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Addressing psychological morbidity in informal carers at the end of life: evidence synthesis and stakeholder consultation to produce tailored, evidence-based information and priorities

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1 FULL TITLE OF PROJECT

Addressing psychological morbidity in informal carers of patients at the end of life (EOL): evidence synthesis and stakeholder consultation to produce tailored, evidence-based information and priorities

2 SUMMARY OF RESEARCH

Family carers provide crucial support for patients at end of life, but suffer considerable impact on their own psychological health. The preservation of carers' own health and their ability to sustain patient care at home is relevant to the health of a substantial proportion of the population, the quality of patient care and the cost to the healthcare system. Synthesis of the expansive evidence on factors affecting carer psychological morbidity to inform remedial initiatives and interventions is likely to be of strategic importance to the NHS, particularly in the face of projected increases in number of deaths[5] and reliance on carers[6]. Whilst we focus on EoL where impact on carers is most acute (and the breadth of conditions widest), findings are likely to have applicability to broader groups of carers.

The project aim is to help reduce psychological morbidity among EOL carers through:
(1) evidence-synthesis of factors affecting EOL carer psychological morbidity
(2) translation of synthesised findings into accessible, tailored information for key stakeholders to enable better targeted efforts to reduce carer psychological morbidity and its impacts.

These aims will be achieved through two work packages (WPs):

WP 1: Comprehensive mixed-method literature review and synthesis
Three reviews will be conducted and their findings integrated into a comprehensive framework:

- Review of quantitative observational studies to identify factors associated with psychological morbidity, using box score and meta-analyses
- Review of qualitative studies to identify factors carers themselves feel have impact on their psychological morbidity, using a thematic best-fit framework synthesis approach
- Review of interventions to examine which of these factors influence effectiveness of existing interventions, using pooled effect sizes and sub-group analyses
- Integration of findings into a framework, informed by current stress models and carer perspectives, using narrative, graphical and numerical display tools.

WP1 will engage carers on a Review Advisory Panel and a carer co-analyst to inform the search strategy, help with the qualitative thematic analysis, and shape the final framework to ensure that the framework contents are relevant and accessible to carers.

WP2: Stakeholder involvement to translate WP1 findings into bespoke information, priorities and procedures
Three stakeholder processes will help us translate empirical evidence into messages that can inform real life decisions and actions by identifying the most relevant and appropriate findings and implications, formats of presentation, and channels of dissemination for each stakeholder group:

- Evidence review stakeholder workshop (N=30) with policy makers, commissioners, researchers, health and social care representatives, and carer representatives. This will enable stakeholders to assess relevance of findings to their respective spheres of influence (settings and systems) and identify the most important information and priorities for their group, whilst promoting interaction between stakeholder groups to help ensure their bespoke materials are still part of a coordinated strategy.

- Translation work with our Review Advisory Panel (N=10) to develop dissemination outputs and dissemination strategies appropriate for each stakeholder group.
- Focus groups with primary care practitioners and carers (N=6x2) to explore how project outputs may be operationalised into primary/ community care procedures

The project will have impact by providing the first comprehensive evidence synthesis of factors affecting the psychological morbidity of carers, and translating it into accessible messages to stakeholders best placed to act on it. Effective knowledge mobilisation will be aided by tailored outputs and dissemination, informed by stakeholders, in addition to publication, presentations, and online/electronic communication.

3 BACKGROUND AND RATIONALE

Value of carers

There are an estimated 6.8 million carers in the UK providing care of an estimated value of £132bn per annum, a sum close to the total cost of UK health spending (£134bn)[6]. Of these, an estimated 500,000 carers provide end of life (EOL) care p.a. in England[7]. The monetary value of EOL caregiving is yet to be established, but the contribution is likely to be substantial: EOL carers report providing a median of 70 hours of care per week in the final months of life[8], whilst the majority of carers in general (62%) provide up to 19 hours[6]. Further, reviews have consistently shown carers to be a main factor in sustaining care at home at EOL[9 10]. This is likely to reduce acute inpatient care costs and pressures on care home beds. EOL carers therefore provide substantial benefit for patient care and the NHS.

The problem being addressed

However, caregiving for patients at EOL has substantial impact on carers' own health. The greatest and most consistent impacts are on carers' psychological health[2]. The project will therefore focus on psychological health as the area where most gains can be made. Reported prevalence of carer anxiety and depression during palliative care are 34-47%[11-14] and 39-57%, respectively[15-16]. However, prevalence of clinically significant carer psychological morbidity was found to be 83% during patients' final three months, in a national census study of cancer deaths in England[2] . Given the numbers affected, these high levels of psychological morbidity arguably represent a sizable public health problem with likely long term effects: carers' pre-bereavement psychological health is a main predictor of post-bereavement psychological health[17 18]. Further, if carers become unable to cope, this is likely to have negative impacts on the quality of patient care and increase likelihood of inpatient hospital admissions.

Opportunity for intervention

Research shows there is large individual variation in level of psychological morbidity from EOL caregiving. Understanding what predicts this variation provides opportunities for identifying those at risk and pointers for intervention. The actual care demands of the patient's illness and hours of care only play a minor, albeit significant role[2]. In contrast, morbidity is considerably influenced by factors internal to the individual carer and by contextual factors. Internal factors may include carers' beliefs about the patient's illness, preparedness for caregiving, and the extent to which they perceive themselves to be in control of the demands they are facing. Contextual factors may relate to demographic, cultural, social or family factors, service provision or carers' financial or work situation.

To date this considerable body of evidence has not been synthesised. Such a synthesis would provide two approaches to reduction in carer psychological morbidity. First, there are factors that cannot realistically be changed (e.g. age and gender), but whose effects can be mitigated through early, targeted support for those at higher risk. Second, there are factors that can be changed, e.g. preparedness for caregiving, that can be subjected to more direct intervention to reduce likelihood of later psychological morbidity. What is non-modifiable or modifiable will partly depend on the stakeholder: for instance, policymakers may through legislation help modify work and financial factors that put carers at risk, while practitioners may improve carers' sense of preparedness through information tailored to their individual caregiving situation, but not vice versa.

A synthesis needs to capture the range of factors affecting carer psychological morbidity to inform a comprehensive, rather than piecemeal, strategy for improving the health of UK EOL caregivers. This synthesis needs to be in an accessible format that can guide policy makers, commissioners, practitioners, and carers, as well as researchers. This may inform decisions about legislation, allocation and distribution of funding, and the fiscal incentives to control quantity and quality of services among policy makers and commissioners (e.g. to improve work and benefits legislation, boost respite provision, or mandate provision for carers within services). It may guide services in design of operational procedures to enable more effective carer and patient support through earlier, targeted carer intervention to prevent later crises, in particular through knowledge of carer resilience or risk factors, how to identify those at higher risk and what is most likely to help those at risk within existing resources. It can help carers identify options for self-help to boost resilience factors, and carer organisations re where to focus their resources and advocacy. Finally, evidence synthesis can guide researchers to design better interventions than can be changed, and address gaps in the evidence, e.g. why carers may be more at risk due to age or sex to identify the underlying mechanisms that may be amenable to change. Considerable gains can therefore be made through synthesis of the existing evidence to provide a comprehensive understanding of factors affecting psychological morbidity at different levels.

What this review will add

We conducted a review of the quantitative and qualitative literature (1998-2008)[18 19] which identified the considerable range of factors affecting carers' psychological morbidity during EOL care. However, although using a systematic, comprehensive search and selection process, this was a simple thematic review with a broader focus than psychological morbidity, summarised findings for each factor in a narrative form and considered quantitative and qualitative results separately. Furthermore, the relevant literature has grown considerably since (see below), but not been synthesised.

Whilst building on the earlier review, the current project will bring added benefit through synthesis of the total body of literature 1998-2018, bringing all factors affecting carer psychological morbidity into a comprehensive framework; providing assessment of the number and quality of the studies for each factor; quantifying number and direction of significant results with effect sizes for quantitative studies; conducting meta-synthesis of qualitative studies; and directly comparing complementarity of quantitative and qualitative evidence. Further, stakeholder consultation will help translate empirical findings into tailored messages and formats that have relevance and utility for the main stakeholders and begin to identify how findings may be operationalised within primary care.

A strength of the review is the inclusion of both quantitative and qualitative literature. Whilst only quantitative studies can systematically test for association and in the case of RCTs, causality, factors selected for quantitative investigation are likely to represent the 'dominant discourse' of academics and healthcare practitioners. Our research shows that practitioners often have little insight into factors that carers see themselves see as critical to their wellbeing[20]. A qualitative review is necessary to capture potential factors contributing to psychological burden as perceived by those experiencing this phenomenon and ensure the voice of carers themselves is heard. A qualitative review is furthermore more likely to uncover enriched, multi-layered perspectives not captured by quantitative methods and add to theory building and models for testing. Methodological advances over the last two decades make qualitative meta-synthesis an optimal way of incorporating this valuable perspective. The combination of both quantitative and qualitative literature review is therefore likely to ensure we incorporate both ‘inside’ and ‘outside’ perspectives and the strengths and insights from both paradigms.

A similar review has not been done elsewhere. A search of the PROSPERO database of registered ongoing reviews reveals no review focusing specifically on predictors of psychological outcomes in carers of people with advanced or EOL disease. Previous reviews of interventions for EOL carers report limited impact on psychological morbidity, but are outdated[21 22]. Although we identified an review of interventions for carers of older adults on PROSPERO, this does not focus on psychological morbidity and EOL[23]. It is currently unknown to what extent existing interventions target factors contributing to psychological morbidity in carers of EOL patients, and the likely benefits of this targeted approach. Overall, fundamental questions remain how we ensure that interventions for carers of end of life patients are targeted at those most likely to benefit.

Why this research is needed now

Government policy and national guidance clearly highlights that carers should be supported during EOL care[24]. This is in recognition of their needs and their importance in supporting patients and enabling EOL care to take place at home, in line with government policy and patient preferences. However, we are currently falling short on supporting carers. The reports on “State of Caring 2016” by Carers UK[25] and “Care Act: One year on” by the Carers Trust[26] indicate that the Care Act 2014 has failed to deliver adequate support for carers in general. Publication of the long awaited new Carers Strategy from the government seems at present to have stalled. Further, our recent national census survey on prevalence of clinically significant psychological morbidity among EOL carers indicates shortfalls in support for carers at EOL in particular[2].

The number of carers in the population has increased by 16.5% from 2001 to 2015, with an increase of nearly 43% in carers providing 20-49 hours and 33% in those providing >50 hours per week[6]. Our reliance on carers is likely to increase further in the future, particularly for EOL care. In the years to come there are projected demographic increases in people over 85, those with life limiting illness[6]; in dependency in the final years of life[27] and number deaths[5]. Health and social care services will struggle to meet increasing future demands, and we need to recognise carers as a vital resource and provide better cross-society initiatives to support carers and prevent adverse health outcomes from caregiving.

This is therefore a crucial time to synthesise evidence on the factors associated with EOL carer psychological morbidity to guide strategic initiatives and interventions to preserve carer health from policy to practice levels. Further, a focus on primary care is opportune. Not only is this where practitioners are most likely to come into contact with carers at an early stage, offering the best opportunity for early identification and intervention (including education and self-care support). Recent national and local initiatives also position carer support within primary care, including the national joint RCGP/ Marie Curie UK General Practice Core Standards for Advanced Serious Illness and End of Life Care, with pilots starting in Spring 2018, and the local Greater Manchester Health and Social Care Strategic Partnership Carers Charter[28]. The devolution of the health and social care budget to Greater Manchester means its service delivery configurations are likely to serve as models for care provision elsewhere. However, these initiatives lack evidence based guidance on early identification and support of carers at risk. The co-applicants are uniquely placed to engage with and directly inform carer support initiatives within these forums.

4 AIMS AND OBJECTIVES

The aim of the project is to help reduce psychological morbidity among EOL carers by
(1) conducting mixed-methods evidence-synthesis of factors that increase or decrease carer psychological morbidity during end of life caregiving, and integrating findings into a coherent framework
(2) translating findings into accessible, bespoke information for key stakeholders to help them better target current and future efforts to reduce psychological morbidity and its impacts.

These two aims will be met through two corresponding Work Packages 1 and 2.

Detailed aims
Work Package 1 (WP1)

- Identify, via quantitative systematic review and meta-analysis, factors associated with psychological morbidity during EOL caregiving
- Explore, via qualitative evidence synthesis, factors carers themselves feel have an impact on their psychological health
- Examine which of these factors influence the effectiveness of existing interventions targeting carers' psychological morbidity
- Critically integrate findings from evidence sources into a coherent, accessible and evidence-based model of psychological morbidity during EOL caregiving, that also includes factors relevant to carers

Work Package 2

- Co-produce with separate stakeholder groups bespoke, accessible and evidence-based summaries relevant to their needs and sphere of influence, to effectively mobilise project learning and help guide targeted use of existing carer support initiatives and interventions
- Explore how synthesised information may form the basis for further development and testing of a future intervention in primary care

Detailed objectives for WP1: Evidence synthesis
1.1 Evidence synthesis of observational quantitative studies

- Agree psychological morbidity outcomes based on measures of anxiety, depression, general psychological morbidity, quality of life and outcomes relevant to carer advisers
- Identification and synthesis of factors associated with carer psychological morbidity using box score and meta-analysis

1.2 Evidence synthesis of qualitative studies

- Identification of factors reported by carers in the literature to be important to their psychological health
- Thematic analysis of factors with a carer co-analysist using a best-fit framework synthesis approach and principles of meta-ethnography

1.3 Evidence synthesis of intervention studies; focusing on intervention components and participant characteristics, their match with factors identified in 1.1-1.2 above and their ability to further inform and expand on identified factors

- Assessing size of the effect of interventions on carer psychological morbidity outcomes
- Examining whether any identified factors associated with psychological morbidity in the observational and qualitative reviews have been accounted for in existing interventions aimed at reducing psychological morbidity in EOL carers.

- Formally testing the impact of these factors in the pooled effect size of the interventions using subgroup analyses or meta-regression analyses (where sufficient data is available for such analyses)
- If formal subgroup or meta-regression analyses are not possible for some factors, we will conduct a conceptual mapping between interventions' active components and factors identified in the observational and qualitative reviews.

1.4 Integration of syntheses into a coherent framework of factors affecting psychological morbidity during EOL caregiving
- Bringing together findings from qualitative and quantitative syntheses (1.1-1.3); mapping agreement, conflict and evidence gaps
- Using narrative, graphical and numerical tools to present combined findings on type of factor, strength of evidence and effect size where evidence permits
- Mapping findings into a factor framework of likely predictors, moderators, mediators and level at which they operate (individual - contextual), guided by main existing carer stress models, and confirming or challenging existing models.
- Consulting with carer advisors to ensure the framework reflect what is meaningful and important to them in an accessible format

Detailed objectives for WP2: Stakeholder consultation
2.1 Translation of evidence synthesis into tailored materials
- Engage stakeholders (policy makers, commissioners, provider representatives, carer representatives, and researchers) in translating findings into tailored information, priorities and procedures accessible and relevant to each group, with appropriate dissemination strategies for each, through
  - One day stakeholder workshop (N=30) to identify the most important information and priorities for each stakeholder group
  - translation work with our Review Advisory Panel (N=10) to develop outputs and dissemination strategies appropriate for each stakeholder group, using iterative cycles of development by the research team and review by the RAP, supported by an infographic specialist.

2.2 Exploring the operationalisation of project outputs into primary care procedures
- Engage primary care practitioners and carers through focus groups (N=6x2) to explore how project outputs may be operationalised into primary care procedures to promote early identification and targeted support for carers at risk of developing psychological morbidity, for further development and testing as a future intervention

5 RESEARCH PLAN / METHODS

WORK PACKAGE 1: EVIDENCE SYNTHESIS (Objectives 1.1 - 1.4)

Design
A comprehensive, structured mixed method review of the qualitative and quantitative literature over the past 20 years will be conducted (see Flow Diagram). This will identify and synthesise factors associated with psychological morbidity in EOL caregivers, which have the potential to inform targeted efforts to reduce morbidity. In reviewing the evidence base relevant to each of our research objectives, a range of study designs (quantitative observational, qualitative and intervention studies) will be synthesised. At all phases of the review we will adhere to accepted guidelines outlined by the Centre for Reviews and Dissemination (CRD) and the Cochrane Collaboration. The final protocol for this review will be registered with PROSPERO, the NIHR International register of systematic reviews.

Search strategy

Research and grey literature will be searched for empirical studies using systematic and comprehensive search strategies in appropriate databases and on the Internet to capture the relevant quantitative observational, qualitative and intervention literature. Working with an information specialist our search terms will be tailored to each electronic database. All databases will be searched for the past 20 years.

- Due to the often dispersed nature of literature on carers, targeted electronic databases will span medical and nursing (e.g. MEDLINE, CINHAL, EMBASE; Database of Abstracts of Reviews of Effects-DARE; Cochrane Central Register of Controlled Trials-CENTRAL; Cochrane Qualitative Reviews), mental health (e.g. PsycINFO) and social science databases (e.g. ASSIA, SCOPUS, WoS including SSCI, AHCI and SCIEXPANDED).
- Dissertations and other grey literature will be searched (e.g. Dissertation Abstracts International; ProQuest Dissertations & Theses Global; OpenGrey, British National Bibliography for Report Literature, GOOGLE Scholar). We will not search the policy and professional literature as we are focusing on rigorous empirical evidence, which is less likely to be found within these latter sources.
- As recommended by Cochrane we will complement database searches with other search strategies: additional studies will be identified by scanning the bibliographies of recent reviews and newly retrieved articles, by brief targeted author searches and forward citation searching, hand-search the publication records of key authors and the establishment of a website for the review through which additional references can be submitted. Authors of ongoing and recently completed research projects will be contacted directly to enquire whether or not the research has been completed and if there are any subsequent publications.

Search terms will build on the comprehensive strategy devised for our two original research publications[18 19] which proved effective in capturing literature relevant to EOL caregiving both for cancer and non-cancer conditions. Terms will be updated and refined via i) discussion between the research team and an information specialist from University of Manchester Library; ii) discussion with the Review Advisory Panel; iii) scanning the background literature and iv) browsing the MEDLINE thesaurus (MeSH).

No design filters will be used as database indexing is often unable to distinguish accurately between different types of design. Optimal identification of the literature most relevant to our review question and objectives will thus require that most resource is targeted at the screening and filtering stages.

Our original review (1998-2008) identified 61 quantitative and 34 qualitative papers on factors affecting EOL carers' psychological morbidity. From our scoping review of the literature since then, using the searches used in our original review in Medline, we estimate that approximately 60 further papers will meet the criteria for the quantitative synthesis and 20 for the qualitative synthesis (totalling 121 quantitative and 54 qualitative papers for the proposed evidence synthesis). Similarly, we updated the searches of the Candy et al (2011)[22] review and, in conjunction with our broader inclusion criteria (which will include controlled intervention designs as described in the Cochrane handbook instead of RCTs only), we estimate that of the quantitative papers, approximately 20-25 of these will be controlled intervention studies and will be included in the synthesis.

PPI involvement in the search strategy and assessment criteria: The Review Advisory Panel will receive an introduction to review methods at their first meeting to subsequently help them review the search strategy, and suggest any additionally important words and phrases. They will also be asked to comment on the suitability of definitions, inclusion and exclusion criteria, to ensure these are most likely to capture their experiences. Furthermore, they will be asked to comment on the data extraction and anything they think the extracted information should be benchmarked against as quality criteria beyond academic criteria.

Definitions and parameters

The following definitions define the parameters for our review:

- *Population* – Lay adults who are supporting and caring for a patient who is at end of life. End of life (EOL) is conceptualised as a palliative, terminal, or otherwise ‘advanced’ or ‘end stage’ phase of care where all or a substantial proportion of patients are likely to die within a year. Additional disease-specific criteria will be employed for chronic disease, e.g. New York Heart Association Class III-IV for heart failure. Any articles not giving enough information to ascertain disease stage/palliative phase will be excluded. Care must be predominantly provided in a home-care setting. Papers which report that most care occurring while the patient is in a facility (i.e. care home, hospital) will be excluded.
- *Factor* - any factor which may affect psychological morbidity in carers (including as a correlating factor, predictor or through moderation or mediation); either as tested in quantitative observational studies (Objective 1.1), or as perceived by carers in qualitative studies (Objective 1.2). In the context of this review this may relate to fixed factors (e.g., carer or patient demographics, disease characteristics) or modifiable factors (e.g. preparedness for caregiving, beliefs about what causes the patient’s illness, etc.).
- *Intervention* – any non-pharmacological intervention designed to reduce psychological morbidity in EOL carers (Objective 1.3)
- *Comparison* – only relating to lay adults caring patients who are at EOL. EOL carers exposed to an intervention or factor will only be compared with other EOL carers, not other carer groups or the general population (e.g. relevant to case control studies Objective 1.1, and interventions Objective 1.3)
- *Outcome* - All studies which assess psychological morbidity as either a primary or secondary outcome will be reviewed. Psychological morbidity will include outcomes such as: anxiety, depression, general psychological morbidity (distress), quality of life and outcomes that carer advisers consider to be important.

Inclusion/ exclusion criteria

Observational quantitative studies (Objective 1.1) must fall within the definitions of Population, Factor, and Outcome as described above. They must also have a primary aim to examine factors associated with our Outcome and provide quantitative data of the association between Factor and Outcome. Eligible designs include cross-sectional, longitudinal or case control studies.

Qualitative studies (Objective 1.2) must fall within the definitions of Population, Factor and Outcome as described above. To be eligible these studies must demonstrate an a priori aim or objective to investigate psychological morbidity in informal carers, and must be based on the perspectives of EOL carers themselves. Qualitative research will be defined as those studies that collect data using specific qualitative techniques such as unstructured interviews, semi-structured interviews or focus groups, either as stand-alone methodology or as a discrete part of a larger mixed-method study.

Intervention studies (Objective 1.3) must fall within the definitions of Population, Intervention, Comparison and Outcome as described above. Interventions must have a primary aim to reduce our Outcome (psychological morbidity) in EOL carers. In terms of comparator groups, we will include usual care, enhanced usual care, ‘no intervention’ or waiting list controls. We will also consider studies which include other ‘active’ types of interventions as comparators (e.g. varying levels of intensity or different forms of delivery of an intervention), although final decisions regarding their eligibility will be made at a later stage. Eligible study designs are controlled intervention designs described in the Cochrane Handbook for Systematic Reviews of Interventions[29], including randomised clinical trials, nonrandomised trials, controlled before-after studies, and interrupted time series.

Only empirical research will be included, and reports, opinion pieces, book chapters will be excluded. For any reviews, we will assess individual papers within the review, rather than the reviews themselves. We will seek translation of relevant non-English papers where relevance is indicated by an abstract is published in English.

Inclusion and exclusion criteria will initially be tested against a small set of studies identified through our search to ensure they are fully operationalisable and clear.

Screening and selection of studies.

All potentially eligible records will be imported into a bibliographic referencing software program (Endnote version 9) and duplicate references will be identified and deleted. Studies will be screened against the inclusion/exclusion criteria in three stages;(i) title screening, (ii) abstract screening, and (iii) full text assessment. If there is ambiguity about inclusion at title or abstract screening, the article will move forward to the next stage of screening. These stages will be reported via a PRISMA flow chart which will include reasons for exclusion. The PRISMA flow-chart will double as a working document and be presented at all project management meetings.

Two reviewers will independently screen titles and abstracts for relevance, using the inclusion criteria outlined above, and a measure of inter-rater reliability (kappa coefficient) will be calculated. Where both reviewers agree on exclusions, titles and abstracts will be excluded and the reasons for exclusion will be recorded. Where both reviewers agree on inclusion, or where there is disagreement, the full text article will be retrieved. The two reviewers will independently assess the full text of the articles against the inclusion criteria. Our scoping suggests that there will be few disagreements but where these occur resolution will be through consultation with a third member of the research group.The resulting set of citations and associated abstracts will be managed in Covidence (www.covidence.org), a web-based systematic review management software program to facilitate reviewing within a research team. Covidence is a core component of Cochrane's review production toolkit that works seamlessly with reference managers such as Endnote.

From the final set, the reviewers will assign studies to the review categories Observational, Qualitative and Intervention studies in accord with Objectives 1.1-1.3, using the same assessment and disagreement resolution strategies as described above.

Data extraction

Data extraction will be guided by pre-specified data extraction forms (DEFs) detailing key features of the study sample, setting, methods, results and conclusions. Two researchers will extract data from all identified studies and systematically code it using DEFs. Discrepancies will be resolved by referral to the original studies and if necessary through arbitration by a third reviewer. Three different DEFs (with common sections for comparison such as country of origin, language, year of publication, aims, design, sample size and composition, definition of family carer and their status, method of data collection/recruitment etc) will be developed which will be tailored to the specific characteristics of the study designs outlined in each objective. The data extraction of the quantitative observational studies will focus on capturing details on predictors of psychological morbidity and data for calculating effect sizes. The data extraction of qualitative studies will involve tabulation of themes/subthemes. The DEF of intervention studies will focus on characteristics of the intervention, likely factors influencing the effectiveness of the intervention, and effect sizes.

We will contact original authors to supplement information where there are ambiguities or further data are needed in order to successfully include a study in our review (e.g. where statistics are reported but, for example, all the information required to calculate effect sizes is not reported). We will attempt to contact authors at their last know institutional address and via professional and academic networks.

Quality assessment

As there will be multiple study designs, tools specific to each will be needed as no single tool is suitable for all designs. For observational quantitative studies the choice of the assessment of will be finalised once all full texts have been identified for review. It is anticipated that we will either use the adapted form of the Newcastle Ottawa scale for cohort and cross-sectional studies[31] or a number of widely used fundamental criteria adapted from guidance on the assessment of observational studies (cross-sectional and cohort studies)[31]. Intervention studies will be assessed for quality according to the Cochrane Collaboration Risk of Bias Assessment Tool for randomised controlled trials and controlled intervention studies. For qualitative studies, drawing on updated guidance from Cochrane Qualitative and Implementation Methods Group (CQIMG), we will appraise study quality against the core set of domains recommended by Cochrane. Quality assessment within each of these domains will be guided by the COREQ tool.

Finally, an overall assessment of the quality (or certainty) of evidence and strength of our recommendations, will be provided by GRADE (for the quant reviews) and GRADE CerQual for the qualitative review.

Data synthesis

Objective 1.1: Evidence synthesis of observational quantitative studies

Our findings will be aggregated in several ways. Initial analysis will be simple categorisation of the characteristics of each study, presented in tables. Findings relating to factors associated with carer psychological morbidity will be grouped into types/ levels of factors.

We will map outcomes to help us visually group presentation of findings and identify common outcomes whose results can be pooled. Main groups of recognised, standard outcomes of psychological morbidity are likely to be measures of depression, anxiety and general psychological morbidity (normally measured in the form of distress through GHQ) and quality of life. Further outcomes may be included if considered important by our carer advisers. We will scrutinise sub-components of standard measures and evidence for correlations between measures to inform any further groupings of outcomes on statistical and conceptual grounds.

Box score analysis

We will use a box score method[32] to present the findings of our review, providing one or more box score tables depending on whether we present all our outcomes together or separately. The box-score table will include the list of factors, grouped by type down the left hand side. We will then classify each study as providing evidence for a statistically significant positive relationship between the factor and outcome, a negative relationship, or no relationship, using the signs + - and 0. By counting the number of signs in each row, we can determine the number of studies testing each relationship and the weight of the evidence amongst those studies. We will also provide a summary of the quality of the relevant studies in the box-score table, in terms of the percentage of included studies which reach a certain pre-determined criterion for quality. Prior to constructing our box-score tables, we will discuss and decide a set of a priori rules for interpreting contents of the table. For example, we will decide the proportion of high quality positive studies in each line that will be required for us to be confident that the variable tested is related the outcome.

Meta-analysis

The main outcome of this evidence synthesis of observational studies will be the effect of a range of factors on psychological morbidity. Where quantitative data permit we will pool data using meta-analyses; we will calculate overall effect sizes for the effects of individual factors on psychological morbidity. Psychological morbidity is mainly expected to be a continuous outcome and therefore Cohen's d together with the 95% confidence intervals will be calculated. Studies will be eligible for inclusion in more than one analysis (e.g. if they report more than factor linked to psychological morbidity) but none of the studies will be represented twice in the same analysis (to avoid double counting). Due to high heterogeneity, random effects models will be applied to calculate pooled effect sizes[33]. Heterogeneity will be assessed using the I^2 statistic with values of 25%, 50%, and 75% indicating low, moderate, and high heterogeneity, respectively[46]. Sensitivity analysis will be performed to evaluate the stability of the results when only studies less susceptible to risk of bias will be retained in the analysis. We will inspect the symmetry of the funnel plots and perform the Egger's test to examine for publication bias[34]. All meta-analyses will be performed in STATA (version 15) using the metaan command[35]. Funnel plots will be constructed using the metafunnel command[36], and the Egger test will be computed using the metabias command[37].

Objective 1.2: Evidence synthesis of qualitative studies

Informed by Cochrane guidance and the RETREAT criteria for selecting methods of qualitative evidence synthesis, we will use thematic synthesis to aggregate qualitative findings on factors carers feel are important to their mental health across our included studies. We will use a best fit framework synthesis approach. This approach is particularly suited to achieve a pragmatic, rapid review of evidence in a way which can generate or inform theory about interventions and their efficacy, presented in ways that are useful to researchers, clinicians and policy makers[38].

Informed by a systems perspective, this approach involves the identification of a "good enough" contingent preliminary conceptual framework as a starting point for deductive data analysis. This framework is formed via the identification of prevalent conceptual models (e.g. by volume of use in relevant literature or informed by expert opinion). The identified models are themselves subject to thematic analysis to identify commonalities and differences. The emergent themes form the preliminary framework for analysis. Data not accommodated within the framework will be identified and in a subsequent inductive phase, new concepts are developed thematically. All data are then coded against the revised framework. The best fit approach represents a first stage in a matrix approach to mixed-methods data synthesis. The integration of qualitative and quantitative evidence is elucidated in Objective 1.4.

Our preliminary conceptual framework will be based on the two main models used to study EOL carer stress: the Transactional Model of Stress and Coping[39] and Pearlin et al's Stress Process Model[4- 41]. These encompass similar concepts and processes to explain carer psychological outcomes. The vast majority of EOL caregiving studies that have considered a model have drawn on one of these models.[18]

Analysis will be conducted by a researcher and carer co-analyst. As with meta-analysis a quality assessment and strength of evidence judgements will be included as part of the analysis and subsequent tabulation of these data. While not as 'thick' and interpretative as synthesis methods such as meta-ethnography, the best fit approach is arguably more pragmatic, transparent and appropriate for multi-disciplinary working and inclusion of PPI/ lay people in the process[38]. Additionally, we will employ principles of meta-ethnography within our analysis plan to ensure that the preconceptions of the proposed conceptual framework can be actively challenged through searches for alternative interpretations and 'deviating' evidence.

The co-analyst and our Review Advisory Panel (RAP) will further help us establish and agree the most suitable categorisation of emergent themes, their fit with the preliminary framework, and to establish the further coding and inclusion of relevant findings falling outside this. Relevance will be determined by our review aims and question and carer perceptions. Carer involvement is particularly important in qualitative analysis where ‘member checks’ with participants or those from a similar background is a key method for validating findings and thus improving rigour. This also provides an important starting point for carer involvement in challenging and refining quantitative research and theory models which often are ‘done to’ users, rather than ‘with’ users, which will be carried through to the final framework integration in Objective 1.4.

Objective 1.3: Evidence synthesis of intervention studies

The main meta-analysis here will evaluate the effectiveness of the interventions in reducing psychological morbidity in end of life carers. Cohen’s d and confidence intervals will be calculated in each study and then the pooled Cohen’s d will be computed using the metaan command (Kontopantelis, 2019) in STATA 15. When data are available for more than one follow-up assessment point, the short-term assessment point (e.g. up to 6-month post-intervention) will be inserted in the main analysis.

Subgroup analyses will be conducted to examine the effect of key study-level factors in the size of the effect. Such factors are likely to be type of interventions (e.g. targeting self-efficacy, perceived control); type of disease and patient disease burden; demographic factors; and key carer psychological factors. The Cochran’s Q test of between group variance will be used to test whether the effectiveness of interventions is significantly different across sub-groups. If the data reporting is consistent across the majority of studies, we might be able to fit a multivariable meta-regression model (using the metareg command)[42] which will account simultaneously for several factors.

Sensitivity analyses will be performed to examine whether the effects are robust when only studies with low risk of bias scores are retained in the analyses. Cluster RCTs (if any) will be identified and the precision of analyses will be adjusted using a sample size/variation inflation method, assuming an intra-class correlation of 0.02[43 44]. Random effects model will be applied throughout; heterogeneity and publication bias will be assessed using the same approach specified in the analysis plan of objective 1.1.

Objective 1.4: Integration of syntheses into a coherent framework

Using narrative graphical and numerical tools we will bring together the findings of our quantitative observational, qualitative and intervention reviews, and map agreement, conflict and evidence gaps between data sources.

For our integration we will build on the revised framework emerging from the qualitative analysis (Objective 1.2) which was informed by stress models, but reshaped and expanded through thematic analysis of carers’ perspectives. The final framework integration will seek to map the quantitative findings onto this framework. The final integration will enable us to assess the fit between models, what matters to carers, and the quantitative empirical evidence.

Research on end of life caregiving is mainly atheoretical, the majority of studies have no theoretical underpinning, and where models have been considered, this has mainly been for post-hoc discussion or explanation of outcomes. There has been little or no a priori empirical testing or systematic assessment of models[18]. It is therefore timely to conduct a systematic, integrated review of the empirical evidence to assess, refine and extend these models, as well as provide a comprehensive overview of factors affecting carer psychological morbidity.

Based on the models, early review and scoping, the initial categories of factors in the framework are likely to include sociodemographic variables (e.g. education), patient factors (e.g. dependency), caregiving context (e.g. family dynamics, work demands, financial pressures), and carer internal psychological factors (e.g. self esteem, mastery). However, our synthesis and integration will refine and extend the framework. This will include classification into modifiable and non-modifiable factors; and furthermore consideration of whether factors affect carer psychological morbidity in the form of predictors (that place carers at initial risk of morbidity), moderators (that moderate the impact of predictors) or mediators (that mediate the relationship between predictors and morbidity).

Our end-product will be a framework based on the empirical evidence, although one whose organisation has been guided by existing models and our RAP. For each factor within the final set of categories we will display the total body of evidence. Some factors are likely to be supported by evidence across all Objective 1.1-3 analyses, for instance ‘perceived control’ is likely to be identified as a factor within observational, qualitative and intervention studies. Thus there will be strong underpinning evidence for this factor under a framework category of ‘carer internal factors’. However, other factors may only be identified from the analysis within one objective, for instance ‘family dynamics’ (part of a ‘caregiving context’ category) may only be identified under Objective 1.1. Conversely, ‘Problem solving skills’ (part of ‘carer internal factors’) may only be identified as an intervention component/ factor under Objective 1.3. These factors would still be integrated into the overall framework, but the limitation of their underpinning evidence would be displayed.

Throughout this integration our Review Advisory Panel (RAP) will help review the summary of the evidence, the proposed framework and the fitting of the evidence to the framework. We will explore whether the RAP can ‘relate’ to the findings (resonance), feel that they ‘make sense’ for them, that they have utility, and how the presentation of findings may need adjustment to be meaningful to carers. Similarly, we will seek the RAP’s feedback on the framework itself, our fitting of the evidence to the framework, and whether the resulting evidence framework appears to have gaps that need to be addressed in further research. This will be done through our scheduled 4-hour RAP meetings and postal/ email review of materials.

WORK PACKAGE 2: STAKEHOLDER CONSULTATION (Objectives 2.1 - 2.2)

Objective 2.1: Translation of evidence synthesis into tailored materials containing accessible information and recommendations for use by stakeholder groups

Stakeholder workshops – evidence review

At review completion, we will convene and host a participatory workshop inviting key stakeholders to review the framework of evidence findings and to consider how these relate to their local settings and systems.

The workshop will comprise a minimum of 30 stakeholders (practitioner representatives from primary, community, social and specialist palliative care provider organisations; policy makers, commissioners, researchers, carer representatives (Carers UK, Carers Trust, and individual carers and patients). We will draw on contacts from networks within our RMG, RAP and previous stakeholder consultations conducted with Hospice UK and CLAHRC Greater Manchester, snowballing and internet searches to identify a set of key informants. Given the potential for schedule clashes we recognise that there may need to be a series of smaller workshops and contingency for electronic input either during workshops, or *post-hoc* in gaining consensus of opinions and drawing together conclusions from the events.

Findings will be presented to workshop stakeholders. A series of small group facilitated exercises will then enable participants to discuss and map the synthesised evidence to current local practice and initiatives while identifying areas of promising practice, and revealing potential opportunities for more impactful action. Iterative group discussions and consensus exercises, using anonymised voting technologies, will enable the identification of evidence-based short, medium and longer-term recommendations for research and key messages for practice priorities about factors associated with carer psychological morbidity, bespoke to each stakeholder group. Whilst enabling stakeholders to identify the most important information and priorities for their group, workshop interaction between groups increases likelihood that their tailored priorities are still part of a coordinated strategy.

Translation of findings from WP1 and workshop

We will develop dissemination outputs based on findings from WP1 and key messages from the workshop. Outputs will be tailored to individual stakeholder group based on the information and priorities identified within the workshop as most relevant to each group. The research team will work with the Review Advisory Panel (RAP) in an iterative cycle of drafting by the research team and review by the RAP. The RAP will furthermore advise on appropriate dissemination strategies and media for the outputs for each stakeholder group. The translation process will be aided by expert input from an infographic specialist.

Objective 2.2: Exploring the operationalisation of project outputs into primary care procedures for further development and testing as a future intervention

We will engage primary care practitioners and carers through focus groups to explore how bespoke outputs developed under Objective 2.1 may be utilised in primary care practice. Evidence synthesis of factors affecting carer morbidity should help inform practitioners what risk factors to look out for and what actions within their repertoire (either in the form of direct input, signposting or referral) are most likely to help.

Focus groups (one for practitioners, N=6; one for carers, N=6) will explore when and how carers may be approached to enable early identification of carers at risk; who would be best placed to do this; how to investigate risk (e.g. feasibility and acceptability of a ‘resilience checklist’); how carers at risk may want to be supported; and what support is feasible within primary care. We will focus primary care practitioners within Greater Manchester who should already be primed to support carers through the GM Carers Charter[28]. The feedback will inform procedures for early identification and support of carers at risk within primary care, sensitive to both practitioner and user perspectives, for future development and testing.

6. DISSEMINATION, OUTPUTS AND ANTICIPATED IMPACT

What will be produced from the research

The project will deliver the following products, each associated with tangible outputs (OP)

- A comprehensive literature review and framework of factors affecting EOL carer psychological morbidity, encompassing factors relevant to carers (WP1)
    - OP: accessible summaries in text and digital formats using language and evidence displays meaningful to carers
    - OP: a scientific report with detailed account of review process, findings and conclusions; peer reviewed publications; and conference presentations
- Overview of evidence gaps and (mis)match between empirical evidence and existing carer stress models (WP1)
    - OP: Strategy for future research, presented in peer reviewed publication, conference presentations

- Tailored and accessible evidence and priorities for key stakeholder groups relevant to their sphere of influence to inform targeted initiatives and interventions (WP2)
    - OP: Bitesize or executive summaries tailored to each stakeholder group, with contents relevant to them in their preferred format.
    - OP: Webinars, blogs and Twitter chats, as recommended by stakeholders
- A process for operationalisation of the review findings and priorities in primary/ community care (WP2)
    - OP: a draft protocol to form basis for further development and testing of a future intervention for early identification and support of carers at risk
- Project website (WP1 & WP2)
    - OP: Website providing project description and latest updates, downloadable project outputs, notification of webinars/ events, blogs from research team and stakeholders, information on how to get involved etc

How we will inform and engage carers, NHS and the wider population
Engagement and communication with carers and other stakeholders is built into project management and WPs from the outset. These stakeholders will further shape the communication and dissemination strategy for wider audiences:

- Our carer and practitioner co-applicants will help ensure the project maintains practical relevance to carers and main practitioners
- An independent Review Advisory Panel (5 carers; 5 other stakeholder representatives) will oversee project conduct and products throughout, help shape further stakeholder involvement and the final tailoring of project outputs and dissemination strategies.
- Our WP2 stakeholder workshop will identify the information and priorities relevant to each stakeholder group and how outputs should be tailored to each in which formats.
- Our WP2 practitioner and carer focus groups will ensure that operationalisation of project outputs in primary / community care fit with practice realities and carer concerns

We will use our already extensive networks (including those built through work with NIHR CLAHRC Greater Manchester, Hospice UK, Royal College of General Practitioners, the Marie Curie charity, Queens Nursing Institute (QNI), NHS England and Public Health England) to bring on board the key informants for our RAP, stakeholder workshop and focus group who are best able to advise on tailoring project outputs and appropriate dissemination. Our co-applicant team and RAP will link the project into other local national and international networks and act as important champions and conduits for our study outputs. Our team is also well placed to ensure that findings are fast tracked in pre and post registration nursing curricula.

How project outputs will enter our health and care system or society as a whole
Project outputs and dissemination strategies will be shaped by our stakeholders (carers and other stakeholders, as described above). We aim to produce bitesize summaries of the project outputs for each stakeholder group (in both text and digital format) and distribute these via a launch event and more widely in electronic, visual and hard-copy format. This is likely to include passive means (posting versions of materials online for people to download; both on our project website and other stakeholder organisational websites, e.g. carer charity hosts); active distribution through stakeholder group mailing lists, forums and newsletters; or more interactive dissemination through webinars, or Twitter-chats. Exact mechanisms for dissemination will be determined by our stakeholder representatives. At the start the dissemination we will liaise with the press offices of University of Manchester, QNI and RCGP/ Marie Curie to raise awareness of the project in the news media, coordinated with the launch event.

Shorter term, our tailored dissemination will provide timely evidence to inform current decision making: policy makers, commissioners and palliative care/ hospice charities are becoming increasingly aware of the need to invest in initiatives to support carers nationally and locally (e.g. the Government's Carers' Strategy still in development, Greater Manchester Health & Social Care Strategic Partnership Commitment to Carers[28]; Hospice UK[45] ;NHS England's MOU for Carers[47]). These stakeholders together with carer charity advocacy organisations need evidence-based information, which so far has been lacking, on where to focus efforts. Contacts within the co-applicant team, RAP and stakeholder workshops should enable us to reach relevant stakeholder audiences with the project outputs.

Medium term the project will deliver an intervention for early identification and support of carers at risk in primary/community care, by providing a practical process for early identification and support of carers at risk for further development and testing. Close links with local primary / community care providers within Greater Manchester and the RCGP/ Marie Curie and QNI representation on our team make us ideally placed to take this forward.

Longer term the project will identify evidence gaps and priorities to drive a coherent strategy for EOL carer research. The combined carer research expertise of team members GG, AW, MF, PB and CR make us ideally placed to take this forward. The evidence synthesis and framework templates once established, would also facilitate work with other carer groups, e.g. carers of people with long term conditions.

What further funding or support will be required if this research is successful
Shorter term, project outputs should aid better decision making within stakeholders' existing remits by providing tailored evidence about which carer groups may be at added risk of psychological morbidity and what early intervention may help[48]. Where additional funding would be required, is in the further development and testing of an intervention in primary/ community care for early identification and support of carers at risk. We will apply for funding for this (e.g. through NIHR RfPB follow on funding). Identified research gaps and priorities are over time likely to underpin an NIHR programme grant application. Our outcomes would also be of interest to research charities, e.g. Marie Curie Research Fund, who we will approach for specific spin-off projects. Finally, we will seek funding to maintain the project website to ensure it remains updated and accessible.

Possible barriers for further research, development, adoption and implementation
Our approach should overcome initial, common barriers to utilisation of evidence synthesis findings by (1) providing tailored, accessible outputs to stakeholder groups, rather than expect them to sift through synthesised evidence to extract what is relevant to them; (2) adopting a proactive approach in dissemination to stakeholder groups rather than expect them to come to us, and engaging in dialogue rather than didactic, top-down approach of communication. Competing priorities of stakeholder groups would still place limitations on the extent of utilisation of outcomes. However, within these constraints, the project would both help raise the awareness of factors placing carers at risk and inform appropriate initiatives to ameliorate these within the options available to stakeholders.

Further, we will begin to address challenges of implementation in healthcare practice by investigating the acceptability and feasibility of assessing carers for early risk and targeted follow up in primary/ community care (e.g. through carer risk checklists), thus aiming to begin to tackle practical issues of implementation of an intervention in this setting.

For research, utilisation of findings to drive further enquiry will depend on funding. However, research projects based on clear evidence gaps and priorities are more likely to meet with success.

What the impact of the research will be and for whom
Both immediate and longer term impacts can be achieved by:

- informing priorities and decision making of stakeholder groups (e.g. policy makers re legislation and health promotion initiatives for carers; commissioners re what services would benefit carers; palliative/ hospice care charities re appropriate carer support services; carer charities re advocacy for change)
- providing carer advice and resources via carer charities and our project website

Longer term impact is likely to be achieved by:

- enabling primary care/ community practitioners to support carers more effectively through earlier, more focused support of those at potential risk, to reduce later, more severe psychological impact
- enabling researchers to address gaps in knowledge and develop better interventions to ameliorate psychological morbidity in EOL carers based on best evidence

Ultimately the project should benefit carers and their patients, and should reduce healthcare costs. Some 400,000 carers p.a. may suffer significant clinical psychological morbidity during the final months of EOL caregiving, based on an estimated 500,000 providing EOL care and a potential 83% prevalence of morbidity[2]. Even one percentage point reduction in this number through earlier intervention and better targeted support would benefit 4,000 carers. The cost of treatment for anxiety and depression is over £1-2,000 per case (with bigger losses from lost employment)[1], which means this reduction in carer morbidity may save £4-8million p.a. at a conservative estimate. Carer input is furthermore the main predictor of death at home. If care at home can be sustained for more patients by supporting carers, this may entail considerable hospital cost savings (estimated at £3,000 per death in hospital)[3] as well as increase likelihood of patients dying in their preferred location[4].

7. PROJECT / RESEARCH TIMETABLE

Utilising existing collaborations and networks, and methods previously used by our team, our rapid evidence synthesis approach can be realistically achieved within 18 months.

Project month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
Review Advisory Panel*	■	■					■				■		■			■		
Research Management Group*	■	■		■			■			■			■			■		
Work Package 1																		
Set up and protocol refinement	■																	
Searches, screening, retrieve full texts		■	■	■														
Data extraction, quality assessment				■	■	■	■	■										
Data analysis, synthesis and interpretation							■	■	■	■	■	■						
Preparation of final report												■	■	■	■			
Dissemination																■	■	■
Work package 2																		
Engage stakeholders									■	■	■							
Evidence Review workshop												■						
Focus Groups												■	■					
Production of dissemination materials													■	■	■	■		
Products launch &																■	■	■

dissemination																■	■	■

Milestones

Month 4:	All papers identified for review
Month 8:	Completion of data extraction and quality assessment of identified papers
Month 12:	Completion of analysis, synthesis and mapping into framework
Month 16:	Completion of translation of synthesis into tailored materials
Month 18:	Completion of launch event and dissemination

8. ETHICS / REGULATORY APPROVALS

There should be no need to gain ethical or governance approval as we propose a secondary synthesis of existing data and stakeholder consultation. We will ensure that work adheres to the UK Framework for Health and Social Care Research where appropriate, and follow INVOLVE guidance for PPI / Stakeholder work.

9. PATIENT AND PUBLIC INVOLVEMENT

PPI will mainly be achieved by having a carer co-applicant on the team and a carer co-analyst for the WP1 qualitative synthesis, by strong representation of carers in our Review Advisory Panel, stakeholder workshop and focus groups (WP2) (see PPI on main form).

10. SUCCESS CRITERIA AND BARRIERS TO PROPOSED WORK

The success of the project will be measured against the following criteria: our ability to synthesise three main bodies of literature; produce a summary of the literature within a comprehensive framework; produce tailored materials for different stakeholder groups; disseminate via key stakeholder channels and forums; and produce a practical process for identifying and supporting carers at risk in primary/ community care. The risks together with mitigating processes are outlined below.

Difficulty of conducting synthesis of three main bodies of literature
The challenges of conducting, in effect, three reviews in one will be mitigated by using a common search and selection process for all reviews before allocating the literature into separate strands for extraction and analysis. Analysis will be staggered, completing the larger quantitative observational review first, with each strand conducted to a clear protocol developed by experts within the team (PB, MP). The full time Research Fellow will be supported by added Research Associate input during the reviews (month 2-13).

Difficulty of synthesising evidence into a framework and creating bespoke materials
Our expertise in caregiver research, previous thematic literature review[18,19] and scoping of recent literature have given us a detailed overview of the likely factors affecting carer psychological morbidity, and a clear vision of how they can be pulled together into a framework to summarise the empirical evidence. Our expertise in, and scoping of, carer stress models make us confident that we can base a first version of this framework on existing models. This is likely to be reshaped into a final framework based on the empirical evidence and carer input, but we will be able to work to a clear template, rather than be subject to the risk and uncertainty of devising a framework from scratch. The final framework will in turn provide a template for tailoring stakeholder materials, where different parts of the framework can be highlighted and elaborated for different stakeholders according to their

needs and perspectives. The involvement with stakeholders throughout (RMG, RAP and workshops) will help ensure that both content and format of materials are relevant and meaningful to stakeholders.

Difficulty of gaining interest and involvement from stakeholder groups
The applicant team already has run successful broad-based stakeholder consultations for NIHR CLAHRC Greater Manchester and Hospice UK, and has links into extensive stakeholder networks, including NIHR CLAHRC GM NHS partners and local carer groups, Hospice UK/ National Council for Palliative Care (*NCPC)***,** RCGP, Marie Curie, Queens Nursing Institute (QNI), NHS England and Public Health England. Further snowballing techniques will be used to bring on board key stakeholder informants to shape the tailoring project output to stakeholder groups.

Difficulty of operationalising project outputs in primary/ community care
We have already discussed practical options for operationalising project outputs with our GP/ community nursing and PPI co-applicants. However, which options are likely to be best will depend on the outcomes of the evidence synthesis and stakeholder consultation.

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