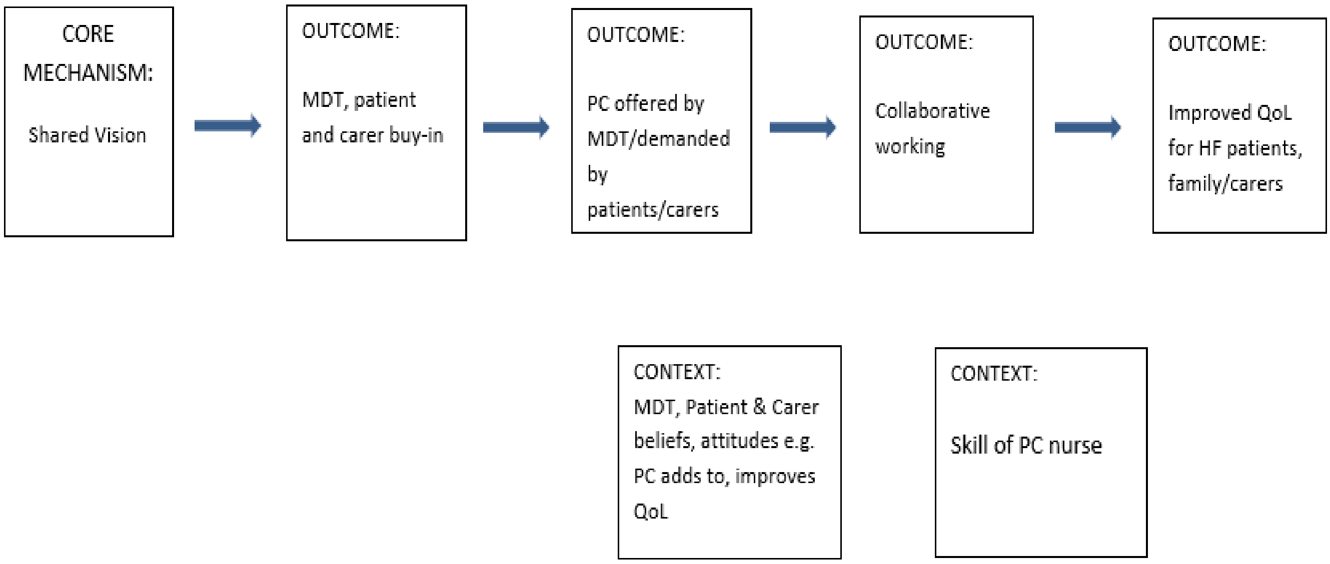
The process for arriving at recommendations for optimal configuration of integrated palliative and heart failure services will begin month 13-15 and be completed months 16 -18 during the 4th and 5th (final) co-production stakeholder meetings. This process is clarified under Objective 2 on page 13 and further clarified under section 6. Dissemination, outputs and anticipated impact on page 13-15. We anticipate that co-production stakeholder group meetings will include commissioners, local, national, international content experts, multidisciplinary practitioners, patients, family members and the public who will each bring their unique perspective to data synthesis and what works, for whom, how, why and in what contexts to inform recommendations for the optimal configuration of integrated palliative and heart failure services. In the first of these meetings we will provide the participants with easy to understand summaries of our findings as well as drafts of what we would recommend in response. We would facilitate the meetings in such a way as to enable the participants to openly discuss and debate each recommendation. Where relevant and necessary we will revise our recommendations based on their feedback and advice. This may be done during the meeting or after it. If there are stakeholders who are not present in the meeting whose feedback and advice we would value, we will approach then individually and use the same process as described above. We will bring our revised recommendations back to the stakeholders in the second meeting and repeat the process outlined above.

During the review we will seek out data on costs and sustainability. Where such data exist, if possible and relevant we will develop CMOCs for these aspects. Any such findings we develop on costs and sustainability of integrated palliative and heart failure services will be provided at the last two stakeholder meetings (see above) along with recommendations for commissioners and providers.

Example of a preliminary 'initial' programme theory

To provide an indication of what we think a programme theory of integrated palliative care and heart failure might look like in practice, we have developed a preliminary 'initial' programme theory of integrated palliative care and heart failure for the purposes of this research proposal (see Figure 1). This theory is based on the research team's content expertise on how integrated palliative care and heart failure could produce its effects. In addition, we have provided details on a CMO configuration to indicate the type of information that a realist synthesis can generate. This CMO configuration is based on a core mechanism; Shared Vision. *"A mechanism is the way in which a programme's resources or* *opportunities interact with the reasoning of individuals and lead to changes in behaviour"* (36, p.3).

Figure 1: Preliminary 'Initial' Programme Theory



A hypothetical CMO Configuration example: Shared Vision Core Mechanism
A shared healthcare vision is essential for patients with heart failure to get the care they need. Without this, it would be a challenge to achieve the desired behaviour change (collaborative working between palliative care and cardiology teams) and therefore improve symptomatic heart failure patient's quality of life. A shared vision refers to a common and clearly defined goal for patient care and outcomes that is shared by and meets the collective interests of the multidisciplinary healthcare team (MDT). This enhances buy-in to new ways of working and produces a feeling of being part of a supportive team, which leads to collaborative working. In integrated palliative care and heart failure, the concept of a shared vision may well function as a mechanism within some of the CMO configurations we will develop as part of this synthesis. For example, having an appreciation of how palliative care can improve the quality of life of patients with advanced heart failure (context) may trigger a shared vision (mechanism) among the clinical cardiology team, patients and their families leading to the offer or demand for integrating palliative care and heart failure management (outcome). Additional important contexts may be in operation that influence the possible mechanism of shared vision. For example, we hypothesise that the clinical cardiology team, patients and their families understand that a palliative care approach *adds* to patient's clinical care, and does not mean that clinical care is reduced or stopped (context), and the palliative care nurse that works as part of the team is highly skilled in educating generalist staff, and building their confidence to deliver basic palliative care (context) then a shared vision (mechanism) will be triggered resulting in collaborative working (outcome) and eventually increase the patient's quality of life (outcome). Thus, whilst we are initially speculating that a 'core' mechanism is shared vision, we hypothesise that different contexts will influence it in different ways to produce different outcomes (as would be expected in a realist understanding of causation). If we were to find that these hypothetical CMO configuration were to be confirmed against available data from the literature, then we might recommend that palliative care nurses who work in collaboration with the clinical cardiology team would need to be highly skilled in both cardiology and palliative care, and understand how to trigger a shared vision in the clinical cardiology team.

Objective 2: To provide recommendations for commissioners, practitioners, patients and the public
Our programme theory will be used to provide recommendations for the optimal configuration and implementation of integrated palliative care and heart failure services across NHS organisations currently implementing or wishing to implement an integrated palliative care and heart failure intervention. We will co-produce recommendations with our key stakeholders (commissioners, local, national, international content experts, multidisciplinary practitioners, patients and the public) as outlined under 6.2 below, to ensure they are feasible, acceptable, and meaningful in practice. Recommendations will also inform specific guidelines for local, national and international professional bodies (37-38), which recommend an integrated palliative care and heart failure approach, on what works, for whom, how, why and in what contexts to bring about the desired outcomes. More information is provided in the following section 6.

6. DISSEMINATION, OUTPUTS AND ANTICIPATED IMPACT

Project Outputs
To ensure that the recommendations and guidelines from this project will be useful to the key audiences we have set out below, the Knowledge-To-Action Cycle Framework provided by the Knowledge Transfer Clearinghouse (http://ktclearinghouse.ca/knowledgebase/knowledgetoaction) will be used. This framework provides knowledge translation resources funded by the Canadian Institute of Health Research. The Knowledge-to-Action Cycle graphically sets out the three steps necessary in bridging the knowledge-to-action gap. Specifically, this realist synthesis will generate knowledge that will inform the following phases of the Knowledge-To-Action Cycle framework:

1. producing stakeholder relevant knowledge;
2. adapting knowledge to local context and;
3. assessing barriers to knowledge use.

We shall operationalise this framework as below:

6.1) Co-producing a practical user guide with key stakeholders

All three phases of the Knowledge-To-Action Cycle will be addressed during co-production of the recommendations with key stakeholders. This co-production work will begin during the fourth stakeholder group meeting in month 14 of the project to ensure adequate time for planning both the dissemination formats and channels to optimise impact of the review findings. This will involve a ‘user guide’ that outlines practical advice to optimise, tailor and implement interventions designed to integrate palliative care and heart failure that takes the local context into consideration.

The user guide will aim to impact on the routine care for patients with advanced heart failure so they can benefit from an evidence-based integrated palliative care approach to heart failure management. This document will be of relevance to commissioners of services, along with managers and providers of heart failure services. These audiences are predominantly responsible for making the necessary changes at the 'coal face' to influence a change in practice. To gain impact we will make our 'How to' publication as relevant and feasible as possible - our goal being to avoid bland sweeping statements that are difficult to operationalise in different settings.

Findings from the review will be presented to key stakeholders at the fourth stakeholder group meeting, and their expert feedback will be used to shape the recommendations. We envisage broadening the membership of the stakeholder group once we start to develop our outputs and recommendations, to gain a wider representation of both PPI members and ‘coalface’ providers. Suggestions made will be noted and discussed in detail to ensure the user guide is acceptable and feasible within different settings i.e. what are the challenges to making this happen and how might they be overcome (if possible). We will ensure that any suggestions made are backed up by evidence from our review. Where there is a discrepancy, we will initiate further discussions about the validity of a suggestion. We will use this iterative dialogue with our stakeholder group to work through our review's findings. We will focus our last stakeholder group meeting (month 17) to confirm and refine our outputs and recommendations for a similar purpose but use email and teleconferencing (as needed) with the group between meetings to continue to work on the 'How to' publication output. We will augment the membership of this last stakeholder group meeting to ensure we have the relevant content expertise present. This strategy has proved successful in a previous realist synthesis to produce relevant and feasible recommendations (39).

6.2) Co-producing user-friendly summaries of the synthesis findings with key stakeholders that are tailored to the needs of interested audiences:

To enhance the understanding, accessibility, impact and reach of our findings to all key audiences mentioned above, along with patients and the public, an independent website will be built, hosted and maintained by Nathan Conn Freelance Designer and Animator, that houses all project information in one place. Hosting will be held by the Designer to enable controlled access and management as this is more cost-effective. A unique domain for the study will be linked to and from QUB online sites. This website will include short animations/illustrations to creatively convey complex synthesis findings. The intended impact of this creative approach is to widen the reach of the 'headline' findings of the realist review to relevant stakeholders in a visually engaging way. These outputs are thus closely linked to our dissemination strategy. We will again draw on the expertise within the research team and stakeholder group to produce creative summaries that are user-friendly and relevant to the audiences we have identified above.

6.3) The synthesis findings will be submitted for publication to a high-impact, open access peer-reviewed journal

The findings paper will be submitted to the European Journal of Heart Failure. This is a high impact journal (11.627), dedicated to advancing knowledge in the field of heart failure management. We anticipate this publication is most likely to impact at an academic level – informing the understanding and theoretical basis of an integrated palliative care and heart failure intervention. There are a number of integrated palliative care and heart failure interventions in place nationally and internationally, thus such a publication will be of relevance to academics and clinicians across the world.

Co-producing dissemination strategies to increase impact

Our dissemination strategy will build on the co-production approach (involving PPI) that we used in the development of this research proposal (see section 10) and in the production of the review outputs. It is clear there will be a number of key audiences, which will each need a slightly different approach to engage. For each audience, therefore, once we have consulted with the stakeholder group and clarified the key contacts, we shall contact the organisation directly to seek further advice on their preferred channels and format for optimal dissemination to their members. This will be assisted by the stakeholder group, JR already having established relationships with the All Ireland Institute of Hospice and Palliative Care (AIIHPC) and the European Association for Palliative Care (EAPC), TM who has established relationships with the British Heart Foundation and hospices through Marie Curie UK; and LH who has established specialist heart failure networks through her connections with the National Heart Failure nurse networks (British Society for Heart Failure Nurse Forum and Scottish Heart Failure Nurse forum) and the Heart Failure Association of the European Society of Cardiology (ESC).

Audience 1: Policymakers, decision-makers and commissioners of heart failure services.

This audience is key to implementing recommendations arising from our realist review. We will engage with our stakeholder group to ensure findings reach all relevant bodies. We will develop briefing materials, tailored to different audiences, including Department of Health, NHS England, the Royal College of General Practitioners (RCGP), Royal Society of Medicine (RSM), Royal Society for Public Health (RSPH), and local government bodies: Recommendations will be disseminated directly to every Health and Social Care Trust in Northern Ireland, England, Scotland and Wales, and presented at the Northern Ireland Assembly Knowledge Exchange Seminar Series (KESS), which is well attended by policymakers and commissioners. We envisage the final report from our study will be hosted on relevant websites with relevant links to our project website. We will work with communication and Public Relations teams at QUB, Marie Curie, BHF, AIIHPC and NIHR to enhance readership.

Audience 2: NHS leaders, managers and practitioners involved in palliative care and heart failure provision

These audiences are key to the delivery of integrated palliative care and heart failure. We will work with our stakeholder group to reach the relevant individuals and practitioner groups across England, Scotland, Wales and Northern Ireland, and prepare tailored briefing documents targeted at the different provider groups.

Audience 3: Members of the public, including those impacted by advanced heart failure

We will work with our University media, NIHR, BHF, AIIHPC and Marie Curie communication services to ensure comprehensive dissemination of our findings to both patients and the public. We will also provide summaries of our findings to all relevant charities. We will engage with our PPI Stakeholder group to maximise dissemination opportunities to the widest possible public audience, for example through social media, ensuring our materials meet their needs.

To ensure that the patient voice is heard, we will invite our PPI stakeholder group members to share their own stories of heart failure management (both with and without the integration of palliative care if possible). These will be used to strengthen the review findings and may be incorporated into the practical user guides, user-friendly summaries, relevant websites and media in the form of anonymised quotes or vignettes in order to encourage uptake of the recommendations by commissioners and providers.

7. PLAN OF INVESTIGATION AND TIMETABLE

The key tasks and their timings are outlined in the Gantt chart. Briefly:

MONTHS -3-0

- Recruit RF

MONTHS 0-3

- Brief, recruit and train (where requested) Stakeholder Group
- Set up and run 1st Stakeholder Group meeting
- Submit realist synthesis protocol for publication
- Start Step 1 of realist synthesis – locate existing theories and build initial programme theory

- Start Step 2 of realist synthesis – searching for evidence and screen search results
- Initial website development

MONTHS 4- 6

- Complete Step 1 of realist synthesis
- Complete Step 2 of realist synthesis
- Start Step 3 of realist synthesis – article selection
- Start Step 4 of realist synthesis – extracting and organising data
- Start Step 5 of realist synthesis – synthesising the evidence part only
- Iteratively refine initial programme theory – based on data from initial search and undertake any additional searching as needed and informed by the programme theory

MONTHS 7-9

- Complete Step 3 of realist synthesis
- Continue with Steps 4 and 5 of realist synthesis
- Iteratively refine initial programme theory
- Run 2nd Stakeholder Group meeting – with updates on progress, findings and expenditure

MONTHS 10-12

- Continue with Steps 4 and 5 of realist synthesis
- Iteratively refine initial programme theory
- Run 3rd Stakeholder Group meeting – with updates on progress, findings and expenditure

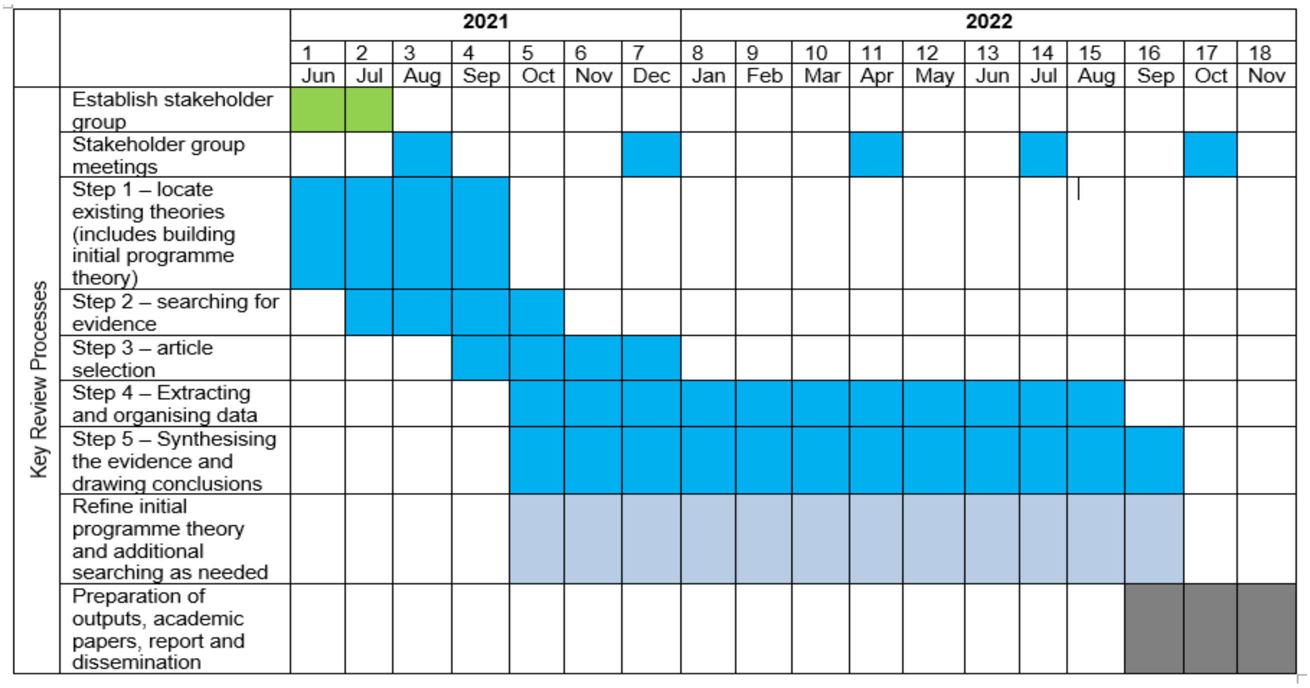
MONTHS 13-15

- Complete Step 4 of realist synthesis
- Continue with Step 5 of realist synthesis
- Iteratively refine initial programme theory
- Begin to co-produce recommendations at 4th Stakeholder Group meeting

MONTHS 16-18

- Complete Step 5 of realist synthesis and recommendations part as well
- Finalise programme theory
- Finalise co-produced recommendations at 5th and final Stakeholder Group meeting and disseminate outputs
- Finalise and submit academic paper for publication
- Write final report

Project Timetable



		2021							2022											
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
		Jun	Jul	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov
Key Review Processes	Establish stakeholder group	🟩	🟩																
	Stakeholder group meetings			🟦				🟦				🟦			🟦			🟦	
	Step 1 – locate existing theories (includes building initial programme theory)	🟦	🟦	🟦	🟦														
	Step 2 – searching for evidence		🟦	🟦	🟦	🟦													
	Step 3 – article selection				🟦	🟦	🟦	🟦											
	Step 4 – Extracting and organising data					🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦			
	Step 5 – Synthesising the evidence and drawing conclusions					🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦	🟦		
	Refine initial programme theory and additional searching as needed					▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨	▨		
	Preparation of outputs, academic papers, report and dissemination																⬛	⬛	⬛

8. PROJECT MANAGEMENT

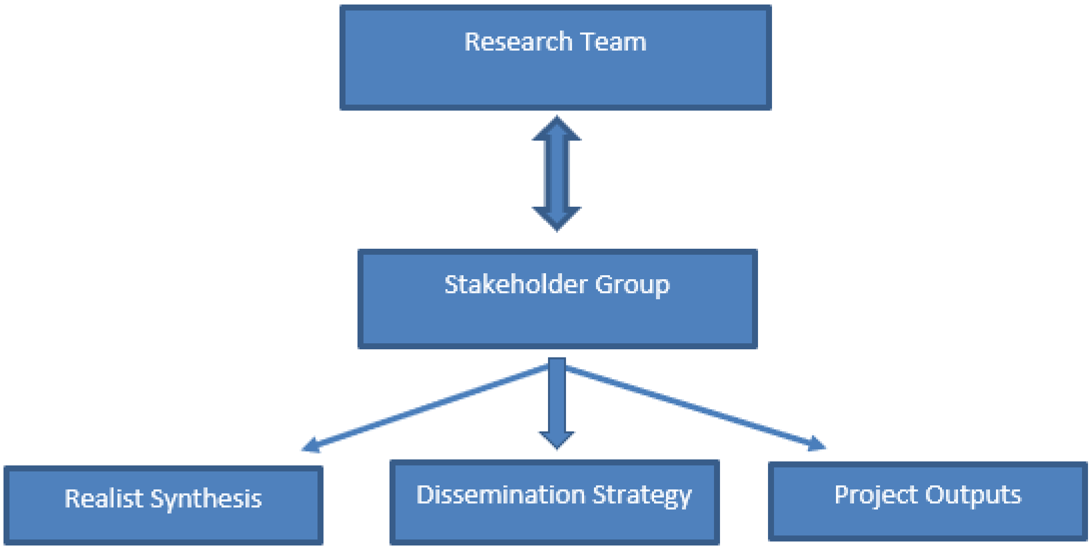
The research team will meet monthly with additional contact as required (e.g. via email, video and tele-conferencing). We shall run five stakeholder group meetings (as set out in the Plan of investigation and timetable section above). We plan to run three of the stakeholder meetings face to face during project set-up and co-producing recommendations (first, fourth and fifth meeting). However, we are mindful of the possible impact of COVID-19 on our project (travel restrictions, social distancing requirements and shielding requirements for PPI members with heart failure), and as such we will be flexible and inclusive. If required, we will run all five meetings online via Zoom or MS Teams depending on Stakeholder preference to ensure the study is executed on time and that all key deadlines are met. We have already held a Zoom meeting with PPI stakeholder group members to discuss the aims, objectives, plain English summary and dissemination plan for this proposed research. This mode of communication provided flexibility and was considered convenient and appropriate by our PPI partners.

The research team, co-led by TM and JR, will include LH, GW, our information specialist (CD) and the RF– to be employed. We shall use QUB's Microsoft Onedrive as needed to enable us to conduct high-quality remote interaction and file sharing. This team will plan and monitor day to day progress, ensure ongoing communication among team members, review quality and timeliness of outputs, and manage day-to-day risks and issues. The research team will be responsible for undertaking the realist synthesis, producing the project outputs and dissemination.

The stakeholder group (Table 1) will also provide advice, promote the project, and help maximise dissemination and impact of findings. All data will be handled in accordance with the Data Protection Policies of our respective institutions.

Figure 2 below provides an outline of the project's organisational structure.

Figure 2: Project's organisational structure



9. APPROVAL BY ETHICS COMMITTEES

We do not anticipate that we will need ethical approval, but we will seek confirmation of this once the project starts.

10. PATIENT AND PUBLIC INVOLVEMENT

We have involved members of the public in the drafting of this proposal. We sought feedback on importance of our proposed study, what we should focus on in our review and our Plain English summary during April 2020 from members of two established public involvement and engagement groups (Marie Curie PPI Research Voices Group London and BHF PPI Heart Failure Group London). We received eight responses from PPI members, three of whom have agreed to membership of our stakeholder group (further details of what they told and what we did in response may be found in the '*Patient and Public Involvement*' section of our application).

During the review, we will ask PPI stakeholder group members:

- to help us develop our initial programme theory;
- for their advice and feedback on our programme theory as it evolves;
- to consider our findings and recommendations from their varied perspectives;
- provide input and support into our dissemination strategy and;
- review and contribute to our materials, to ensure they meet the needs of patients and the wider public.

Where needed we will provide training to the PPI members so that they understand what their roles will be and will be able to meaningfully contribute. If necessary and requested, we will meet with PPI members of the stakeholder group before the main stakeholder meeting to provide any support needed. More details may be found in the 'Patient and Public Involvement' section of our application.

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