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Assessing impact, needs and quality-of-life among informal carers of people with pancreatic cancer: The PAN-CARER study Protocol

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ASSESSING IMPACT, NEEDS AND QUALITY-OF-LIFE AMONG INFORMAL CARERS OF PEOPLE WITH PANCREATIC CANCER: THE PAN-CARER STUDY PROTOCOL

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ABSTRACT

Introduction

Approximately 10,300 people are diagnosed with pancreatic cancer each year in the UK. The cancer and its treatment inflict a significant physical, functional and emotional burden on patients. Research suggests that patients have many ongoing needs for support and care, but that these needs are not met by existing services. Family members often step in to fill this gap and provide support and care during and after treatment. Research in other cancers shows that this informal caregiving can place a very heavy burden on carers. However, there are few studies in the international literature that have focussed on informal carers in pancreatic cancer; none have been conducted in the UK.

Methods and analysis

Two complementary research methods will be utilised. Firstly, a longitudinal quantitative study of 300 carers will investigate, using validated questionnaires, the impact of caregiving (Caregiver Reaction Assessment), the unmet needs of carers (Supportive Care Needs Survey), and their quality-of-life (short form 12 item health survey), will be conducted. Secondly, qualitative interviews will be conducted with 30 carers to explore their experiences in more depth. Mixed effects regression models will be applied to survey results to determine how impact, needs and quality-of-life vary over time, compare outcomes between carers of patients with operable and inoperable disease and identify social factors which affect outcomes. Interview data will undergo reflexive thematic analysis.

Ethics and dissemination

The protocol has been approved by the Health Research Authority of the UK (Ethical approval IRAS ID 309503). Findings will be published in peer-reviewed journals and presented at national and international conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study will examine an under-investigated area in pancreatic cancer research and generate novel data on how carer impact evolves over time from diagnosis
- A high number of participants will be recruited from different locations in England
- Both quantitative (survey) and qualitative (interview) data will be utilised to provide complementary data and give depth to the analysis
- Both operable and inoperable patients will be included to ascertain the burden of caregiving for each group.
- Carers with high levels of anxiety, or burden, may not agree to participate in the study, resulting in an under-estimation of the burden of caregiving

INTRODUCTION

Pancreatic cancer patients have a significant symptom burden and many unmet physical and psychological needs. Family and friends increasingly take on the role of informal caregivers, providing social, emotional and practical care during and following treatment. Research in other cancers indicates that informal caregiving can place a heavy burden on people and that carers can have many unmet needs. However, there is paucity of data on informal caregiving in pancreatic cancer.

The last decade has brought major changes in pancreatic cancer treatment. Significant progress has been made in chemotherapy regimens in the adjuvant and metastatic settings, with 5-year survival up to 37% for patients with resectable disease who complete adjuvant chemotherapy (https://www.cancer.net/cancer-types/pancreatic-cancer/statistics). However, only 10-15% of patients are suitable for surgery and surgery is associated with high morbidity and often prolonged hospital stay. Furthermore, chemotherapy, whether used as neoadjuvant or adjuvant treatment, is associated with challenging side-effects. During and following treatment, patients can have a high and debilitating symptom burden including severe pain, fatigue, jaundice and nausea (1). Levels of anxiety and depression are high (2). Indeed, research has shown that some physical and psychological effects (e.g. pain, distress) are more common in pancreatic cancer patients than those with other cancers (2). Consequently, patients have significant, and persistent, supportive care needs in a range of areas, which are largely unmet by existing services (3,4).

For pancreatic cancer (as for other cancers) family members and friends often step into the gap left by services, providing practical, emotional and social support and care for patients during treatment, recovery and afterwards – so-called informal caregiving. Emerging evidence for other cancers indicates that informal caregiving for patients with cancer places a heavy burden on the individual. Family members and friends are seldom prepared to be carers (5), and are thrust into the role at the time when they are struggling to come to terms with the diagnosis. Although there can be positive aspects of caregiving (6), carers often report difficulties in undertaking complex caring activities (e.g. symptom management, treatment monitoring) while lacking the information, support, and self-confidence to perform these tasks (7;8). Disruptions to carers' lives and work can be significant (9) and many, including those who do not regard caregiving negatively, suffer from a wide range of problems, such as practical and financial difficulties, sleep disturbance, psychological problems, and decrements in their own health (10-13). These effects impact quality-of-life (14), can persist long after care activities have ceased, and can have significant long-term sequalae (15). Few services exist specifically for carers, and they may be unable to access support available for patients. Consequently, carers themselves often have extensive unmet needs for support (13;16), which not only correlate with carer burden (17) and decrease their own quality-of-life, but also negatively affect the patient's wellbeing and health outcomes (18).

For pancreatic cancer specifically, there have been very few studies of informal caregiving. In a US study of 8 carers of patients with advanced pancreatic cancer, carers reported spending, on average,

9 hours/ day on caregiving activities and losing more than 5 hours sleep/night (19). Stressors experienced by carers included not knowing what to expect, trying to be strong for the care recipient and managing the wider family. In a study of 78 carers in Ireland, caregiving responsibilities had greatest impact on carers' schedules and their health (20). A US study of 22 family members of pancreatic cancer patients (not all of whom were informal carers), reported carers struggle to balance their feelings with those of the patient (21), while the largest study, of 84 carers in Australia reported that 58% had below average quality-of-life and, importantly, a higher proportion of carers than patients had significant anxiety (22).

While these data point towards a significant burden on informal carers in pancreatic cancer, there are important limitations in the work, and major gaps in knowledge. Studies were small and from different healthcare systems, so findings may not generalise to the UK. How caring for someone with pancreatic cancer impacts people's lives, and their physical and emotional wellbeing is not understood. Furthermore, it is unknown how the impact of caring changes over time from diagnosis or how it varies for carers of patients with resectable compared to metastatic or locally advanced tumours. Carers' own support needs have not been investigated, and which carers experience the greatest impact or most unmet needs is unknown. Moreover, the factors that mitigate against negative impacts of caregiving in pancreatic cancer have never been explored.

The proposed pilot project will – for the first time in the UK - investigate and characterise informal caregiving in pancreatic cancer. It will provide the first complementary qualitative and quantitative data on this topic. Using these methods together provides a better understanding of complex phenomena than either approach alone and, here, will reveal the "big picture" of the impact of caregiving in pancreatic cancer and a detailed understanding of that experience.

The study will generate completely novel data on how carer impact evolves over time from diagnosis, compares in those caring for patients with operable and inoperable disease, and affects carer quality-of-life. It will shed new light on whether carers feel equipped to support their care recipients and whether they experience issues and problems that are distinct from the needs of the care recipient. Moreover, it will provide the first data on carers' needs for support and how impacts, needs and quality-of-life inter-relate. Finally, it will provide novel information on which subgroups of carers experience greatest impact and needs, and what may mitigate against negative effects of caregiving.

The pilot will confirm feasibility, design and methods for a future nationwide study including all major pancreatic units, enabling recruitment from all regions and socio-economic and ethnic groups. The work will have important long-term implications. It will inform the need for interventions and services for informal carers, and provide information on the content and shape of these. It will also help identify carers at greatest risk of adverse effects, who might benefit from targeted support and provide data to inform development of a screening tool which could be used to identify these carers. Ultimately, it has significant potential to improve pancreatic cancer patient support and outcomes.

METHODS AND ANALYSIS

This protocol design was based on the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Statement (23) and will be conducted in accordance with the principles of Good Clinical Practice.

Study design and setting

PAN-CARER is a multi-centre multi-method prospective study with two phases. Phase 1 will establish a cohort of informal carers from whom quantitative data will be collected. Phase 2 will involve in-depth interviews with informal carers, primarily sampled from the cohort.

The study will be conducted at five tertiary centres (Freeman Hospital, Newcastle-Upon-Tyne; Queen Elizabeth Hospital, Birmingham; Royal Surrey County Hospital, Guilford; Manchester Royal Infirmary. Manchester and Oxford Radcliffe hospital, Oxford) and two district general hospitals (Sunderland Royal Hospital, Sunderland and James Cook Hospital, Middlesbrough). These sites have been chosen because they have socio-economic and ethnically diverse catchment populations, and differ in their pancreatic cancer patient populations and in supports offered by, and services allied with, the hospital.

The recruiting centres currently undertake around 500 pancreatic resections per year for resectable pancreatic cancers and manage a further 1000 patients with inoperable cancer through their multidisciplinary team meetings.

To supplement recruitment in phase 2, and allow the study to be completed in a timely fashion, carers will also be identified outwith these NHS sites, including through social media and charities (specifically Pancreatic Cancer UK (PCUK)).

Eligibility criteria

Carers of patients with operable and inoperable (including locally advanced and metastatic) pancreatic cancer who are greater than 18 years of age will be included in the study. Those unable to give informed consent will be excluded. Carers will be those who identify themselves with this term, or as someone who provides (or has provided) support for a family member or friend diagnosed with pancreatic cancer.

Study tests

Phase 1 – questionnaire

The questionnaire will include questions on carer circumstances (e.g. relationship to patient, gender, age, employment status), and validated, and recommended, instruments to measure impact, unmet needs and quality-of-life. Impact will be assessed using the Caregiver Reaction Assessment (CRA) which measures four negative domains of caregiving impact (effects of caregiving on carers' daily activities; financial strain due to caregiving tasks; perceived deterioration in health from caring; lack of family support) and one positive domain (impact on self-esteem) (24). Unmet needs will be measured

using the Supportive Care Needs Survey Partners and Caregivers (SCNS-P&C45), which captures information needs, healthcare service needs, work and social needs, and psychological and emotional needs (25). Mental and physical quality-of-life will be measured using the short form 12 item health survey (SF12_v2) quality of life questionnaire (26). Questionnaires will be administered at three time points (Table 1) by research nurses in the NHS sites.

Phase 2 - interview

Interviews will be guided by a topic guide and explore experiences of caregiving (activities undertaken, etc), preparedness for taking on caregiving role, how well-equipped the carer feels to fulfil caregiving responsibilities, carer's own support needs and how these have evolved since the care recipient's diagnosis, carer's perceptions of existing and potential services/supports, and supports/services carers would like to see provided. The topic guide will be used flexibly to allow interviewees to raise issues they consider important and new areas raised will be explored in subsequent interviews to ensure sufficient depth is reached. Interviews will be undertaken by a trained qualitative researcher, with experience in research among potentially vulnerable participants or those in potentially challenging emotional situations.

Management of participant distress

It is recognised that participating in research may have emotional consequences for the individual and may involve them considering and discussing potentially upsetting issues related to their own experiences. If a participant does not wish to answer any question during either the quantitative or qualitative interviews, this will be respected. If they become upset, the researcher/research nurse will ask them if they wish to halt the interview, either temporarily or permanently. If they become very distressed, the researcher/research nurse will ask whether they would like her/him to contact someone (a family member, friend, GP, consultant) on their behalf. Participants will also be offered a useful contacts sheet which will list contact details for members of the study team and organisations such as PCUK, who offer support for patients with pancreatic cancer.

Study outcomes

Study outcomes include the subjective impact of caregiving on the carer, the extent of unmet care supportive needs and carer quality of life.

Participant Timeline

The participant schedule of events is summarised in Table 1.

Phase 1

For the inoperable group (ie carers of inoperable patients) , participants will be recruited approximately 6 weeks post-diagnosis to allow the patient and carer time to come to terms with the diagnosis. For the operable group, we will aim to collect the first questionnaire prior to surgery to provide a "baseline",

and therefore recruit 2-4 weeks post-diagnosis. The questionnaire will then be repeated at 3 and 6 months following diagnosis. Prior to data collection at 3 and 6 months, research nurses will contact the patient's GP to obtain information on current health status. Carers will be contacted by telephone; contacts will be sensitive to circumstances and clarify whether the individual wishes to continue in the study.

Phase 2

Most interviews will take place approximately 3-6 months post-diagnosis to allow carers time to reflect post-diagnosis. A few (among participants recruited through non-NHS routes) will be conducted 6-12 months from diagnosis, to provide some information on carer experience later in the disease trajectory.

Table 1 – Schedule of enrolments, tests and assessments

Timepoint	D0 diagnosis	2-6 weeks	3 months	6 months
Enrolment – Phase 1				
- Eligibility screen		X		
- Consent for quantitative study		X		
Enrolment – Phase 2				
- Eligibility screen			◆	◆
- Consent for qualitative interview			◆	◆
Test				
- Carer characteristics		X		
- Patient characteristics		X		
- Caregiver reaction assessment (CRA)		X	X	X
- Supportive Care Needs Survey (SCNS-P&C45)		X	X	X
- Quality of life (SF12_v2)		X	X	X
- Semi-structured interview			◆	◆
Assessments				

• Carer characteristics: Age, sex, relationship to patient, co-morbidities		X		
• Patient characteristics: Age, sex, disease profile, management, vital status		X	X	X
• Impact assessment		X	X	X
• Unmet needs assessment		X	X	X
• Mental and physical QoL score		X	X	X
• Experiences of caregiving			◆—	—◆

Sample Size

In phase 1 (quantitative), 300 carers of patients with operable (n=~150) and inoperable (including locally advanced and metastatic, n=~150) pancreatic cancer will be enrolled in the study. The sample size assessment was based on the number of cases diagnosed, estimated numbers with carer involvement, and likely response rates. No sample size calculations were undertaken as this is a pilot study.

In phase 2 (qualitative), recruitment will continue until reasonable data saturation is reached. Experience suggests up to 30 interviews are likely to be required.

Recruitment & data collection

Phase 1:

Recruitment will be undertaken by research nurses when carers accompany patients to hospital soon after diagnosis. Patients who attend alone will be asked whether they can nominate a carer and, if so, to pass on study information. Research nurses (or other research staff) will administer questionnaires by telephone or video conferencing software, if preferred. Patients will also be given the option to complete the questionnaire themselves at home and return them by mail.

Phase 2:

Selected participants from the phase 1 cohort will be invited to participate in phase 2. Maximum variation purposive sampling will be used to ensure elicitation of varied experiences. Sampling strata will include whether patient has operable/inoperable disease, time since diagnosis, site, and carer gender. Interviews will last 60-90 minutes and take place remotely, by video (e.g. Zoom) or telephone, at a time convenient for the interviewee. They will be audio-recorded and transcribed for analysis.

Data management

All data will be stored in secure electronic database protected by two factor authentication (REDCap), and only accessible by research staff. Data integrity will be maintained with data validation tools built

into the database and with regular checks by the data manager for accuracy and prevention of missing data. The database will be backed up daily.

Statistics and analysis plan

Phase 1:

Statistical analysis will be conducted in Stata. Mean carer impact (overall and by domain), mean mental and physical quality-of-life, and proportion with unmet needs (any and by domain) will be computed. Mixed effects regression models (linear or logistic as appropriate) will be used to: (i) determine how impact, needs and quality-of-life vary over time; (ii) compare outcomes between carers of patients with operable and inoperable disease; and (iii) identify factors (e.g. carer age, employment status) associated with outcomes. Mixed-effects models allow all surveys completed at every time-point to be included in analysis, taking within-subject correlations into account to produce robust error estimates (27). Associations between both impact and unmet needs and quality-of-life will be assessed using similar approaches.

Phase 2:

Interview recordings will be transcribed and reflexive thematic analysis undertaken (28). Data collection and analysis will occur concurrently to ensure any new issues raised are explored in subsequent interviews. Analysis and organisation of data will be facilitated by NVivo software. A few interviews will be independently coded by two team members to agree emergent themes, which will form an analytical "framework". Remaining interviews will be coded to this framework, with novel issues incorporated as analysis progresses. Standard approaches for analytical rigour will be applied (e.g. constant comparison, deviant case analysis). Interpretation and drawing out pertinent findings will involve the entire applicant team.

ETHICS AND DISSEMINATION

Local Hospital Trust sponsorship and UK Health Research Authority (HRA) Research ethics committee (REC) approval has been obtained (Ethical approval IRAS ID 309503. East of England - Cambridge Central Research Ethics Committee, REC reference 22/EE/0072 18th May 2022).

Non-identifiable and anonymised data and findings will be published in peer-reviewed journals and presented at national and international conferences. Lay summaries will be developed and disseminated, including through the networks of PCUK. Patient consent includes granting permission for sharing non-identifiable data with other groups to advance understanding of caregiving in pancreatic cancer.

There are no conflicts of interest to declare.

PUBLIC AND PATIENT INVOLVEMENT

Feedback on the project, and advice on methods, was obtained from the PCUK Research Involvement Network (RIN), a PPI group which includes those affected by pancreatic cancer. The RIN will be consulted throughout the project. Their reflection and comments on emergent findings will be sought and they will be asked to highlight key messages for carers and patients. Feedback will also be obtained on lay summaries to ensure findings are clear and understandable and reported sensitively. Moreover, the RIN will be asked to suggest areas for follow-on research.

CONCLUSION

In other cancers, evidence is growing that a cancer diagnosis can have a major impact on the lives and wellbeing of informal carers – family members or friends who provide day-to-day support and care for patients. Given the nature of pancreatic cancer, it seems likely that the impact on carers may be especially significant. Tentative international data suggests this is the case, but that data is very limited and major gaps in evidence remain.

The proposed pilot project will – for the first time in the UK - investigate and characterise informal caregiving in pancreatic cancer. It will provide the first complementary qualitative and quantitative data on this topic. Using these methods together provides a better understanding of complex phenomena than using either approach alone and, here, will reveal the "big picture" of the impact of caregiving in pancreatic cancer and a detailed understanding of that experience.

The study will generate completely novel data, internationally, on how carer impact evolves over time from diagnosis, compares in those caring for patients with operable and inoperable disease, and affects carer quality-of-life. It will shed new light on whether carers feel equipped to support their care recipients and whether they experience issues and problems that are distinct from the needs of the care recipient. Moreover, it will provide the first data on carers' needs for support and how impacts, needs and quality-of-life inter-relate. Finally, it will provide novel information on which subgroups of carers experience greatest impact and needs, and what may mitigate against negative effects of caregiving.

The work will have important long-term implications. It will inform the need for interventions and services for informal carers and provide information on the content and shape of these. It will also help identify carers at greatest risk of adverse effects, who might benefit from targeted support and provide data to inform development of a screening tool which could be used to identify these carers. Furthermore, the pilot will confirm feasibility, design and methods of a nationwide study including all major pancreatic units, enabling recruitment from all regions and socio-economic and ethnic groups. Ultimately, it has significant potential to improve pancreatic cancer patient support and outcomes.

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Prof Linda Sharp: Co-Principal investigator, study design, protocol co-author
Dr Keno Mentor: Study design, protocol co-author & submission
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COMPETING INTERESTS STATEMENT

The authors have no competing interests to declare.

DATA AVAILABILITY STATEMENT:

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

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ASSESSING IMPACT, NEEDS AND QUALITY-OF-LIFE AMONG INFORMAL CARERS OF PEOPLE WITH PANCREATIC CANCER: THE PAN-CARER STUDY PROTOCOL

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ABSTRACT

Introduction

Approximately 10,300 people are diagnosed with pancreatic cancer each year in the UK. The cancer and its treatment inflict a significant physical, functional and emotional burden on patients. Research suggests that patients have many ongoing needs for support and care, but that these needs are not met by existing services. Family members often step in to fill this gap and provide support and care during and after treatment. Research in other cancers shows that this informal caregiving can place a very heavy burden on carers. However, there are few studies in the international literature that have focussed on informal carers in pancreatic cancer; none have been conducted in the UK.

Methods and analysis

Two complementary research methods will be utilised. Firstly, a longitudinal quantitative study of 300 carers will investigate, using validated questionnaires, the impact of caregiving (Caregiver Reaction Assessment), the unmet needs of carers (Supportive Care Needs Survey), and their quality-of-life (short form 12 item health survey), will be conducted. Secondly, qualitative interviews will be conducted with 30 carers to explore their experiences in more depth. Mixed effects regression models will be applied to survey results to determine how impact, needs and quality-of-life vary over time, compare outcomes between carers of patients with operable and inoperable disease and identify social factors which affect outcomes. Interview data will undergo reflexive thematic analysis.

Ethics and dissemination

The protocol has been approved by the Health Research Authority of the UK (Ethical approval IRAS ID 309503). Findings will be published in peer-reviewed journals and presented at national and international conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study will examine an under-investigated area in pancreatic cancer research and generate novel data on how carer impact evolves over time from diagnosis
- A high number of participants will be recruited from different locations in England
- Both quantitative (survey) and qualitative (interview) data will be utilised to provide complementary data and give depth to the analysis
- Both operable and inoperable patients will be included to ascertain the burden of caregiving for each group.
- Carers with high levels of anxiety, or burden, may not agree to participate in the study, resulting in an under-estimation of the burden of caregiving

INTRODUCTION

Pancreatic cancer patients have a significant symptom burden and many unmet physical and psychological needs. Family and friends increasingly take on the role of informal caregivers, providing social, emotional and practical care during and following treatment. Research in other cancers indicates that informal caregiving can place a heavy burden on people and that carers can have many unmet needs. However, there is paucity of data on informal caregiving in pancreatic cancer.

The last decade has brought major changes in pancreatic cancer treatment. Significant progress has been made in chemotherapy regimens in the adjuvant and metastatic settings, with 5-year survival up to 37% for patients with resectable disease who complete adjuvant chemotherapy (https://www.cancer.net/cancer-types/pancreatic-cancer/statistics). However, only 10-15% of patients are suitable for surgery and surgery is associated with high morbidity and often prolonged hospital stay. Furthermore, chemotherapy, whether used as neoadjuvant or adjuvant treatment, is associated with challenging side-effects. During and following treatment, patients can have a high and debilitating symptom burden including severe pain, fatigue, jaundice and nausea (1). Levels of anxiety and depression are high (2). Indeed, research has shown that some physical and psychological effects (e.g. pain, distress) are more common in pancreatic cancer patients than those with other cancers (2). Consequently, patients have significant, and persistent, supportive care needs in a range of areas, which are largely unmet by existing services (3,4).

For pancreatic cancer (as for other cancers) family members and friends often step into the gap left by services, providing practical, emotional and social support and care for patients during treatment, recovery and afterwards – so-called informal caregiving. Emerging evidence for other cancers indicates that informal caregiving for patients with cancer places a heavy burden on the individual. Family members and friends are seldom prepared to be carers (5), and are thrust into the role at the time when they are struggling to come to terms with the diagnosis. Although there can be positive aspects of caregiving (6), carers often report difficulties in undertaking complex caring activities (e.g. symptom management, treatment monitoring) while lacking the information, support, and self-confidence to perform these tasks (7;8). Disruptions to carers' lives and work can be significant (9) and many, including those who do not regard caregiving negatively, suffer from a wide range of problems, such as practical and financial difficulties, sleep disturbance, psychological problems, and decrements in their own health (10-13). These effects impact quality-of-life (14), can persist long after care activities have ceased, and can have significant long-term sequalae (15). Few services exist specifically for carers, and they may be unable to access support available for patients. Consequently, carers themselves often have extensive unmet needs for support (13;16), which not only correlate with carer burden (17) and decrease their own quality-of-life, but also negatively affect the patient's wellbeing and health outcomes (18).

For pancreatic cancer specifically, there have been very few studies of informal caregiving. In a US study of 8 carers of patients with advanced pancreatic cancer, carers reported spending, on average,

9 hours/ day on caregiving activities and losing more than 5 hours sleep/night (19). Stressors experienced by carers included not knowing what to expect, trying to be strong for the care recipient and managing the wider family. In a study of 78 carers in Ireland, caregiving responsibilities had greatest impact on carers' schedules and their health (20). A US study of 22 family members of pancreatic cancer patients (not all of whom were informal carers), reported carers struggle to balance their feelings with those of the patient (21), while the largest study, of 84 carers in Australia reported that 58% had below average quality-of-life and, importantly, a higher proportion of carers than patients had significant anxiety (22).

While these data point towards a significant burden on informal carers in pancreatic cancer, there are important limitations in the work, and major gaps in knowledge. Studies were small and from different healthcare systems, so findings may not generalise to the UK. How caring for someone with pancreatic cancer impacts people's lives, and their physical and emotional wellbeing is not understood. Furthermore, it is unknown how the impact of caring changes over time from diagnosis or how it varies for carers of patients with resectable compared to metastatic or locally advanced tumours. Carers' own support needs have not been investigated, and which carers experience the greatest impact or most unmet needs is unknown. Moreover, the factors that mitigate against negative impacts of caregiving in pancreatic cancer have never been explored.

The proposed pilot project will – for the first time in the UK - investigate and characterise informal caregiving in pancreatic cancer. It will provide the first complementary qualitative and quantitative data on this topic. Using these methods together provides a better understanding of complex phenomena than either approach alone and, here, will reveal the "big picture" of the impact of caregiving in pancreatic cancer and a detailed understanding of that experience.

The study will generate completely novel data on how carer impact evolves over time from diagnosis, compares in those caring for patients with operable and inoperable disease, and affects carer quality-of-life. It will shed new light on whether carers feel equipped to support their care recipients and whether they experience issues and problems that are distinct from the needs of the care recipient. Moreover, it will provide the first data on carers' needs for support and how impacts, needs and quality-of-life inter-relate. Finally, it will provide novel information on which subgroups of carers experience greatest impact and needs, and what may mitigate against negative effects of caregiving.

The pilot will confirm feasibility, design and methods for a future nationwide study including all major pancreatic units, enabling recruitment from all regions and socio-economic and ethnic groups. The work will have important long-term implications. It will inform the need for interventions and services for informal carers, and provide information on the content and shape of these. It will also help identify carers at greatest risk of adverse effects, who might benefit from targeted support and provide data to inform development of a screening tool which could be used to identify these carers. Ultimately, it has significant potential to improve pancreatic cancer patient support and outcomes.

METHODS AND ANALYSIS

This protocol design was based on the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Statement (23) and will be conducted in accordance with the principles of Good Clinical Practice.

Study design and setting

PAN-CARER is a multi-centre multi-method prospective study with two phases. Phase 1 will establish a cohort of informal carers from whom quantitative data will be collected. Phase 2 will involve in-depth interviews with informal carers, primarily sampled from the cohort.

The study will be conducted at five tertiary centres (Freeman Hospital, Newcastle-Upon-Tyne; Queen Elizabeth Hospital, Birmingham; Royal Surrey County Hospital, Guilford; Manchester Royal Infirmary. Manchester and Oxford Radcliffe hospital, Oxford) and two district general hospitals (Sunderland Royal Hospital, Sunderland and James Cook Hospital, Middlesbrough). These sites have been chosen because they have socio-economic and ethnically diverse catchment populations, and differ in their pancreatic cancer patient populations and in supports offered by, and services allied with, the hospital.

The recruiting centres currently undertake around 500 pancreatic resections per year for resectable pancreatic cancers and manage a further 1000 patients with inoperable cancer through their multidisciplinary team meetings.

To supplement recruitment in phase 2, and allow the study to be completed in a timely fashion, carers will also be identified outwith these NHS sites, including through social media and charities (specifically Pancreatic Cancer UK (PCUK)).

Eligibility criteria

Carers of patients with operable and inoperable (including locally advanced and metastatic) pancreatic cancer who are greater than 18 years of age will be included in the study. Those unable to give informed consent will be excluded. Carers will be those who identify themselves with this term, or as someone who provides (or has provided) support for a family member or friend diagnosed with pancreatic cancer.

Study tests

Phase 1 – questionnaire

The questionnaire will include questions on carer circumstances (e.g. relationship to patient, gender, age, employment status), and validated, and recommended, instruments to measure impact, unmet needs and quality-of-life. Impact will be assessed using the Caregiver Reaction Assessment (CRA) which measures four negative domains of caregiving impact (effects of caregiving on carers' daily activities; financial strain due to caregiving tasks; perceived deterioration in health from caring; lack of family support) and one positive domain (impact on self-esteem) (24). Unmet needs will be measured

using the Supportive Care Needs Survey Partners and Caregivers (SCNS-P&C45), which captures information needs, healthcare service needs, work and social needs, and psychological and emotional needs (25). Mental and physical quality-of-life will be measured using the short form 12 item health survey (SF12_v2) quality of life questionnaire (26). Questionnaires will be administered at three time points (Table 1) by research nurses in the NHS sites.

Phase 2 - interview

Interviews will be guided by a topic guide and explore experiences of caregiving (activities undertaken, etc), preparedness for taking on caregiving role, how well-equipped the carer feels to fulfil caregiving responsibilities, carer's own support needs and how these have evolved since the care recipient's diagnosis, carer's perceptions of existing and potential services/supports, and supports/services carers would like to see provided. The topic guide will be used flexibly to allow interviewees to raise issues they consider important and new areas raised will be explored in subsequent interviews to ensure sufficient depth is reached. Interviews will be undertaken by a trained qualitative researcher, with experience in research among potentially vulnerable participants or those in potentially challenging emotional situations.

Management of participant distress

It is recognised that participating in research may have emotional consequences for the individual and may involve them considering and discussing potentially upsetting issues related to their own experiences. If a participant does not wish to answer any question during either the quantitative or qualitative interviews, this will be respected. If they become upset, the researcher/research nurse will ask them if they wish to halt the interview, either temporarily or permanently. If they become very distressed, the researcher/research nurse will ask whether they would like her/him to contact someone (a family member, friend, GP, consultant) on their behalf. Participants will also be offered a useful contacts sheet which will list contact details for members of the study team and organisations such as PCUK, who offer support for patients with pancreatic cancer.

Study outcomes

Study outcomes include the subjective impact of caregiving on the carer, the extent of unmet care supportive needs and carer quality of life.

Participant Timeline

The participant schedule of events is summarised in Table 1.

Phase 1

For the inoperable group (ie carers of inoperable patients) , participants will be recruited approximately 6 weeks post-diagnosis to allow the patient and carer time to come to terms with the diagnosis. For the operable group, we will aim to collect the first questionnaire prior to surgery to provide a "baseline",

and therefore recruit 2-4 weeks post-diagnosis. The questionnaire will then be repeated at 3 and 6 months following diagnosis. Prior to data collection at 3 and 6 months, research nurses will contact the patient's GP to obtain information on current health status. Carers will be contacted by telephone; contacts will be sensitive to circumstances and clarify whether the individual wishes to continue in the study.

Phase 2

Most interviews will take place approximately 3-6 months post-diagnosis to allow carers time to reflect post-diagnosis. A few (among participants recruited through non-NHS routes) will be conducted 6-12 months from diagnosis, to provide some information on carer experience later in the disease trajectory.

Table 1 – Schedule of enrolments, tests and assessments

Timepoint	D0 diagnosis	2-6 weeks	3 months	6 months
Enrolment – Phase 1				
• Eligibility screen		X		
• Consent for quantitative study		X		
Enrolment – Phase 2				
• Eligibility screen			◆	◆
• Consent for qualitative interview			◆	◆
Test				
• Carer characteristics		X		
• Patient characteristics		X		
• Caregiver reaction assessment (CRA)		X	X	X
• Supportive Care Needs Survey (SCNS-P&C45)		X	X	X
• Quality of life (SF12_v2)		X	X	X
• Semi-structured interview			◆	◆
Assessments				

• Carer characteristics: Age, sex, relationship to patient, co-morbidities		X		
• Patient characteristics: Age, sex, disease profile, management, vital status		X	X	X
• Impact assessment		X	X	X
• Unmet needs assessment		X	X	X
• Mental and physical QoL score		X	X	X
• Experiences of caregiving			◆——	——◆

Sample Size

In phase 1 (quantitative), 300 carers of patients with operable (n=~150) and inoperable (including locally advanced and metastatic, n=~150) pancreatic cancer will be enrolled in the study. The sample size assessment was based on the number of cases diagnosed, estimated numbers with carer involvement, and likely response rates. No sample size calculations were undertaken as this is a pilot study.

In phase 2 (qualitative), recruitment will continue until reasonable data saturation is reached. Experience suggests up to 30 interviews are likely to be required.

Recruitment & data collection

Phase 1:

Recruitment will be undertaken by research nurses when carers accompany patients to hospital soon after diagnosis. Patients who attend alone will be asked whether they can nominate a carer and, if so, to pass on study information. Research nurses (or other research staff) will administer questionnaires by telephone or video conferencing software, if preferred. Patients will also be given the option to complete the questionnaire themselves at home and return them by mail.

Phase 2:

Selected participants from the phase 1 cohort will be invited to participate in phase 2. Maximum variation purposive sampling will be used to ensure elicitation of varied experiences. Sampling strata will include whether patient has operable/inoperable disease, time since diagnosis, site, and carer gender. Interviews will last 60-90 minutes and take place remotely, by video (e.g. Zoom) or telephone, at a time convenient for the interviewee. They will be audio-recorded and transcribed for analysis.

Data management

All data will be stored in secure electronic database protected by two factor authentication (REDCap), and only accessible by research staff. Data integrity will be maintained with data validation tools built

into the database and with regular checks by the data manager for accuracy and prevention of missing data. The database will be backed up daily.

Statistics and analysis plan

Phase 1:

Statistical analysis will be conducted in Stata. Mean carer impact (overall and by domain), mean mental and physical quality-of-life, and proportion with unmet needs (any and by domain) will be computed. Mixed effects regression models (linear or logistic as appropriate) will be used to: (i) determine how impact, needs and quality-of-life vary over time; (ii) compare outcomes between carers of patients with operable and inoperable disease; and (iii) identify factors (e.g. carer age, employment status) associated with outcomes. Mixed-effects models allow all surveys completed at every time-point to be included in analysis, taking within-subject correlations into account to produce robust error estimates (27). Associations between both impact and unmet needs and quality-of-life will be assessed using similar approaches.

Phase 2:

Interview recordings will be transcribed and reflexive thematic analysis undertaken (28). Data collection and analysis will occur concurrently to ensure any new issues raised are explored in subsequent interviews. Analysis and organisation of data will be facilitated by NVivo software. A few interviews will be independently coded by two team members to agree emergent themes, which will form an analytical “framework”. Remaining interviews will be coded to this framework, with novel issues incorporated as analysis progresses. Standard approaches for analytical rigour will be applied (e.g. constant comparison, deviant case analysis). Interpretation and drawing out pertinent findings will involve the entire applicant team.

ETHICS AND DISSEMINATION

Local Hospital Trust sponsorship and UK Health Research Authority (HRA) Research ethics committee (REC) approval has been obtained (Ethical approval IRAS ID 309503. East of England - Cambridge Central Research Ethics Committee, REC reference 22/EE/0072 18th May 2022).

Non-identifiable and anonymised data and findings will be published in peer-reviewed journals and presented at national and international conferences. Lay summaries will be developed and disseminated, including through the networks of PCUK. Patient consent includes granting permission for sharing non-identifiable data with other groups to advance understanding of caregiving in pancreatic cancer.

There are no conflicts of interest to declare.

PUBLIC AND PATIENT INVOLVEMENT

Feedback on the project, and advice on methods, was obtained from the PCUK Research Involvement Network (RIN), a PPI group which includes those affected by pancreatic cancer. The RIN will be consulted throughout the project. Their reflection and comments on emergent findings will be sought and they will be asked to highlight key messages for carers and patients. Feedback will also be obtained on lay summaries to ensure findings are clear and understandable and reported sensitively. Moreover, the RIN will be asked to suggest areas for follow-on research.

CONCLUSION

In other cancers, evidence is growing that a cancer diagnosis can have a major impact on the lives and wellbeing of informal carers – family members or friends who provide day-to-day support and care for patients. Given the nature of pancreatic cancer, it seems likely that the impact on carers may be especially significant. Tentative international data suggests this is the case, but that data is very limited and major gaps in evidence remain.

The proposed pilot project will – for the first time in the UK - investigate and characterise informal caregiving in pancreatic cancer. It will provide the first complementary qualitative and quantitative data on this topic. Using these methods together provides a better understanding of complex phenomena than using either approach alone and, here, will reveal the "big picture" of the impact of caregiving in pancreatic cancer and a detailed understanding of that experience.

The study will generate completely novel data, internationally, on how carer impact evolves over time from diagnosis, compares in those caring for patients with operable and inoperable disease, and affects carer quality-of-life. It will shed new light on whether carers feel equipped to support their care recipients and whether they experience issues and problems that are distinct from the needs of the care recipient. Moreover, it will provide the first data on carers' needs for support and how impacts, needs and quality-of-life inter-relate. Finally, it will provide novel information on which subgroups of carers experience greatest impact and needs, and what may mitigate against negative effects of caregiving.

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AUTHORS' CONTRIBUTIONS

Prof Linda Sharp and Mr Sanjay Pandanaboyana conceived of the study concept and were responsible for the study design and writing of the protocol. Dr Keno Mentor contributed to the study design and was responsible for editing and submission of the protocol. Ella Watson, Keith Roberts, Michael Silva, Mary Phillips, Ajith K Siriwardena, John Hammond, Alex Bradshaw, Catherine Exley, Jennifer Deane reviewed and contributed to the protocol.

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COMPETING INTERESTS STATEMENT

The authors have no competing interests to declare.

DATA AVAILABILITY STATEMENT:

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

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ABSTRACT

Introduction

Approximately 10,300 people are diagnosed with pancreatic cancer each year in the UK. The cancer and its treatment inflict a significant physical, functional and emotional burden on patients. Research suggests that patients have many ongoing needs for support and care, but that these needs are not met by existing services. Family members often step in to fill this gap and provide support and care during and after treatment. Research in other cancers shows that this informal caregiving can place a very heavy burden on carers. However, there are few studies in the international literature that have focussed on informal carers in pancreatic cancer; none have been conducted in the UK.

Methods and analysis

Two complementary research methods will be utilised. Firstly, a longitudinal quantitative study of 300 carers will investigate, using validated questionnaires, the impact of caregiving (Caregiver Reaction Assessment), the unmet needs of carers (Supportive Care Needs Survey), and their quality-of-life (short form 12 item health survey), will be conducted. Secondly, qualitative interviews will be conducted with 30 carers to explore their experiences in more depth. Mixed effects regression models will be applied to survey results to determine how impact, needs and quality-of-life vary over time, compare outcomes between carers of patients with operable and inoperable disease and identify social factors which affect outcomes. Interview data will undergo reflexive thematic analysis.

Ethics and dissemination

The protocol has been approved by the Health Research Authority of the UK (Ethical approval IRAS ID 309503). Findings will be published in peer-reviewed journals and presented at national and international conferences.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study will examine an under-investigated area in pancreatic cancer research and generate novel data on how carer impact evolves over time from diagnosis
- A high number of participants will be recruited from different locations in England
- Both quantitative (survey) and qualitative (interview) data will be utilised to provide complementary data and give depth to the analysis
- Both operable and inoperable patients will be included to ascertain the burden of caregiving for each group.
- Carers with high levels of anxiety, or burden, may not agree to participate in the study, resulting in an under-estimation of the burden of caregiving

INTRODUCTION

Pancreatic cancer patients have a significant symptom burden and many unmet physical and psychological needs. Family and friends increasingly take on the role of informal caregivers, providing social, emotional and practical care during and following treatment. Research in other cancers indicates that informal caregiving can place a heavy burden on people and that carers can have many unmet needs. However, there is paucity of data on informal caregiving in pancreatic cancer.

The last decade has brought major changes in pancreatic cancer treatment. Significant progress has been made in chemotherapy regimens in the adjuvant and metastatic settings, with 5-year survival up to 37% for patients with resectable disease who complete adjuvant chemotherapy (https://www.cancer.net/cancer-types/pancreatic-cancer/statistics). However, only 10-15% of patients are suitable for surgery and surgery is associated with high morbidity and often prolonged hospital stay. Furthermore, chemotherapy, whether used as neoadjuvant or adjuvant treatment, is associated with challenging side-effects. During and following treatment, patients can have a high and debilitating symptom burden including severe pain, fatigue, jaundice and nausea (1). Levels of anxiety and depression are high (2). Indeed, research has shown that some physical and psychological effects (e.g. pain, distress) are more common in pancreatic cancer patients than those with other cancers (2). Consequently, patients have significant, and persistent, supportive care needs in a range of areas, which are largely unmet by existing services (3,4).

For pancreatic cancer (as for other cancers) family members and friends often step into the gap left by services, providing practical, emotional and social support and care for patients during treatment, recovery and afterwards – so-called informal caregiving. Emerging evidence for other cancers indicates that informal caregiving for patients with cancer places a heavy burden on the individual. Family members and friends are seldom prepared to be carers (5), and are thrust into the role at the time when they are struggling to come to terms with the diagnosis. Although there can be positive aspects of caregiving (6), carers often report difficulties in undertaking complex caring activities (e.g. symptom management, treatment monitoring) while lacking the information, support, and self-confidence to perform these tasks (7;8). Disruptions to carers' lives and work can be significant (9) and many, including those who do not regard caregiving negatively, suffer from a wide range of problems, such as practical and financial difficulties, sleep disturbance, psychological problems, and decrements in their own health (10-13). These effects impact quality-of-life (14), can persist long after care activities have ceased, and can have significant long-term sequalae (15). Few services exist specifically for carers, and they may be unable to access support available for patients. Consequently, carers themselves often have extensive unmet needs for support (13;16), which not only correlate with carer burden (17) and decrease their own quality-of-life, but also negatively affect the patient's wellbeing and health outcomes (18).

For pancreatic cancer specifically, there have been very few studies of informal caregiving. In a US study of 8 carers of patients with advanced pancreatic cancer, carers reported spending, on average,

9 hours/ day on caregiving activities and losing more than 5 hours sleep/night (19). Stressors experienced by carers included not knowing what to expect, trying to be strong for the care recipient and managing the wider family. In a study of 78 carers in Ireland, caregiving responsibilities had greatest impact on carers' schedules and their health (20). A US study of 22 family members of pancreatic cancer patients (not all of whom were informal carers), reported carers struggle to balance their feelings with those of the patient (21), while the largest study, of 84 carers in Australia reported that 58% had below average quality-of-life and, importantly, a higher proportion of carers than patients had significant anxiety (22).

While these data point towards a significant burden on informal carers in pancreatic cancer, there are important limitations in the work, and major gaps in knowledge. Studies were small and from different healthcare systems, so findings may not generalise to the UK. How caring for someone with pancreatic cancer impacts people's lives, and their physical and emotional wellbeing is not understood. Furthermore, it is unknown how the impact of caring changes over time from diagnosis or how it varies for carers of patients with resectable compared to metastatic or locally advanced tumours. Carers' own support needs have not been investigated, and which carers experience the greatest impact or most unmet needs is unknown. Moreover, the factors that mitigate against negative impacts of caregiving in pancreatic cancer have never been explored.

The proposed pilot project will – for the first time in the UK - investigate and characterise informal caregiving in pancreatic cancer. It will provide the first complementary qualitative and quantitative data on this topic. Using these methods together provides a better understanding of complex phenomena than either approach alone and, here, will reveal the "big picture" of the impact of caregiving in pancreatic cancer and a detailed understanding of that experience.

The study will generate completely novel data on how carer impact evolves over time from diagnosis, compares in those caring for patients with operable and inoperable disease, and affects carer quality-of-life. It will shed new light on whether carers feel equipped to support their care recipients and whether they experience issues and problems that are distinct from the needs of the care recipient. Moreover, it will provide the first data on carers' needs for support and how impacts, needs and quality-of-life inter-relate. Finally, it will provide novel information on which subgroups of carers experience greatest impact and needs, and what may mitigate against negative effects of caregiving.

The pilot will confirm feasibility, design and methods for a future nationwide study including all major pancreatic units, enabling recruitment from all regions and socio-economic and ethnic groups. The work will have important long-term implications. It will inform the need for interventions and services for informal carers, and provide information on the content and shape of these. It will also help identify carers at greatest risk of adverse effects, who might benefit from targeted support and provide data to inform development of a screening tool which could be used to identify these carers. Ultimately, it has significant potential to improve pancreatic cancer patient support and outcomes.

METHODS AND ANALYSIS

This protocol design was based on the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) Statement (23) and will be conducted in accordance with the principles of Good Clinical Practice.

Study design and setting

PAN-CARER is a multi-centre multi-method prospective study with two phases. Phase 1 will establish a cohort of informal carers from whom quantitative data will be collected. Phase 2 will involve in-depth interviews with informal carers, primarily sampled from the cohort.

The study will be conducted at five tertiary centres (Freeman Hospital, Newcastle-Upon-Tyne; Queen Elizabeth Hospital, Birmingham; Royal Surrey County Hospital, Guilford; Manchester Royal Infirmary. Manchester and Oxford Radcliffe hospital, Oxford) and two district general hospitals (Sunderland Royal Hospital, Sunderland and James Cook Hospital, Middlesbrough). These sites have been chosen because they have socio-economic and ethnically diverse catchment populations, and differ in their pancreatic cancer patient populations and in supports offered by, and services allied with, the hospital.

The recruiting centres currently undertake around 500 pancreatic resections per year for resectable pancreatic cancers and manage a further 1000 patients with inoperable cancer through their multidisciplinary team meetings.

To supplement recruitment in phase 2, and allow the study to be completed in a timely fashion, carers will also be identified outwith these NHS sites, including through social media and charities (specifically Pancreatic Cancer UK (PCUK)).

Eligibility criteria

Carers of patients with operable and inoperable (including locally advanced and metastatic) pancreatic cancer who are greater than 18 years of age will be included in the study. Those unable to give informed consent will be excluded. Carers will be those who identify themselves with this term, or as someone who provides (or has provided) support for a family member or friend diagnosed with pancreatic cancer.

Study tests

Phase 1 – questionnaire

The questionnaire will include questions on carer circumstances (e.g. relationship to patient, gender, age, employment status), and validated, and recommended, instruments to measure impact, unmet needs and quality-of-life. Impact will be assessed using the Caregiver Reaction Assessment (CRA) which measures four negative domains of caregiving impact (effects of caregiving on carers' daily activities; financial strain due to caregiving tasks; perceived deterioration in health from caring; lack of family support) and one positive domain (impact on self-esteem) (24). Unmet needs will be measured

using the Supportive Care Needs Survey Partners and Caregivers (SCNS-P&C45), which captures information needs, healthcare service needs, work and social needs, and psychological and emotional needs (25). Mental and physical quality-of-life will be measured using the short form 12 item health survey (SF12_v2) quality of life questionnaire (26). Questionnaires will be administered at three time points (Table 1) by research nurses in the NHS sites.

Phase 2 - interview

Interviews will be guided by a topic guide and explore experiences of caregiving (activities undertaken, etc), preparedness for taking on caregiving role, how well-equipped the carer feels to fulfil caregiving responsibilities, carer's own support needs and how these have evolved since the care recipient's diagnosis, carer's perceptions of existing and potential services/supports, and supports/services carers would like to see provided. The topic guide will be used flexibly to allow interviewees to raise issues they consider important and new areas raised will be explored in subsequent interviews to ensure sufficient depth is reached. Interviews will be undertaken by a trained qualitative researcher, with experience in research among potentially vulnerable participants or those in potentially challenging emotional situations.

Management of participant distress

It is recognised that participating in research may have emotional consequences for the individual and may involve them considering and discussing potentially upsetting issues related to their own experiences. If a participant does not wish to answer any question during either the quantitative or qualitative interviews, this will be respected. If they become upset, the researcher/research nurse will ask them if they wish to halt the interview, either temporarily or permanently. If they become very distressed, the researcher/research nurse will ask whether they would like her/him to contact someone (a family member, friend, GP, consultant) on their behalf. Participants will also be offered a useful contacts sheet which will list contact details for members of the study team and organisations such as PCUK, who offer support for patients with pancreatic cancer.

Study outcomes

Study outcomes include the subjective impact of caregiving on the carer, the extent of unmet care supportive needs and carer quality of life.

Participant Timeline

The participant schedule of events is summarised in Table 1.

Phase 1

For the inoperable group (ie carers of inoperable patients) , participants will be recruited approximately 6 weeks post-diagnosis to allow the patient and carer time to come to terms with the diagnosis. For the operable group, we will aim to collect the first questionnaire prior to surgery to provide a "baseline",

and therefore recruit 2-4 weeks post-diagnosis. The questionnaire will then be repeated at 3 and 6 months following diagnosis. Prior to data collection at 3 and 6 months, research nurses will contact the patient's GP to obtain information on current health status. Carers will be contacted by telephone; contacts will be sensitive to circumstances and clarify whether the individual wishes to continue in the study.

Phase 2

Most interviews will take place approximately 3-6 months post-diagnosis to allow carers time to reflect post-diagnosis. A few (among participants recruited through non-NHS routes) will be conducted 6-12 months from diagnosis, to provide some information on carer experience later in the disease trajectory.

Table 1 – Schedule of enrolments, tests and assessments

Timepoint	D0 diagnosis	2-6 weeks	3 months	6 months
Enrolment – Phase 1				
• Eligibility screen		X		
• Consent for quantitative study		X		
Enrolment – Phase 2				
• Eligibility screen			◆	◆
• Consent for qualitative interview			◆	◆
Test				
• Carer characteristics		X		
• Patient characteristics		X		
• Caregiver reaction assessment (CRA)		X	X	X
• Supportive Care Needs Survey (SCNS-P&C45)		X	X	X
• Quality of life (SF12_v2)		X	X	X
• Semi-structured interview			◆	◆
Assessments				

• Carer characteristics: Age, sex, relationship to patient, co-morbidities		X		
• Patient characteristics: Age, sex, disease profile, management, vital status		X	X	X
• Impact assessment		X	X	X
• Unmet needs assessment		X	X	X
• Mental and physical QoL score		X	X	X
• Experiences of caregiving			◆—	—◆

Sample Size

In phase 1 (quantitative), 300 carers of patients with operable (n=~150) and inoperable (including locally advanced and metastatic, n=~150) pancreatic cancer will be enrolled in the study. The sample size assessment was based on the number of cases diagnosed, estimated numbers with carer involvement, and likely response rates. No sample size calculations were undertaken as this is a pilot study.

In phase 2 (qualitative), recruitment will continue until reasonable data saturation is reached. Experience suggests up to 30 interviews are likely to be required.

Recruitment & data collection

Phase 1:

Recruitment will be undertaken by research nurses when carers accompany patients to hospital soon after diagnosis. Patients who attend alone will be asked whether they can nominate a carer and, if so, to pass on study information. Research nurses (or other research staff) will administer questionnaires by telephone or video conferencing software, if preferred. Patients will also be given the option to complete the questionnaire themselves at home and return them by mail.

Phase 2:

Selected participants from the phase 1 cohort will be invited to participate in phase 2. Maximum variation purposive sampling will be used to ensure elicitation of varied experiences. Sampling strata will include whether patient has operable/inoperable disease, time since diagnosis, site, and carer gender. Interviews will last 60-90 minutes and take place remotely, by video (e.g. Zoom) or telephone, at a time convenient for the interviewee. They will be audio-recorded and transcribed for analysis.

Data management

All data will be stored in secure electronic database protected by two factor authentication (REDCap), and only accessible by research staff. Data integrity will be maintained with data validation tools built

into the database and with regular checks by the data manager for accuracy and prevention of missing data. The database will be backed up daily.

Statistics and analysis plan

Phase 1:

Statistical analysis will be conducted in Stata. Mean carer impact (overall and by domain), mean mental and physical quality-of-life, and proportion with unmet needs (any and by domain) will be computed. Mixed effects regression models (linear or logistic as appropriate) will be used to: (i) determine how impact, needs and quality-of-life vary over time; (ii) compare outcomes between carers of patients with operable and inoperable disease; and (iii) identify factors (e.g. carer age, employment status) associated with outcomes. Mixed-effects models allow all surveys completed at every time-point to be included in analysis, taking within-subject correlations into account to produce robust error estimates (27). Associations between both impact and unmet needs and quality-of-life will be assessed using similar approaches.

Phase 2:

Interview recordings will be transcribed and reflexive thematic analysis undertaken (28). Data collection and analysis will occur concurrently to ensure any new issues raised are explored in subsequent interviews. Analysis and organisation of data will be facilitated by NVivo software. A few interviews will be independently coded by two team members to agree emergent themes, which will form an analytical “framework”. Remaining interviews will be coded to this framework, with novel issues incorporated as analysis progresses. Standard approaches for analytical rigour will be applied (e.g. constant comparison, deviant case analysis). Interpretation and drawing out pertinent findings will involve the entire applicant team.

ETHICS AND DISSEMINATION

Local Hospital Trust sponsorship and UK Health Research Authority (HRA) Research ethics committee (REC) approval has been obtained (Ethical approval IRAS ID 309503. East of England - Cambridge Central Research Ethics Committee, REC reference 22/EE/0072 18th May 2022).

Non-identifiable and anonymised data and findings will be published in peer-reviewed journals and presented at national and international conferences. Lay summaries will be developed and disseminated, including through the networks of PCUK. Patient consent includes granting permission for sharing non-identifiable data with other groups to advance understanding of caregiving in pancreatic cancer.

There are no conflicts of interest to declare.

PUBLIC AND PATIENT INVOLVEMENT

Feedback on the project, and advice on methods, was obtained from the PCUK Research Involvement Network (RIN), a PPI group which includes those affected by pancreatic cancer. The RIN will be consulted throughout the project. Their reflection and comments on emergent findings will be sought and they will be asked to highlight key messages for carers and patients. Feedback will also be obtained on lay summaries to ensure findings are clear and understandable and reported sensitively. Moreover, the RIN will be asked to suggest areas for follow-on research.

DISCUSSION

In other cancers, evidence is growing that a cancer diagnosis can have a major impact on the lives and wellbeing of informal carers – family members or friends who provide day-to-day support and care for patients. Given the nature of pancreatic cancer, it seems likely that the impact on carers may be especially significant. Tentative international data suggests this is the case, but that data is very limited and major gaps in evidence remain.

The proposed pilot project will – for the first time in the UK - investigate and characterise informal caregiving in pancreatic cancer. It will provide the first complementary qualitative and quantitative data on this topic. Using these methods together provides a better understanding of complex phenomena than using either approach alone and, here, will reveal the "big picture" of the impact of caregiving in pancreatic cancer and a detailed understanding of that experience.

The study will generate completely novel data, internationally, on how carer impact evolves over time from diagnosis, compares in those caring for patients with operable and inoperable disease, and affects carer quality-of-life. It will shed new light on whether carers feel equipped to support their care recipients and whether they experience issues and problems that are distinct from the needs of the care recipient. Moreover, it will provide the first data on carers' needs for support and how impacts, needs and quality-of-life inter-relate. Finally, it will provide novel information on which subgroups of carers experience greatest impact and needs, and what may mitigate against negative effects of caregiving.

The work will have important long-term implications. It will inform the need for interventions and services for informal carers and provide information on the content and shape of these. It will also help identify carers at greatest risk of adverse effects, who might benefit from targeted support and provide data to inform development of a screening tool which could be used to identify these carers. Furthermore, the pilot will confirm feasibility, design and methods of a nationwide study including all major pancreatic units, enabling recruitment from all regions and socio-economic and ethnic groups. Ultimately, it has significant potential to improve pancreatic cancer patient support and outcomes.

AUTHORS' CONTRIBUTIONS

Prof Linda Sharp and Mr Sanjay Pandanaboyana conceived of the study concept and were responsible for the study design and writing of the protocol. Dr Keno Mentor contributed to the study design and was responsible for editing and submission of the protocol. Ella Watson, Keith Roberts, Michael Silva, Mary Phillips, Ajith K Siriwardena, John Hammond, Alex Bradshaw, Catherine Exley, Jennifer Deane reviewed and contributed to the protocol.

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COMPETING INTERESTS STATEMENT

The authors have no competing interests to declare.

DATA AVAILABILITY STATEMENT:

The authors confirm that the data supporting the findings of this study are available within the article [and/or] its supplementary materials.

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