STUDY TITLE: A randomised controlled trial and feasibility study of the effects of an e-health intervention 'iSupport' for reducing distress of dementia carers, especially in the ongoing pandemic of COVID-19.

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Contents

Contents 3
Table of Figures 5
Note on the structure of this protocol 6
1. Background and rationale 6
1.1 What is the problem being addressed? 6
1.2 Why is this research important? 6
1.3 Brief review of published evidence 7
2. Trial objectives and design 7
2.1 Trial objectives and design 7
2.2 Research questions 8
2.3 Trial expected duration 9
2.4 Trial flowchart 9
3. Selection and withdrawal of trial participants 10
3.1 Inclusion criteria 10
3.2 Exclusion criteria 10
3.3 Trial consent procedure 11
3.4 Randomisation procedure 12
3.5 Unblinding procedure 13
3.6 Withdrawal of participants 13
4. Trial procedures 13
4.1 Planned intervention 13
4.2 Comparison group 14
4.3 Setting and context 15
4.3.1 Research sites 15
4.3.2 Organogram of research sites and study reporting 16
4.4 Sampling and sample size 16
4.5 WS1 Randomised controlled trial 17
4.5.1 Internal pilot study 18
4.5.2 Selection of participants 18
4.5.3 Primary outcome measures 19
4.5.4 Secondary outcome measures 20
4.5.5 Data collection 21
4.5.6 Data analysis 21
4.6 WS2 Process evaluation 21
4.6.1 Quantitative data collection 22

4.6.2 Qualitative data collection 22
4.6.3 Data analysis 22
4.7 WS3 health economics 23
4.7.1 Outcome measures 23
4.7.2 Data collection 24
4.7.3 Data analysis 24
5. Feasibility study objectives and design 25
5.1 Feasibility study objectives and design 25
5.2 Research questions 25
5.3 Feasibility study expected duration 25
5.4 Feasibility study flowchart 26
6. Selection and withdrawal of feasibility study participants 26
6.1 Inclusion criteria 26
6.2 Exclusion criteria 27
6.3 Feasibility study consent procedure 27
6.4 Randomisation and unblinding 27
6.5 Withdrawal of participants 27
7. Feasibility study procedures 27
7.1 Planned intervention 27
7.2 Setting and context 27
7.3 Feasibility study 27
7.3.1 Phase 1: Adaptation of ‘iSupport’ for younger dementia carers 27
7.3.2 Phase 2: Feasibility testing ‘iSupport’ for younger dementia carers 28
7.3.3 Sampling and sample size 28
7.3.4 Selection of participants 28
7.3.5 Data collection 29
7.3.6 Data analysis 29
8. Translating ‘iSupport’ into Welsh 30
9. Assessment of safety 30
9.1 Definitions 30
9.2 Collecting, recording and reporting of adverse events 30
10. Project management 31
10.1 Trial Steering Committee 31
10.2 Independent Data Monitoring Committee 32
10.3 Trial Management Group 32
10.4 Patient and public involvement (PPI) 32
10.5 Coronavirus (COVID-19) mitigation 33

11. Ethics and regulatory approvals 33
12. Monitoring 34
12.1 Quality Assurance (QA) and Quality Control (QC) of data 34
12.2 Risk assessment 34
12.3 Monitoring plan 35
12.4 Source data 35
12.5 Direct access to source data and documents 35
12.6 Confidentiality 35
13. Data handling 35
14. Pathways to impact 36
15. Indemnity 36
16. Financial aspects 37
17. Definition of end of study 37
18. Archiving 37
19. Research expertise 37
20. Research collaborators 38
21. Protocol amendments 38
21.1 Current version of the protocol 38
21.2 Amendments 39
21. Appendices 40
22. References 42

Table of Figures

Figure 1: Trial flowchart including sample sizes 9
Figure 2: Consent procedure flowchart 11
Figure 3: Overview of 'iSupport' intervention 14
Figure 4: Organogram of research sites and study reporting 16
Figure 5: Feasibility study flowchart including sample sizes 26

Note on the structure of this protocol

For the purposes of this Protocol, the randomised controlled trial will be outlined first, and the feasibility study second. The randomised controlled trial will henceforth be referred to as the "trial".

1. Background and rationale

1.1 What is the problem being addressed?

Estimates suggest 850,000 people in the UK live with dementia. Most (700,000) are cared for at home,[1] supported by a family member or friend who has little knowledge of the condition and how to best manage it. This is often described as 'informal care', in contrast to professional care provision. Informal carers (henceforth referred to as 'carers') are unpaid, often performing care tasks similar to those carried out by paid health or social service providers.[2] This raises two important points. First, there is a well-documented detrimental impact of caregiving on the physical and mental health of dementia carers.[3] Second, despite this detrimental impact to carers, informal care benefits their relatives and also society. For example, the total cost of dementia to society in the UK is £26.3 billion. £11.6 billion of this is contributed by the work of unpaid carers of people with dementia, higher than the £4.3 billion spent on healthcare costs and £10.3 billion spent on social care.[4] Given the financial contribution of informal caring on the one-hand, and the negative health impact on the other, Action area 5 of the global action plan on the public health response to dementia 2017-2025 prioritises supporting carers, calling for the provision of accessible evidence based information to improve knowledge and skills and prevent stress and health problems.[5] Although health is a devolved area of government policy, UK national dementia strategies[6,7,8] all make commitments to support the health and wellbeing of dementia carers. NICE [9] recommend informal carers of people living with dementia should be offered training and psychoeducation to help them develop care skills and manage their own physical and mental health. Therefore access to appropriate, useful, low-cost, effective support for carers, with effective implementation strategies, is a priority for people living with dementia, their carers and service providers, and the focus of this research. This is especially important given the current pandemic, when many carers no longer have access to usual respite, leisure, and support services, finding themselves distanced and isolated.

1.2 Why is this research important?

Sustained interest and intent: The number of people with dementia in the UK is predicted to increase to 1,142,677 within 5 years and 2,092,945 by 2051, an increase of 40% and 156% respectively from the 2013 estimate.[4] Currently there is no cure, with limited medical treatment options. Most people living with dementia are supported by informal carers. Sustaining the health and capabilities of these dementia carers is a public health priority.[5]

Health need: A meta-review concluded that being an informal carer for people with dementia is associated with psychological stress and physical ill-health.[3] A meta-analysis comparing carers and non-carers found carers were more stressed, depressed, and had lower levels of subjective well-being, physical health, and self-efficacy than non-carers.[2] The

evidence generated from this research will examine how a low cost, accessible and scalable e-health intervention 'iSupport' may alleviate the detrimental human and economic impact of dementia. The WHO describes e-health as "the use of information and communication technologies (ICT) for health".

Expressed need: A systematic review of dementia carers' needs, as voiced themselves (i.e. not by a care professional) found that carers need: a) relevant information and knowledge; b) support with the management of care recipients' functioning, behavioural and psychological symptoms; c) support with their own physical and mental health; d) support regarding their unbalanced social life.[10] The intervention to be tested 'iSupport' is specifically designed to address these needs of carers.

Capacity to generate new knowledge: This will be the first study in the UK and the first in a majority English-speaking population of a globally targeted e-health intervention for dementia carers. 'iSupport' is a recently developed evidence-informed online training and support programme for adult dementia carers to help them provide good care and take care of themselves. It was developed by the World Health Organisation in collaboration with Alzheimer's Disease International and international experts, consequently 'iSupport' has the potential for significant global reach and impact.

1.3 Brief review of published evidence

Our ongoing systematic reviews found the most effective interventions for carers' psychological health should incorporate both an educational component to enhance knowledge and a therapeutic component, such as CBT/cognitive reframing.[11] 'iSupport' incorporates both these components.

To date, there is no published evidence of the effectiveness of 'iSupport'. In contrast to the Dutch, Portuguese and Indian evaluations of 'iSupport',[12,13,14] we will not screen participants and restrict our inclusion to those reporting clinically relevant levels of distress, depression or anxiety, we will instead use self-recognition of such outcomes from carers themselves. This 'real world' application will generate new knowledge about 'iSupport' as a public health approach to prevention.

The proposed feasibility study will also provide new knowledge about the impact of an adapted version of 'iSupport' on younger populations of carers. No published works of online interventions for young carers were identified in core databases.

2. Trial objectives and design

2.1 Trial objectives and design

The objectives of the trial can be separated into three work-streams (WS):

WS1. A definitive pragmatic individually randomised controlled trial across Wales, Scotland and England, with a six-month nested internal pilot. This will:

- Determine progression of the definitive trial based on a go/review/stop criteria (nested internal pilot).
- Determine the effectiveness of 'iSupport' in reducing symptoms of distress and/or depression.
- Determine the effectiveness of 'iSupport' in reducing symptoms of anxiety.
- Determine the effectiveness of 'iSupport' in improving dementia knowledge, relationship quality and resilience.
- Describe the trial sample according to demographic/socioeconomic characteristics.

WS2. A process evaluation will be conducted in line with the established guidelines for process evaluations of complex evaluations[15,16] to determine the barriers and facilitators to the implementation of 'iSupport' at scale, and the extent it supports carers in the face of the ongoing or future COVID-19 pandemic. This will:

- Determine participant engagement and adherence to 'iSupport'.
- Explore the mechanisms of change.
- Identify the external factors to 'iSupport' which influence the delivery and function of the intervention.
- Explore the contextual factors that influence the scalability of 'iSupport' into wider contexts using the CICI framework.[17]

WS3. A parallel cost-effectiveness analysis, undertaken from both a public sector perspective (NHS, personal social services and local authorities), and a societal perspective (public sector plus opportunity costs). This will:

- Calculate the costs of implementing 'iSupport', including technical support and time spent supporting carers to use the tool.
- Explore patterns of, and estimate the cost of, health and social care resource use for carers in the 'iSupport' and comparison arms of the trial.
- Explore patterns of, and estimate the cost of, health and social care resource use for the care recipients of carers in the trial.
- Explore the opportunity cost of informal care through the measurement of informal care time, types of care task, impacts on carer's leisure and employment hours, and carers' willingness to pay for more support.
- Using QALYs derived from the EQ-5D-5L, determine the cost-effectiveness of 'iSupport' compared to the control condition; conduct secondary cost-effectiveness analyses using the Zarit Burden Interview[18] and the Centre for Epidemiological Studies of Depression Scale (CES-D10).[19,20]

2.2 Research questions

1. Is carer distress and/or symptoms of depression (primary outcomes) significantly reduced in participants allocated to receive 'iSupport' compared to participants allocated to a comparison group?
2. Are symptoms of anxiety (secondary outcome) significantly reduced, and resilience, relationship quality and dementia knowledge (secondary outcomes) significantly increased in

participants allocated to receive 'iSupport' compared to participants allocated to a comparison group receiving standardised information about dementia?
3. What are participant and contextual barriers and facilitators to implementation of 'iSupport'?
4. What potential mechanisms might underpin changes in outcomes from using 'iSupport'?
5. What is the cost-effectiveness of 'iSupport' compared to standardised information about dementia?
6. What are the carers' perspectives of 'iSupport' in relation to supporting them in an ongoing or future repeated pandemic such as COVID-19?

2.3 Trial expected duration

The total time scheduled for the trial is 36 months. Key milestones will be monitored as part of overall project management.

2.4 Trial flowchart

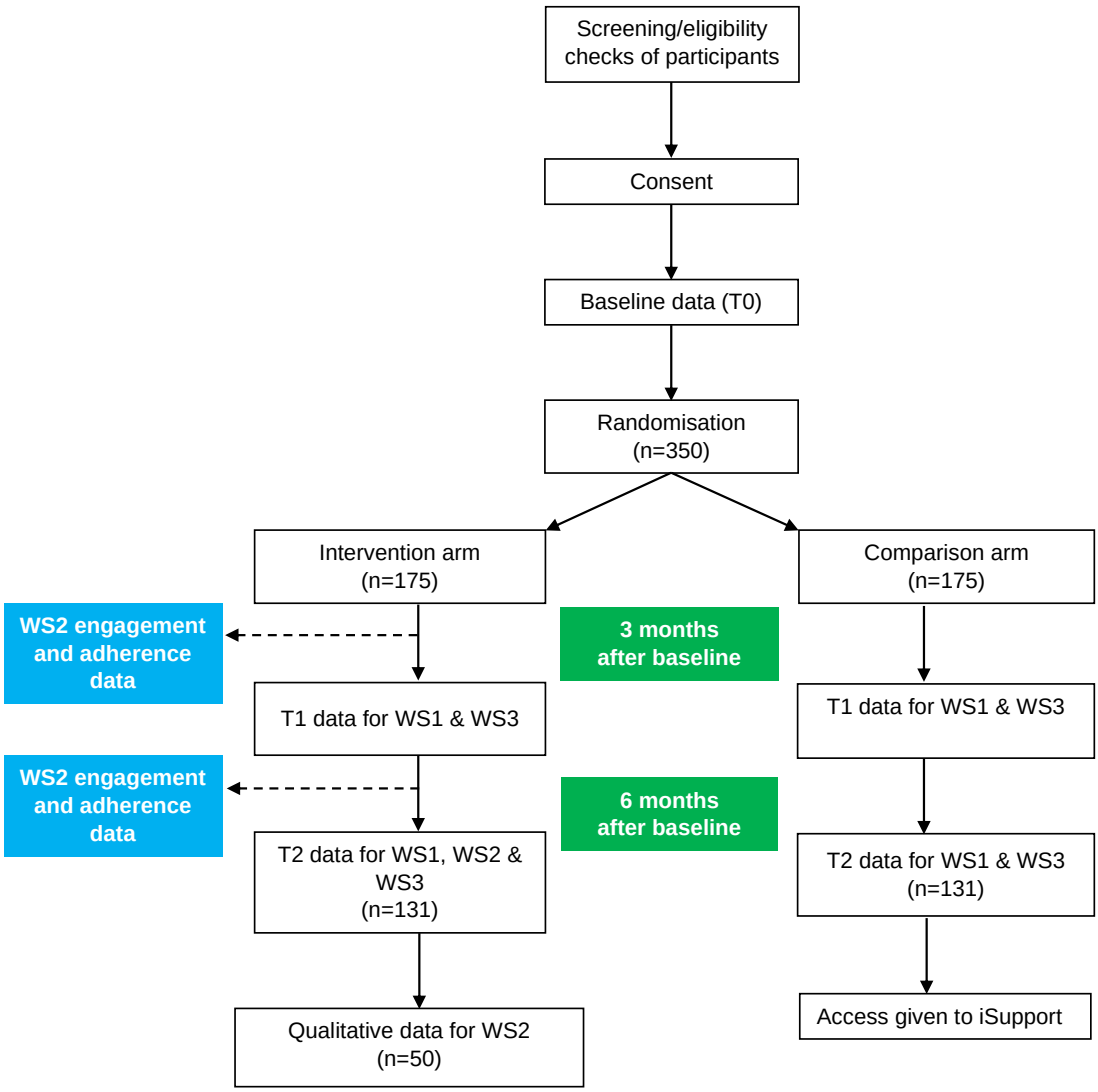


Figure 1: Trial flowchart including sample sizes

3. Selection and withdrawal of trial participants

Dementia carers (age 18+) in Wales, Scotland and England will be recruited through a range of approaches. Research Assistants will work with our Patient and Public Involvement (PPI) groups to promote the trial through social media to promote self-referral, and will use Join Dementia Research (JDR)[21] as a tool to identify potential participants. This is an online self-registration service that enables volunteers with memory problems or dementia, carers of those with memory problems or dementia and healthy volunteers to register their interest in taking part in research. Researchers can then contact volunteers, in line with the volunteers' preferred method of contact, to further discuss potential inclusion.

Our study partners (Carers Trust and Alzheimer Scotland) and other non-statutory organisations will promote the study through their networks and to regional groups (including England), in order to reach a diverse range of dementia carers across different regions.

If recruitment from our collaborators is not happening to target, Research Assistants will approach memory clinics and dementia support groups to identify participants. This would first require NHS ethical approval. An IRAS form would be completed and approved prior to commencing recruitment from clinics. An amendment request would also be submitted to this ethics committee.

All public facing documents, including a plain English/Cymraeg clir trial leaflet explaining the purpose of the research will be finalised in collaboration with our PPI group. We will establish a webpage explaining the study purpose and procedures. This will be hosted by the lead institution. Interested participants will be able to register through this website. All carers expressing interest in taking part will be provided with the leaflet and information sheet and have the opportunity to discuss the trial with the research assistants before committing.

3.1 Inclusion criteria

1) Adults (18+) who self-identify as an unpaid carer (partners, children, friends, etc.) of a person with dementia who is not living in a full-time care facility, caring at least weekly for at least 6 months.
2) Self-identify as experiencing at least some stress, depression or anxiety.
3) The care recipient has to have a confirmed diagnosis of dementia (through self-report of the carer, to reflect the 'real world' application of 'iSupport').

3.2 Exclusion criteria

1) Receiving psychological treatment from a mental health specialist at the time of recruitment.
2) Unable to comprehend written English.
3) No access to the internet.
4) Unable to give informed consent to the trial.
5) Have previously used 'iSupport' materials (in the last 12 months).

3.3 Trial consent procedure

We will use a remote method for assessing eligibility and taking consent, following a procedure successfully implemented in other studies by our co-investigators at UCL. Participants will electronically "sign" a statement of consent after having received the study information and consent forms via email, and having had a one-to-one phone or internet-based meeting with a researcher to ask questions. A flowchart of the consent procedure is below:

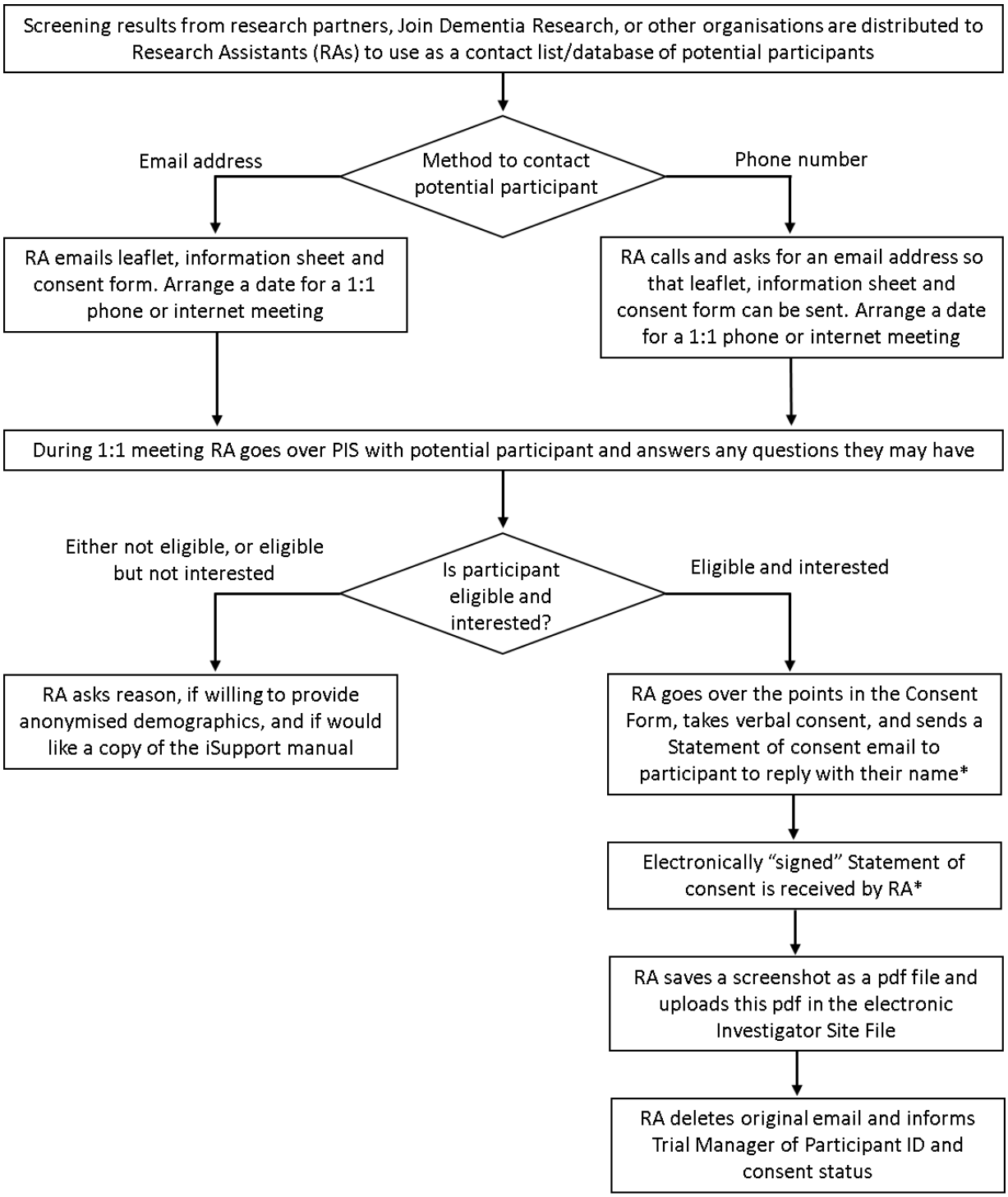


Figure 2: Consent procedure flowchart

The Statement of consent will read:

> "I [NAME], have read the information sheet and consent forms for the study titled 'iSupport for Dementia Carers'. With this email, I hereby electronically 'sign' and consent to taking part in the study and to the [NUMBER] items outlined on the consent form."

*In the event participants do not use email or other messaging services (e.g. Whatsapp), paper versions of documents will be posted to their address and the procedure for taking consent would slightly differ: The participant would sign while on the phone with the researcher, post their signed consent form to the researcher to be copied and put in the Investigator Site File (ISF), and a copy would then be returned to the participant.

In the unlikely event the participant cannot return either the statement of consent or a paper consent form, verbal consent would be sought. The research assistant would audio record the participant consenting to the trial and the recording would be securely stored as an audio file (e.g. MP3, WAV) in the electronic ISF.

3.4 Randomisation procedure

Randomisation will be performed by dynamic allocation to protect against subversion.[22] The algorithm will ensure that the trial maintains good balance to the allocation ratio of 1:1 both within each stratification variable and overall for the trial. Stratification variables will be site, along with age and gender, previously found to influence the outcome measure of caregiver distress.[23]

Randomisation will be performed by the Research Assistant after completing the baseline assessment with the participant (see section 2.4 Trial flowchart). The Trial Manager and Chief Investigator will also be able to perform randomisations if required. The randomisation system will allow the user to check entry details before randomisation is performed. A simple confirmation email will be sent to the person who performed the randomisation. For research assistants these will not include any allocation information in order to keep them blinded.

The randomisation system will send a second unblinded email to the Trial Manager and Chief Investigator, informing them of all randomisations performed and the group allocations. They can then inform the participant of their allocation to either the intervention or comparison arm of the study. This will be done by emailing the details contained in the randomisation letter template (uploaded as part of research ethics submission). If the participant does not use email, they will be informed by phone and a letter will be sent to their address.

Randomisation will be achieved by secure web access to the remote randomisation centre at NWORTH, Bangor University. The randomisation system will be set up, maintained, and monitored independently of the trial statistician or other trial staff. A detailed randomisation specification will be drawn up prior to set up of the system that will detail the technical system requirements, this will be guided by NWORTH's Standard Operating Procedures (SOPs).

3.5 Unblinding procedure

It is not possible to blind the individual participants in this trial, but the research assistants, health economists, co-investigators and trial statistician will remain blind until the blinded analysis detailed in the Statistical Analysis Plan has been conducted and reported to the trial team. The exception will be one of the co-investigators leading the process analysis. Unblinding will be performed following procedures outlined in NWORTH SOPs.

3.6 Withdrawal of participants

Participants are free to withdraw at any time during the trial without any impact on their future health and care. Participant data collected to the point of withdrawal will be used in the analysis set unless consent for this is specifically withdrawn.

4. Trial procedures

4.1 Planned intervention

'iSupport' is an internet-based psychoeducation and skills development intervention. The theoretical underpinnings of 'iSupport' are based on person-centred care, which recognises that dementia care should reflect the individual's needs, personality and ability.[24] These elements are integrated into the interactive content of 'iSupport'. The self-care techniques are based on theoretically informed programmes with some evidence for benefits, including psychoeducation, relaxation, behavioural activation, cognitive reframing, and problem-solving.[25]

'iSupport' consists of five main themes and twenty-three accompanying exercises, namely: (i) introduction to dementia; (ii) being a carer; (iii) caring for me; (iv) providing everyday care; and (v) dealing with behaviour changes. Each exercise takes approximately 5-15 minutes and follows the same format: information about a topic presented; short interactive exercises and questions with instant feedback on responses; a summary of the lesson; a relaxation exercise.

'iSupport' is based on personal choice: carers can construct their own personalised plan and access which sessions they feel are most relevant to them at that point in time. It is anticipated the whole programme can be completed in 3 months. The programme can be followed via the internet using a personal computer or a tablet (e-health), or through a mobile phone accessing a 'mobile friendly' version of the platform (m-health).

To address potential inequity of uptake, a short video tutorial on how to use the programme will be developed and sent to all participants randomised to the intervention group. For the purpose of this research, participants will be advised to use 'iSupport' regularly in order to obtain the most benefit. They will be provided with the contact details of an 'e-coach', who will be trained to explain anything that is not clear about the 'iSupport' programme. This training will follow many of the good practice principles in this document:

https://www.onlinecentresnetwork.org/sites/default/files/a6_your_guide_to_helping_older_people_use_the_internet.pdf [accessed 10/03/2021]. The 'e-coach' will contact participants randomised to intervention shortly after randomisation, 1 month later and 2 months later (if required by the participant).

We will translate 'iSupport' into Welsh following WHO adaptation guidelines (see section 8. Translating 'iSupport' into Welsh). Approximately one-fifth of the Welsh population speak Welsh[26] and the Welsh Government is committed to offering bilingual services as part of health care provision.[27] A bilingual resource being widely available at no cost to the user will add value beyond the trial. To improve access, we will also develop audio/read aloud function for inclusion in the platform.

The figure below shows a visual overview of the intervention, and more information can be viewed in a short video produced by the WHO: https://youtu.be/_g2KMgjukzs [accessed 10/03/2021]

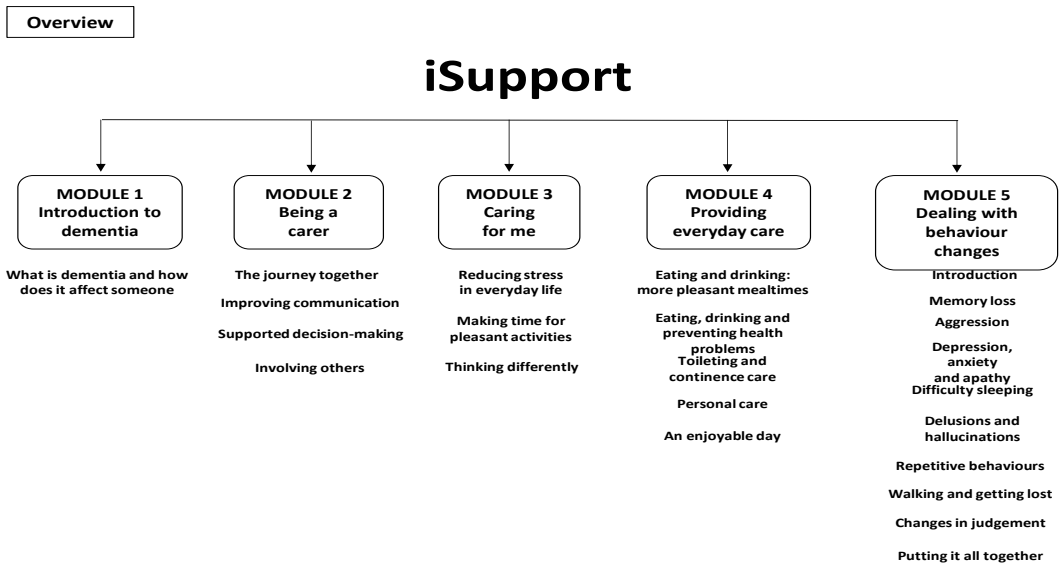


Figure 3: Overview of 'iSupport' intervention

4.2 Comparison group

Participants assigned to the comparison group will receive information about dementia developed by the Alzheimer's Society.[28] This covers the topics of understanding the diagnosis, taking on the caring role, looking ahead, understanding and supporting the person with dementia, services, support and housing, finances, the later stages of dementia, end of life care and support, contact details of useful organisations. This information will be available online and/or in printed format. Carers can choose which format they prefer. Alongside this education, carers will receive care-as-usual. They can search for other information or seek help from other providers. Information about local context support and

services will be obtained at baseline. Following the final data collection the participants allocated to the comparison group will be provided with access to ‘iSupport’.

4.3 Setting and context

The research will be undertaken with dementia carers who live in Wales, Scotland and England. Researchers will recruit and assess participants during a one-to-one interview over an internet-based service (e.g. Zoom, Teams or Skype) or telephone. The intervention – ‘iSupport’ – will be hosted by the Pan American Health Organisation (PAHO), the regional office of the World Health Organization (WHO) for the Americas.

For the trial, carers who meet the inclusion criteria, consent to take part, and are randomised to the intervention arm will be provided with access to the platform by the research team for six months. They will be able to access it at their own pace and time from wherever they feel is convenient.

Analysis plans relevant to the WSs will be written, scrutinised and agreed before recruitment has been completed for all quantitative analyses. This will ensure that variables potentially contributing to missing data will be considered a priori. Independent committees will have the opportunity to comment on these plans.

4.3.1 Research sites

Bangor University is the lead research site for this study and researchers working for this institution will lead the Welsh arm of the study. University College London and the University of Strathclyde are collaborating research sites. Researchers from these institutions will lead the English arm and Scottish arm respectively. All researchers will follow the same working procedures, as described in this protocol.

4.3.2 Organogram of research sites and study reporting

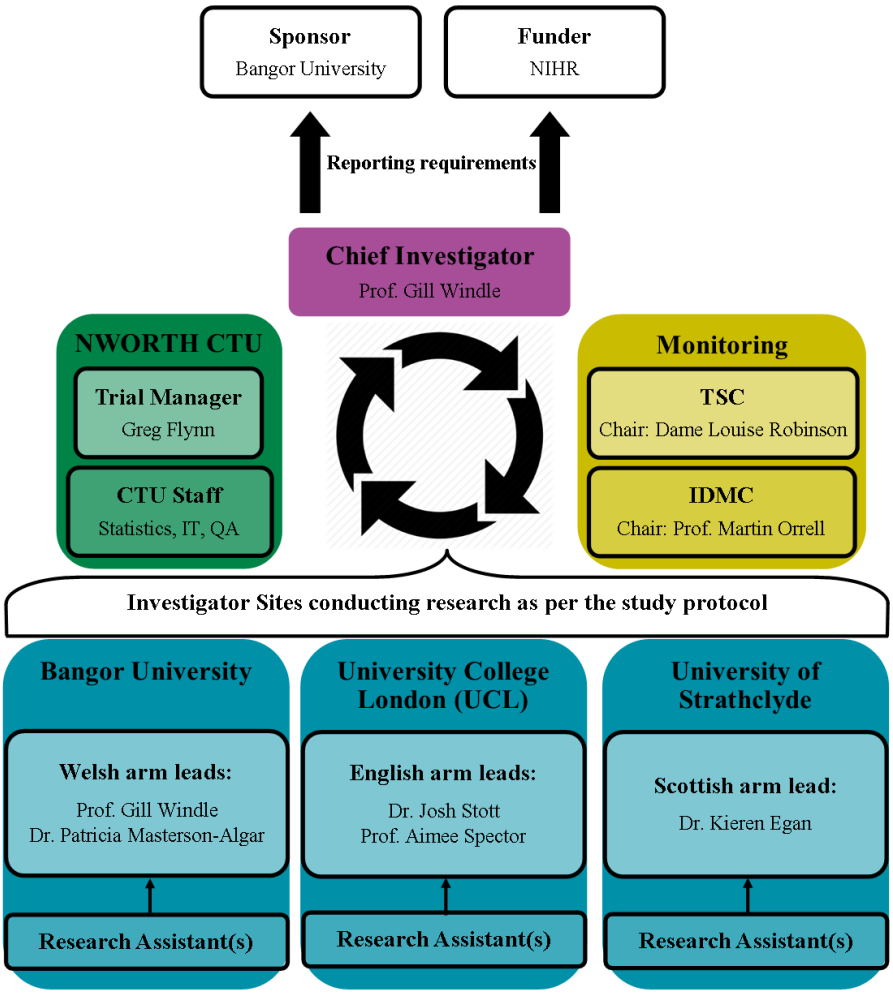


Figure 4: Organogram of research sites and study reporting

4.4 Sampling and sample size

Both primary outcomes (Zarit Burden scale and CES-D10) are important to the participants and have potential to indicate an effect, a successful trial would be one which detected an effect in either of these outcomes. Therefore, the sample size has been approached considering these as multiple primary endpoints at six months.

The Portuguese RCT of 'iSupport' has set an effect size of 0.5[14] and a meta-analysis of multicomponent interventions for carers found a standardized effect size of 0.65 [CI=0.46-0.84] for the ZBI[23]. Being conservative we have assumed a standardised effect size of 0.4 for the ZBI, which is equivalent to a 4-point difference on the scale and assuming a standard deviation of 10 as derived from scale validation with dementia carers.[29]

Meta-analysis by Leng et al.[30] indicated that the standardised effect size possible for the CES-D10 would be in the order of 0.2. Ying et al.[31] denote that the correlation between these two measures is approximately 0.7.

Using the multiple primary endpoint estimator in the R package mpe with power of 90% and significance set to 2.5% established a sample of 262 would be required to have the potential to detect an effect in at least one of these outcomes. The mpe package uses the methodology of Sugimoto et al.[32] and Suzo[33] to estimate the sample size required based on the defined effect sizes and the correlation between the measures. The attrition rate is estimated as 25%, based on 9 dementia intervention studies, where the mean retention rate was 15.33% (range 2%-24%). Accommodating a 25% attrition rate by six months, we will need to recruit and randomise 350 participants.

For WS2, sociodemographic factors collected at baseline will inform the purposive sampling strategy. The choice of sample size in qualitative research is an area of debate.[34] The sample size (up to n=50) will be determined by thematic saturation, along with pragmatic considerations, e.g. it is recommended that studies employing individual interviews undertake no more than 50 interviews in order to manage the complexity of the analysis.[35] The purposive sampling will include a diverse range of participant characteristics such as age, gender, ethnicity, location, caring responsibilities, as well as the extent to which they used/didn't use 'iSupport' and level of support from the 'e-coach'. Motives for declining participation will also be noted where consent is given, to understand barriers for participation and selection bias.

To address possible socioeconomic inequalities, we intend to collect the following information:

- The number of people who express an interest in the trial but are unable to take part because they do not have access to the internet.
- The number of people who express an interest in the trial and have access to the internet but are unable to take part as their internet is unreliable.
- The number of people who express an interest in the trial but are unable to take part because they do not have a PC, tablet or smart phone.
- The number of people who express an interest in the trial but do not join as they feel their IT skills are not sufficient.
- The number of people who express an interest in the trial but are unable to take part because the intervention languages are not compatible with their first language.
- Anonymised data on the age, gender and ethnicity of people who express interest in the trial but do not consent to take part.

4.5 WS1 Randomised controlled trial

WS1 is a multi-centre, pragmatic, single-blinded, two-arm randomised controlled trial (with a nested internal pilot). It will evaluate the effectiveness of 'iSupport' in reducing carer distress and symptoms of depression (primary outcomes). Secondary outcomes will assess reductions in anxiety, and improvements in resilience, relationship quality and dementia knowledge. Assessments will be completed at baseline (T0), 3 months after baseline (post-intervention, T1), and 6 months after baseline (follow-up, T2). NWORTH will provide a randomisation system maintained by a team independent of the trial. Randomisation will use a secure web-

based dynamic adaptive randomisation algorithm[22] and be stratified for site along with age and gender, previously found to influence the outcome measure of caregiver distress.[23] If more than one person identifies as the carer for the same person (e.g. spouse/partner, adult child, or friend) we would allocate one person as the 'index carer' (based on caring frequency, or if caring frequency is equal between carers, then the carers will nominate who will be 'index carer').

4.5.1 Internal pilot study

A six-month internal pilot will be nested in WS1 at each site. Progression criteria will be assessed as a whole, and will guide decisions on a go/review/stop basis. A successful outcome of the internal pilot would be to have all criteria assessed as go. Continuation will still be possible with a combination of stop, review and go flags, but will require additional discussion within the Trial Steering Committee (TSC), research team and the funder prior to proceeding (to mitigate risks highlighted in the pilot study). The discussions would consider the overall context in which the criteria have been assessed, and if a decision is reached which indicates that either the design or processes need to be overhauled, this might suggest termination of the trial. Termination would be fully discussed in collaboration with the funder and independent committees. All thresholds have been set based on levels that would enable completion of the trial objectives within the proposed timeframe (Go without adaptation, Review with adaptations to trial processes, Stop may not be possible to complete).

- Recruitment and set up/ training of sites within time allocated: Go: 3, Review: 2, Stop: 1.
- Recruitment of participants based on target of n=110 by month 6 of recruitment: Go:>= 94 (>=85%), Review:55-93 (50 - 84%), Stop:<55 (<50%).
- Retention of recruited participants to 6 months, assessed as a percentage of those who should have reached 6 months at the time of internal pilot assessment: Go:>=75%, Review:40-74%, Stop:<40%.
- Acceptability of intervention: assessed by utilisation of 'iSupport' (the number of participants who have logged in and used the system more than once): Go:>=70%, Review:50-69%, Stop:<50%.
- Ability to collect outcome data (assessed on baseline and first follow-ups only). A measure would be a candidate for removal if less than 85% of participants attempt to complete a measure: Go:>=85%, Review:70-84%, Stop:<70%. This only becomes a trial termination criteria if this were in relation to the primary outcome. Missing data within an outcome measure will be assessed separately.

4.5.2 Selection of participants

Potential participants who express an interest in the project but do not meet the inclusion criteria will be provided with information about relevant organisations (including our own support groups) and a copy of the 'iSupport' manual.

Participants who meet the inclusion criteria for WS1, provide informed consent and complete the baseline assessments (see section 4.5.5 Data collection for further details), will be

randomised and the outcome communicated to them in an email, internet-based service (e.g. Zoom, Teams or Skype) or telephone by the Trial Manager or Chief Investigator. Participants randomised to the 'iSupport' group will receive the intervention log-in details and they will have access to the intervention for 6 months. To help retention, participants in the comparison group will be given access to 'iSupport' at the end of the data collection. Excluded participants will also be able to use 'iSupport' after study completion.

At the end of the trial, both intervention and comparison groups will receive information on national and regional organisations that can provide help, such as those provided by our charity partners, and information about support groups that our respective institutions (UCL and Bangor) host. To aid recruitment and retention in line with suggestions from Carer's Trust Wales, all eligible randomised participants will be reimbursed with a gift voucher to thank them for their contributions.

4.5.3 Primary outcome measures

Reflecting the intentions of the intervention, the outcome measures assess reductions in psychological morbidity and the promotion of personal capabilities to mitigate against morbidity.

There will be two primary outcome measures for WS1. Sample size has been based on considering both outcomes as primary outcomes where a successful trial would be noted if at least one of the outcomes indicated a statistically significant effect. This choice is justified as a meta-analysis evaluating the efficacy of technology-based interventions for informal carers of people living with dementia found they had a significant effect on reducing depression and burden outcomes.[36]

The first primary outcome measure will assess reductions in carers' distress, measured by the 12-item Zarit Burden Interview.[18] Item responses range from 0 (never) to 4 (almost always), and higher scores indicate greater distress. The original 22-item ZBI is used widely in research with dementia caregivers and internal consistency of the 12-item version, as measured by Cronbach's alpha, is $\alpha = .85$.[37] Concurrent validity of responses to the 12-item version has been examined and found to be good relative to indices of patient behavioural disturbance and ADL impairment in dementia.[18] The ZBI-12 is considered valid for evaluation of burden in clinical practice and research as a fast, efficient option for screening burden among older caregivers of community-dwelling older adults.[38]

The second primary outcome measure is the Centre for Epidemiological Studies of Depression Scale (CES-D10),[20] a very widely used 10-item measure of depression. Ratings relate to the past week with eight items measuring frequency of depressive symptoms and two measuring positive affect. Response categories range from 0 (rarely or none of the time present) to 3 (most or all of the time present). Scores range from 0 (no depression) to 30 (very depressed). Internal consistency ranges between Cronbach α=.86 -.88 in an older caregiver population.[20] CES-D is a valid and reliable scale for detecting caregiver depression in

dementia. It has added utility, beyond that of a caregiver burden scale, in identifying a subgroup of caregivers with depression but not burden.[39]

4.5.4 Secondary outcome measures

Generalised Anxiety Disorder Questionnaire (GAD-7)[40] is a widely used 7-item measure rating the frequency of common symptoms of anxiety in the past two weeks. Response categories range from 0 (not at all) to 3 (nearly every day). Scores of 15 indicate severe anxiety. GAD-7 has excellent internal consistency (Cronbach α=.92), good sensitivity, is a valid and reliable measure for detecting generalised anxiety disorder in the general population. It has been used with carers of people living with dementia.[41] GAD-7 was selected by the NHS England Improving Access to Psychological Therapies (IAPT) programme as the gold-standard measure of anxiety.[42]

Following the recommendations of a 12-country European working group to include measures of 'living as well as possible' with dementia,[43] improvements in the way the carers perceive they can manage the situation will be assessed through the Resilience Scale-14 (RS-14).[44] Derived from the original 25-item Resilience Scale, this 14-item version is strongly correlated with the original (r=0.97, p>0.001) and has an excellent internal consistency ranging from Cronbach α = .89 to .96. Response options range from 1 (Strongly disagree) to 7 (strongly agree). Higher scores are indicative of resilience level. Construct validity has been established in a wide range of previous research and it has been used in previous research with dementia caregivers.[45]

We will examine the influence of 'iSupport' on the quality of the caregiving relationship, using the quality of the carer-patient relationship (QCPR).[46] The QCPR is a measure of relationship quality, comprising 14 items designed to assess warmth, levels of conflict and criticism in the caregiving relationship. Previous studies have shown that the QCPR has good internal consistency and concurrent validity and it has been used in relation to online interventions for dementia carers.[36]

Improvements in how the carer understands their relative will be assessed with a measure of dementia knowledge (DKAS).[47] The 25-item measure exhibits good reliability (α = .85; ωh = .87; overall scale), with acceptable subscale internal consistency (α ≥ .65; subscales). Subscales showed acceptable correlation without any indication of redundancy. Total and DKAS subscale scores show good discrimination between cohorts of respondents who would be anticipated to hold different levels of knowledge on the basis of education or experience related to dementia.

To ascertain the impact on the health-related quality of life of the person being cared for, we will use the DEMQOL-Proxy. This is a widely-used instrument for measuring the health-related quality of life of people living with dementia, completed by the carer. It is adapted for use as a preference-based measure in economic evaluations.[48]

4.5.5 Data collection

The primary mode of data collection for all the outcome measures will be technology mediated, i.e. interviews over an internet-based service (e.g. Zoom, Teams or Skype) or telephone. The outcome measures will be collected first on paper Case Report Forms (CRFs) and then entered into an online data management system (MACRO) by a member of the research team. Assessments will be done at baseline (T0), 3 months after baseline (T1), and 6 months after baseline (follow-up, T2). Demographic data will be collected at baseline (e.g. age, gender, marital status, ethnicity, education, occupation, length and frequency of caring, dementia diagnosis of family member). The researcher will also collect the country/area specific COVID-19 restrictions at the time of data collection.

Whilst every effort will be made to follow-up participants as close as possible to the defined time point this may prove difficult. In these instances T1 and T2 data collection would be acceptable 2 weeks early and up to 4 weeks late. Date of data collection will be recorded in the CRF.

4.5.6 Data analysis

Primary analysis will be conducted on an intention to treat (ITT) basis, blinded to treatment allocation. The primary assessment for effectiveness will be adjusted estimates of the ZBI scores and CES-D10 scores between the two groups assessed at 6 months. A linear mixed effects model adjusting for baseline scores, randomising site (random effect) and stratification variables will be fitted for each of the two primary outcomes. Similar models will be fitted for all continuous secondary outcomes.

All estimates of effect will be presented together with 95% confidence intervals. The aim is to minimise missing data; however, predictors of missingness will be investigated using regression models and any predictors found will be considered for inclusion in the models. Multiple imputation will be employed to address missing scores where appropriate. CACE analysis will be utilised to assess the impact of the number of times the ‘iSupport’ intervention is accessed. A sensitivity analysis will be utilised to assess whether there is any impact resulting from participants completing outcome measures in Welsh.

A full Statistical Analysis Plan will be written and agreed before completion of data collection. The independent committees will have the opportunity to comment on this plan. If any deviations from the planned statistical analysis are required these will be fully documented and justified in the final analysis report.

4.6 WS2 Process evaluation

Process evaluation will run alongside WS1 and will apply mixed-methods (semi-structured interviews, quantitative questionnaires and analysis of data from the online platform). It will be conducted in line with established guidance frameworks.[15,16] It will examine throughout the intervention period how participants engage with and adhere to particular aspects of ‘iSupport’ (e.g. most/least frequently visited pages, the most ‘popular’ modules/sessions, sessions with quizzes with the highest rates of wrong responses).

Change mechanisms will be investigated by exploring the barriers, facilitators and contextual factors which influence the uptake and implementation of 'iSupport' (i.e. the sociodemographic diversity of participants). The extent to which 'iSupport' may have changed behaviours beyond the intervention (e.g. help-seeking) will be explored, as will the extent to which it is beneficial in the current circumstances of distancing and isolating in an ongoing or future repeated pandemic such as COVID-19.

4.6.1 Quantitative data collection

A System Usability Scale (SUS)[49] will be administered at 6-month follow-up. This 10-item scale will quantitatively evaluate the overall usability of the 'iSupport' platform. Each item is a statement (e.g. "I thought 'iSupport' was easy to use") and responses given on a 5-point Likert scale 0 (strongly agree) to 4 (strongly disagree). Total scores range from 0 to 40 which are then converted to 0-100 and normalised to produce a percentile ranking. The SUS is easy to administer, reliable and valid and effectively differentiates between usable and unusable systems. To avoid unblinding the research assistants, they will contact the Trial Manager following the 6-month follow-up. The Trial Manager will send out a thank-you email with a link to the SUS, which will be self-completed online (e.g. through Qualtrics or Survey Monkey).

WS2 will collect data from the online platform regarding usability (e.g. frequency and length of use, which modules/ lessons / pages users most frequently visit; average length of time spent on each module / lesson / page per user; from tablet or PC). The number of contacts with the 'e-coach' will also be recorded.

4.6.2 Qualitative data collection

Semi-structured interviews will be undertaken using an internet-based service (e.g. Zoom, Teams, Skype, or GoToMeeting) or telephone, with a sub-sample of the intervention participants. These will be recorded and professionally transcribed. The topic guides will be guided by the process evaluation parameters described in recognised frameworks,[15,16] and drawing upon theoretical models such as Normalisation Process Theory (NPT).[50] They will be developed in partnership with the PPI group and our collaborators. Regular meetings will be held with the Research Assistants and 'e-coach' to identify any new questions which arise from emerging themes.

4.6.3 Data analysis

Quantitative data from the online platform will be analysed descriptively by calculating total numbers, percentages, means and standard deviations, or, the median and range if not normally distributed. This will provide information on the intervention. Descriptive statistics of sociodemographic characteristics of intervention participants will demonstrate the reach of the project and will then be compared with Office For National Statistics data to preliminarily investigate sample representativeness.

Interview data will be recorded either by the videoconferencing software, or via an encrypted digital recorder and then professionally transcribed verbatim. Transcripts will be checked for accuracy against the recordings and any corrections made. The researchers will re-read all transcripts to gain familiarity with the data which will then be coded, informed by a coding framework based on proposed/hypothesised mechanisms identified in the study's logic model (see Appendix 1) and informed by NPT.[47] Analysis will follow the phases of thematic analysis by Braun and Clarke[51] using NVivo. This analysis will reveal the experiences of 'iSupport' and its delivery, the barriers and facilitators to its uptake and continued use, and the perceived benefits for the carer participating in 'iSupport' and for the person they are caring for and how were these realised (mechanism of change).

Results will also be applied to aspects of the 'Context and Implementation of Complex Interventions' (CICI) checklist[17] to generate recommendations for the WHO that pay particular attention to the contextual factors (e.g. personal characteristics) that may influence, or be influenced by the trial setting (e.g. online access) and their relationship with the trial recruitment and intervention delivery, which may reflect implementation in a real world setting (see Appendix 1).

4.7 WS3 health economics

WS3 will collect health economics data to calculate the cost-effectiveness of 'iSupport'. Cost-effectiveness analysis will be undertaken from two perspectives; the base case analysis will adopt a public sector perspective (NHS, personal social services and local authorities) in line with NICE public health guidance,[52] and a secondary analysis will be undertaken from a societal perspective using an opportunity cost method. Here, the value of the carer's next best use of time is calculated (the value of their leisure time or paid employment) to ascertain changes in employment hours (productivity losses) due to caring. If the internal pilot phase of WS1 indicates <60% of carers provide sufficient information on these two indicators to use this method, we will use the proxy-good method. Here a market price for substitute labour to carry out care-related tasks is applied to informal care hours. Out of pocket expenses, such as travel expenses, will be captured through a Service Use questionnaire developed for 'iSupport'.

4.7.1 Outcome measures

The primary outcome measure for the cost-effectiveness will be Quality-Adjusted Life Years (QALYs) at T2. Utility values for the QALY will be obtained from responses to the EQ-5D-5L[53] at T0, T1 and T2. The EQ-5D-5L is a generic, preference based, health-related quality of life (HRQoL) measure widely applied in economic evaluation, and in dementia research with both people living with dementia and dementia caregivers. It consists of two parts, a five-item questionnaire and a visual analogue scale (EQ-VAS). The first part asks the respondent about the level of difficulty they have in the following domains: mobility, self-care, usual activities, pain / discomfort, anxiety / depression. The second part asks respondents to rate their overall health using a visual-analogue scale, where health is rated anywhere between 0 (worst imaginable health) and 100 (best imaginable health). Previous studies have shown that the

EQ-5D-5L has a good construct validity and good reliability compared with two dementia specific measures.[54]

As mentioned in WS1 secondary outcome measures, the DEMQOL-Proxy will be adapted for use as a preference-based measure in economic evaluations.[45]

Resource use data will be collected using a study-specific Service Use questionnaire at T0, T1 and T2. Some examples of the topics carers will be asked to report on are their own frequency of contacts with health and social care professionals and that of the person that they care for. We will ask carers to report on the use of respite care and sitting services to allow us to consider the impact of 'iSupport' on the person being cared for. Health and social care service use will be costed using national unit costs.[55,56] To incorporate opportunity costs, we will ask carers to report on changes in employment hours (productivity losses) due to caring, employment status and hours, income (including carers allowance and attendance allowance), hours spent caring, types of care tasks undertaken, whether people carry out paid/unpaid care, and carers' willingness to pay for more support or more leisure time. The Erasumus iMTA informal care questionnaire will be adapted for this aspect.[57] The cost of technical support for 'iSupport' over the intervention period will be calculated. Records will be kept of the time spent supporting carers to use the tool, and the staff costs associated with this activity will be calculated.

4.7.2 Data collection

See section 4.5.5 Data collection (collected in same CRF as for WS1).

4.7.3 Data analysis

WS3 will adopt an intention to treat approach. A scoring algorithm using UK tariff values[58] will be used to convert carer EQ-5D-5L responses into an index score of between -0.594 and 1, with 1 representing full HRQoL. Care recipient utility values will be derived using the DEMQOL-proxy scoring algorithm. These index values will then be used to calculate QALYs. An appropriate regression model will be used to adjust for imbalances in baseline utility. Cost and QALY data will be combined to calculate an incremental cost-effectiveness ratio (ICER). As the intervention follow-up period is less than 1 year it will not be necessary to discount costs. The nonparametric bootstrapping approach[59,60] will be used to determine the level of sampling uncertainty surrounding the mean ICER by generating 5,000 estimates of incremental costs and benefits. Cost effectiveness acceptability curves[61] will be produced to show the probability that 'iSupport' is cost-effective compared to standard care for a range of willingness-to-pay thresholds. Secondary cost-effectiveness analyses will calculate the cost per unit change in carer distress using the 12-item Zarit Burden Interview[18], and cost per unit change in carer anxiety and depression using the 10-item CES-D[20]. A subgroup analysis will be conducted on the number of times that carers in the intervention group access 'iSupport' (low/ moderate/ high user categories to be classified during the internal pilot). Sensitivity analyses will be conducted to vary the costs of inputs (e.g. the cost of the staff supporting carers to use 'iSupport'). The economic evaluation will be reported according to the Consolidated Health Economic Evaluation Reporting Standards.[62]

A full Health Economics Analysis Plan (HEAP) will be written and agreed before completion of data collection. The independent committees will have the opportunity to comment on this plan. If any deviations from the planned analysis are required these will be fully documented and justified in the final analysis report.

5. Feasibility study objectives and design

5.1 Feasibility study objectives and design

The feasibility study is a non-randomised feasibility study of intervention refinement for younger dementia carers. This will:

- Explore the potential of 'iSupport' to address the required support that is unique to young carers, including the potential of the platform in the face of the ongoing or future COVID-19 pandemic.
- Work with young carers to refine 'iSupport' to fit their needs.
- Identify what outcomes are most important and relevant to young carers in relation to 'iSupport'.
- Identify the best ways to increase the accessibility and uptake of 'iSupport' for young carers.
- Explore the feasibility of the refined 'iSupport' intervention.

5.2 Research questions

1. Is it feasible, useful and acceptable to digitally deliver a refined 'iSupport' to young carers?
2. What are the carers' perspectives of 'iSupport' in relation to supporting them in an ongoing or future repeated pandemic such as COVID-19?

5.3 Feasibility study expected duration

The total time scheduled for the feasibility study is 36 months. Key milestones will be monitored as part of overall project management.

5.4 Feasibility study flowchart

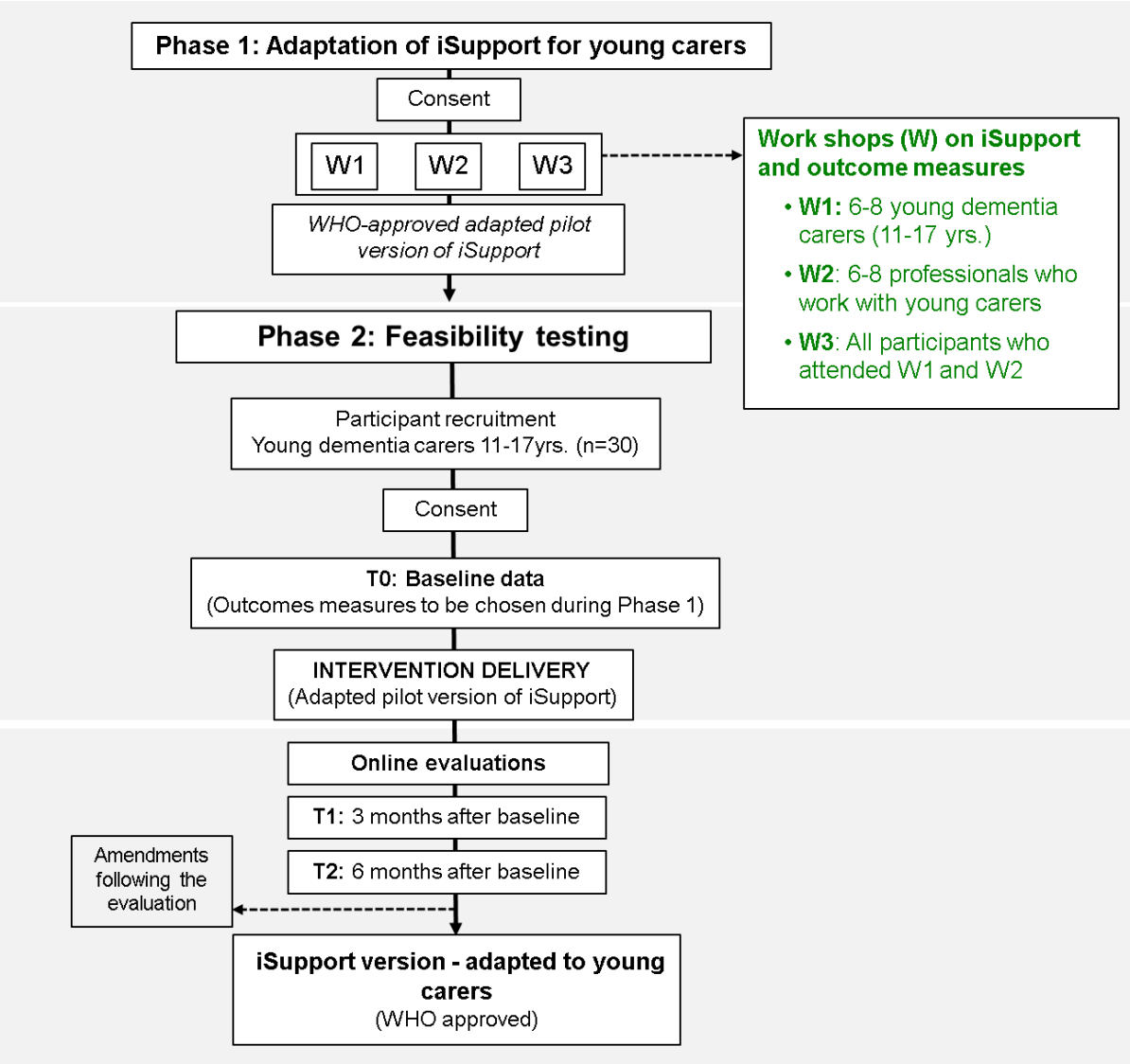


Figure 5: Feasibility study flowchart including sample sizes

6. Selection and withdrawal of feasibility study participants

Young carers (ages 11 - 17) will be recruited through stakeholder and research teams' networks (including secondary schools), social media, and national carers associations (e.g. Carers Trust).

6.1 Inclusion criteria

1) Young people between the ages of 11 - 17 (secondary school age) who self-identify as a carer of a person with dementia who is not living in a full-time care facility, caring at least weekly for at least 6 months.
2) The care recipient has to have a confirmed diagnosis of dementia (through self-report of the carer, to reflect the 'real world' application of 'iSupport').

6.2 Exclusion criteria

1) Receiving treatment from Child and Adolescent Mental Health Services (CAMHS) at the time of recruitment.
2) Unable to comprehend written English.
3) No access to the internet.
4) Have previously used 'iSupport' materials (in the last 12 months).

6.3 Feasibility study consent procedure

For young carers between the ages of 11 - 15, consent will be taken from the parent or legal guardian. Young carers aged 16 or 17 can provide consent independently. Age-specific documentation has been produced, and researchers taking consent will be trained on which participant information sheet to use.

Please see section 3.3 Trial consent procedure.

6.4 Randomisation and unblinding

As this is a non-randomised feasibility study, randomisation and unblinding are not applicable.

6.5 Withdrawal of participants

Please see section 3.6 Withdrawal of participants.

7. Feasibility study procedures

This is a refinement and feasibility study of 'iSupport' for young carers, delivered in two phases: Phase 1 (adapting the intervention) applies principles of co-design reflecting co-applicant Masterson-Algar's expertise.[63] It will involve three sequential co-design workshops with young carers and professionals; Phase 2 (feasibility testing) will then explore the refined 'iSupport' from phase 1.

7.1 Planned intervention

The intervention – as laid out in section 4.1 Planned intervention – will be adapted for the specific needs of young carers as explained below.

7.2 Setting and context

The research will be undertaken with young carers who live in Wales, Scotland or England. Researchers will recruit and assess participants in a one-to-one meeting using an internet-based service (e.g. Zoom, Teams or Skype) or over the telephone. The adapted version of the intervention will be hosted by the PAHO/WHO.

7.3 Feasibility study

7.3.1 Phase 1: Adaptation of 'iSupport' for younger dementia carers

Phase 1 will follow WHO adaptation guidelines to tailor the programme for young carers. This will consist of three workshops. Depending on the government guidelines regarding

COVID-19 and safety, workshops will either be held in-person at Bangor University, or they will be technology mediated i.e. using an internet-based service (e.g. Zoom, Teams or Skype). The first (Workshop 1) will explore with 6-8 young carers, their experiences of caring, what is important to them and how this might be reflected (or not) in 'iSupport'. They will provide in-depth feedback on the content and style of each of the 5 modules. Workshop 2 will undertake a similar exercise with 6-8 professionals who work with young carers. The refined 'iSupport' will be shared in Workshop 3 with all participants who attended the first two workshops, along with discussion regarding outcomes and measures. Modifications will be made before being sent to WHO for approval.

The workshops will draw on participants' experiences, using creative activities to stimulate and encourage reflectivity. These activities will simultaneously engage, reveal tacit knowledge and generate ideas. Participants will be given access to 'iSupport' at least 2-weeks before the workshops and will be instructed to note what is useful, what is clearly explained (or not), what could be made better, the extent to which it is beneficial in circumstances of isolating and distancing, etc. They will also be provided with a printed version of 'iSupport' content for them to make further annotations. They will identify what outcomes are most important to young carers in relation to 'iSupport', using the measures in the trial as discussion points. Following this, the final WHO-approved version will be produced for phase 2 (feasibility testing).

7.3.2 Phase 2: Feasibility testing 'iSupport' for younger dementia carers

The WHO-approved version will test the feasibility of the refined 'iSupport' intervention with a group of 30 young dementia carers. The outcome measures selected as important in Phase 1 will be used to collect data, as per the data collection process for WS1 of the trial (see section 4.5.5 Data collection), with some questions relating to demographic information tailored for younger carers (e.g. how many older siblings do you have, how many younger siblings do you have, do you go to school/college).

7.3.3 Sampling and sample size

No formal sample calculation has been conducted due to the nature of this feasibility study. However, informed by the methodological framework proposed by Lancaster et al.,[64] it is envisaged that a sample of n=30 for phase 2 will provide enough information on the acceptability of the intervention, the appropriateness of data collection forms, the feasibility of recruitment and consent procedures and the most appropriate primary outcome measure. Hence, indicating whether further investigation of the developed intervention is warranted.

7.3.4 Selection of participants

Young carers will be recruited through stakeholder and research teams' networks (including secondary schools), social media, and national carers associations (e.g. Carers Trust).

Professionals will be recruited through stakeholder and research teams' networks (including secondary schools), social media, local authorities, national carers associations (e.g. Carers Trust) for workshops 2 and 3. To be eligible they will need to be professionals who, as part of

their professional role, have regular contact with young people and young carers (e.g. teaching staff involved in pastoral care, young carer charity workers and social workers in children's services.)

7.3.5 Data collection

Phase 1 workshops will either be held in-person at Bangor University, or they will be technology mediated i.e. using an internet-based service (e.g. Zoom, Teams or Skype) depending on the government guidelines regarding COVID-19 and safety. Workshops will be video recorded and will be approximately 3 hours long. PPI co-applicant Hughes is a fluent Welsh speaker and will co-facilitate all workshops. Decisions on outcome measures for phase 2 will be informed by data collected during Phase 1.

Phase 2 will be conducted as per the data collection process for WS1 of the trial (see section 4.5.5 Data collection). Participants will also be asked to complete an online evaluation of their experiences using 'iSupport' after T2 data collection, similar to that of WS2 (see section 4.6.1 Quantitative data collection).

7.3.6 Data analysis

Data from Phase 1 workshops will be selectively transcribed, and hand-written field notes will be converted into electronic text. Masterson-Algar and the research assistant will re-visit the recordings and take written notes to gain familiarity with the data. This qualitative data will inform modifications to 'iSupport' with the aim to make it more relevant for younger carers. The work will be undertaken in line with the FRAME[65] and with the WHO adaptation and implementation guide (2018).

All quantitative data collected during phase 2 will be presented descriptively. No inferential testing will be undertaken for this feasibility data. The mean change from baseline, associated variances and 95% confidence intervals will be calculated for all selected outcomes. Consideration will be given to the applicability of these outcomes for development into a protocol for a defined randomised controlled trial (RCT) if the acceptability of the intervention is proven. Success will be defined as acceptability of the recruitment and consent procedure, data collection tools, intervention content and delivery to participants, as well as compliance.[59] An estimation of the precision of the means and variances will be made to inform the power calculation for a future RCT protocol.

The online evaluation in phase 2 will include Likert-like and open-ended questions and will be informed by NPT and the mechanisms of change through the application of frameworks.[15,16] It will aim at exploring young carer's thoughts about the content, accessibility and perceived benefits of the refined version of 'iSupport'.

8. Translating 'iSupport' into Welsh

We will follow the WHO standardised guide for translation and adaptation to translate 'iSupport' into the Welsh language for WS1. Following professional translation the full text will be independently checked by two experts in the field (already known to the research team). This may lead to suggestions for minor modifications following the original translation. Following any modifications the subsequent procedures will be applied.

Up to 10 caregivers and 6 professionals (Welsh speaking) will be recruited following the procedures outlined for WS1. They will be invited to share their expertise by working through the Welsh version of 'iSupport'. They will be provided with prior guidance by the researcher through either a group meeting or individually, depending on their availability. They will be asked to individually go through 'iSupport', examine the exercises and write down their opinions about content that needs attention. Following this phase the researcher will convene either a group meeting or meet each person individually to discuss their suggestions and send any final modifications to the WHO. All meetings will be undertaken using an internet-based service (e.g. Zoom, Teams or Skype). The final version of the Welsh 'iSupport' will be implemented in WS1.

9. Assessment of safety

9.1 Definitions

Adverse Event (AE): Any untoward medical occurrence in either a trial or feasibility study participant which does not necessarily have a causal relationship with the intervention.

Serious Adverse Event (SAE): Any adverse event that a) Results in death; (b) Is life threatening; (c) Requires hospitalisation or prolongation of existing hospitalisation; (d) Results in persistent or significant disability or incapacity; or (e) Is otherwise considered medically significant by the investigator.

Pre-existing conditions do not qualify as adverse events unless they worsen over the course of the trial or feasibility study.

9.2 Collecting, recording and reporting of adverse events

Assessment of harm will be undertaken and overseen by an Independent Data Monitoring Committee (IDMC), who will report to the Trial Steering Committee (TSC). The IDMC will be able to advise on changes to the conduct of the trial via recommendations to the TSC and will also receive regular safety reports from the team.

The adverse event reporting period for the trial and feasibility study begins as soon as participants consent to take part and one month after their final data collection ends. All adverse event data will be collected and recorded in line with NWORTH's SOP on Safety monitoring. Reporting of SAEs will also form part of the delegation log and be covered in training.

Reports will be sent to the Sponsor, the Research Ethics Committee, IDMC and TSC within the required timelines from the SOP. Other adverse events will be noted in the same log as the SAEs and a monthly report will be compiled by the Trial Manager.

Safety analysis will be pre-specified analyses in the statistical plan and can be represented graphically e.g. as volcano plots[66] or in the usual tabular format. The former plots all SAEs and provides a visual representation of outliers. This method is preferred to inferential analysis, as they would be under-powered. Using graphical methods will allow the IDMC to identify any potential safety signals and these will be reported to the TSC.

A copy of the AE and SAE CRF will be stored at the recruiting site in the ISF, and those signed by the Chief Investigator stored in the Trial Master File (TMF).

Given the nature of the intervention, we do not feel there are serious safety concerns for the person being cared for. However we will be collecting data on health and social care usage, and also the DEMQOL-proxy, which assesses the health-related quality of life of the care recipient. This data will be available to the IDMC during the course of the trial. In the reporting of unanticipated harms, we will include an assessment of whether the reported event could have an impact on the person being cared for.

10. Project management

The study is sponsored by Bangor University and the governance and management of the study will be undertaken by NWORTH. As a result, the study will adhere to NWORTH's SOPs for all study and data management, statistical and regulatory matters. Study-specific SOPs will be developed as required and will be addressed throughout the study period and regularly reviewed. Best practice will be employed throughout to ensure both the trial and feasibility study are managed to the highest possible standard. Appropriate supervision and training of research staff and training in Good Clinical Practice (GCP) will be ensured. NWORTH's Trial Manager will provide advice to the sites on all aspects of the running of the trial and feasibility study and will supply appropriate templates.

We have established a Trial Steering Committee (TSC), an Independent Data Monitoring Committee (IDMC) and a Trial Management Group (TMG). The TSC and IDMC will meet at agreed time intervals, which will be documented in the committees terms of reference or charter. Both will consist of an independent chair and an independent statistician. The IDMC will be able to advise on changes to the conduct of the trial and feasibility study via recommendations to the TSC and will also receive regular safety reports from the TMG.

10.1 Trial Steering Committee

The project's TSC will oversee the running of the study on behalf of the sponsor and funder and will have overall responsibility for the continuation or termination of the trial and/or feasibility study. It will ensure that both the trial and feasibility study are conducted in

accordance with the principles of GCP and the relevant regulations, and to provide advice on all aspects of the study.

10.2 Independent Data Monitoring Committee

The project's IDMC will monitor the data and ethics aspects of the study and provide advice on changes to the conduct of the trial and feasibility study via recommendations to the TSC.

10.3 Trial Management Group

A TMG will oversee the day-to-day running of the trial and feasibility study and is composed of research team members, including the Chief Investigator, Trial Manager, Statistician etc. In addition, the group may include other members of the trial team with specific expertise, such as the Senior Software Engineer, Health Economists, and site Principal Investigators. The TMG will meet frequently during set up and subsequently on an agreed periodic basis once the trial is open to recruitment, and will monitor all aspects of conduct and progress, and ensure the protocol is adhered to.

10.4 Patient and public involvement (PPI)

Our PPI colleagues will be involved throughout the duration of the study and the CABAN group will formally meet twice a year in relation to 'iSupport'. Masterson-Algar will support the CABAN group's involvement with the trial and feasibility study. Co-applicant Hughes will join the TSC and contribute to the ongoing progress of the trial and feasibility study. She will jointly work with Masterson-Algar, assisting the development and facilitation of the feasibility study co-design workshops.

All public-facing documents will be finalised in consultation with our PPI group to ensure they are user-friendly and suitable for all levels of literacy skills. At the start of the project, all colleagues will contribute to the design of information sheets to help aid recruitment. After the intervention platform has been developed, our PPI group will help us make a short video to show other carers how to use 'iSupport'. Some Welsh speaking members will help with pilot testing the Welsh version of 'iSupport' and research documents.

Throughout years 1 and 2, colleagues will help promote the trial and feasibility study to assist the recruitment of participants. They will discuss the development of interview questions for the process analysis. In year 3, they will advise on the interpretation of the research results and the production of a plain English/Cymraeg clir summary and assist with the dissemination of the study findings. The trial team will develop and deliver short and simple research methods sessions if required, e.g. 'what is a randomised controlled trial?' to help colleagues understand this specific research process.

The group will hold the project management team accountable for maintaining the DEEP-Ethics Gold Standards for Dementia Research.[67] The six principles include: Working in real partnership; respect and acknowledgement; safety and wellbeing; informed consent and capacity; confidentiality and anonymity; and information that is simple, accessible, and open.

Collaborators the Carers Trust will send relevant documentation and discuss specific issues with a virtual reference group, which meets monthly.

All PPI colleagues will be reimbursed for any travel expenses and will be thanked for their contributions with shopping vouchers. All payments will be recorded in line with the Monitoring Plan.

10.5 Coronavirus (COVID-19) mitigation

Due to the Coronavirus pandemic (COVID-19), we are following government guidelines regarding working from home. Remote contact will be privileged over in-person meetings (including for site initiation visits and training), where possible, to ensure that all staff are protected. Remote contact will be conducted using an internet-based service (e.g. Zoom, Teams or Skype), and through email communication.

Following any subsequent relaxing of the guidelines, if any in-person site visit need to be performed, these will only be undertaken where sites have been COVID-free for at least 14 days.

Both the staff conducting the site visit and all staff at the site will provide the answers to the following screening questions prior to the in-person visit to ensure risk is minimised:

- Have any staff been unwell recently (that could be attributable to COVID-19)?
- Have any staff had a recent onset of a new continuous cough?
- Have any staff had a high temperature? (temperatures may be checked and recorded).
- Have any staff noticed a loss or change in normal sense of taste or smell?
- Have any staff had recent contact (in the last 14 days) with anyone with COVID-19 symptoms or come into contact with someone who has been confirmed as COVID-19 positive?*

*If yes, they must follow the local rules and national regulations on self-isolation

Site visits will then be booked. During the visit all staff present will wear a mask, ensure social distancing and handwashing/hand sanitisation are performed, in line with local rules and national regulations. The provision and recording of details for all staff present will ensure ‘track and trace’ can be performed, should this be necessary. Approval from our respective institutions will be sought, and this procedure will only be implemented following approval.

11. Ethics and regulatory approvals

The study protocol, associated documentation, and all substantial amendments thereof will be submitted for review by Bangor University Schools of Health and Medical Sciences Research Ethics Committee (REC). The main ethical concern for both the trial and feasibility study are

the process of gaining informed consent. The consent procedure is detailed in 3.3 Trial consent procedure and 6.3 Feasibility study consent procedure.

All researchers will have been fully trained in consent procedures and mental capacity. Applying the principles of the Mental Capacity Act (MCA), the researcher will support the potential participants to fully understand the nature of the trial and what is required of them. In line with the MCA Code of Practice this involves ascertaining the capacity to understand information, retain information and use or weight up the information to arrive at a decision/choice. This will be assessed by the researcher at each point of data collection at the point it needs to be made, i.e. when discussing the trial or feasibility study with a view to gaining consent, by going through the information sheet with them.

Good supervision will ensure a sensitive approach, and dilemmas will be discussed in regular meetings with the team, which include senior clinicians with many years of experience assessing capacity. If there is an indication of a lack of capacity, and a person is unable to give informed consent, the researcher will be trained how to manage that situation.

All information provided will be prepared in an acceptable manner that is clear and understandable. Bilingual information will be provided in Wales. The researchers will undertake the necessary checks (e.g. DBS) and be given full training and support in all procedures. In order to elicit data in a sensitive and appropriate manner and to ensure the questions are asked in a meaningful order, the interview schedule/questionnaires will first be piloted and revised as necessary. The research assistant in Wales will speak Welsh, should any participants prefer to undertake the study in Welsh.

12. Monitoring

12.1 Quality Assurance (QA) and Quality Control (QC) of data

QA includes all the planned and systematic actions established to ensure the trial and feasibility study are performed and data generated, documented/recorded and reported in compliance with the principles of GCP and applicable regulatory requirements.

QC is the operational techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the research-related activities are fulfilled.

12.2 Risk assessment

A risk assessment has been conducted by a cross functional team in order to identify the potential risks/hazards associated with the trial and inform the appropriate approach to monitoring. It was also used in the composition of this protocol.

12.3 Monitoring plan

A Monitoring Plan will be prepared prior to participant recruitment detailing the monitoring strategy for the trial and feasibility study. The plan will include requirements for day-to-day centralised monitoring, and any requirements identified in the risk assessment.

12.4 Source data

The CRF will be considered the source data and should be consistent and verifiable with the information recorded in MACRO. Information regarding how the data is to be collected, stored, and transferred is included in the Data Management Plan which will be stored in the TMF.

12.5 Direct access to source data and documents

In order to perform their role effectively, monitors and persons involved in QA and inspection may need direct access to source data. Since this affects the participant's confidentiality, this fact will be included on the Patient Information Sheet and Informed Consent Form.

12.6 Confidentiality

All data will be handled in accordance with General Data Protection Regulation (2018). The CRFs will not include the participant's name or other personal identifiable data. Audio recordings containing personal identifiers will be substituted for pseudo names during transcription.

All trial staff and members of the research team will preserve the confidentiality of participants taking part in the trial or feasibility study, and the Sponsor is registered as a Data Controller with the Information Commissioners Office.

All interviews will be conducted in a way to ensure privacy and confidentiality (e.g. there is no-one else in the room with the researcher at the time) and all data will be securely stored in lockable areas.

13. Data handling

All aspects of the trial and feasibility study will be managed in accordance with General Data Protection Regulations (GDPR), principles of GCP, and relevant NWORTH SOPs.

In light of the current COVID-19 pandemic, all members of the research team are currently working from home. The security of confidential data will be upheld in line with governing policies of the research team's respective institutions. This will ensure that all data is securely stored electronically using password protected computers and in lockable areas in the home, or if working in offices in a locked filing cabinet.

Participants will be allocated a unique study number, which will be used in any documentation associated with the trial or feasibility study. Participants' names will not appear on any documentation associated with the trial or feasibility study.

A Data Management Plan will be developed to outline the responsibilities of all staff and the procedures for collecting, handling, and transferring data. This will be developed in line with NWORTH SOPs.

14. Pathways to impact

The Chief Investigator and all co-applicants will prepare and agree a publication policy, which will be reviewed by the TMG, to agree on authorship of future papers and other outputs from the study. Multiple routes will be taken to the dissemination of the study:

A dedicated 'iSupport' project webpage will be developed. All participants will receive up to 4 study updates during the project timescale. The 'iSupport' intervention platform and an adapted version of 'iSupport' for young carers will be widely available across the UK and globally at the end of the research. We will produce data on the recruitment, retention, data quality and acceptability of 'iSupport' for young carers to inform a larger definitive study, along with exploring a range of appropriate outcome measures for this group. This could give an indication of the likely magnitude of possible movement within an outcome measure and some suggestion of variability, which could inform a future sample size calculation, along with further evidence from the literature.

We will develop a 'how to use 'iSupport'' video to help other carers who may lack confidence with using technology. We will produce at least 5 academic papers that will be published open access to ensure maximum use, and an article for a practitioner magazine (e.g. Journal of Dementia Care). We will present the findings at academic conferences (e.g. Alzheimer's Europe; Alzheimer's Disease International). We will work with our stakeholders and PPI group to deliver up to three stakeholder and public events, and to produce plain English/Cymraeg clir summaries of the research findings that are visually appealing. Findings will be presented at the Carers Trust annual conference. We will develop policy briefings for our respective devolved governments. A short video developed with young carers will capture some of the main aspects of the adaptation (including methodological guidance) which will be of use to others who may also want to adapt 'iSupport' for young carers in other countries. Carers Trust will disseminate information via their magazine to over 150 carers services in the UK.

15. Indemnity

Cover for harm as a result of the design or conduct of the study has been arranged with the study Sponsor.

16. Financial aspects

This study is funded by the National Institute for Health Research (NIHR) Public Health Research and will be managed in accordance with the relevant policies and procedures.

17. Definition of end of study

This is defined as the date of the last assessment of the last participant.

18. Archiving

Archiving will be conducted in line with NWORTH's SOP on Archiving. The Data Management Plan will also describe the requirements for data archiving, and responsibilities will be documented in the Delegation Log.

19. Research expertise

GW is a Professor of Ageing and Dementia Research and Associate Director of the Wales Centre for Ageing and Dementia Research, with extensive expertise in the leadership of research studies. GW will lead the trial.

RTE is a Professor of Health Economics and Co-Director of Health and Care Economics Cymru (formerly WHESS). She has extensive experience of research involving people living with dementia and their carers, and will lead WS3.

PMA is an experienced researcher within the field of neurological conditions and their impact on individuals and their families. Her recently completed research fellowship explored, applying innovative co-design approaches, the experiences of young people living in families affected by neurological conditions such as dementia. PMA will lead the feasibility study and process evaluation.

JS is an Associate Professor of clinical psychology at UCL and clinical psychologist with a track record in leading dementia research projects including development of clinical interventions for people affected by dementia and evaluating online support for carers. He will lead the English arm of the trial. He is also clinical director of the largest clinical psychology training course in the country (150 active students at any one time).

AS is a Professor of Old Age Clinical Psychology. She has extensive experience in the development and evaluation of psychosocial interventions, including Cognitive Stimulation Therapy (CST), which is recommended by UK government guidelines and is the primary psychosocial intervention offered by UK memory clinics.

KE is an experienced researcher and core member of the Digital Health and Wellness team at the University of Strathclyde. He gained prominent international experience within the World Health Organization developing 'iSupport', and has worked on a number of technology-based studies including Randomised Controlled Trials in Dementia. Since moving to Strathclyde in early 2018 he has established strong working links with Alzheimer Scotland and clinical NHS colleagues making an ideal recruitment base within the Scottish setting. He will lead the Scottish arm of the trial.

ZH, as principal statistician of NWORTH CTU, will provide statistical and methodological oversight for the project and will supervise all statistical analysis.

GH is a young carer of a family member with dementia. She is a member of the TSC and is the research assistant for the Welsh arm of the trial, where she has assisted in adapting iSupport for Welsh language speakers and will undertake bilingual assessments. .
GF, as Trial Manager at NWORTH, will co-ordinate all aspects of quality management and regulatory issues, and will provide advice to the team on all aspects of the running of the trial.
RI, FAI, JC and SK are research assistants working on the Scottish and English arms of the trial, and all have prior experience of conducting quantitative and qualitative research. All research assistants will be fully trained in all the trial procedures.
BA is an experienced health economist with expertise in designing and conducting cost-effectiveness analyses in both health and social care research, and will work on WS3 under the supervision of RTE.

20. Research collaborators

Carers Trust will promote the programme, support recruitment and help ensure the programme is designed to be equitable, accessible and effective, based on in-depth knowledge of working with unpaid carers from across the UK.
Alzheimer Scotland are a leading and innovative dementia charity with over 9,000 members, 90,000 dementia friends and support from 1,000 volunteers. The organisation currently has 21 Dementia Resource Centres (DRCs) spread geographically right across Scotland, regularly supporting individuals with a wide variety of services including obtaining information, training and peer support. Their localised efforts, health and social care links and involvement in developing National Dementia Strategies for Scotland make them an ideal partner for this 'iSupport' study across platform development, recruitment and ensuring impact and implementation.
Professor Anne Margriet Pot is strategic advisor Care for Older People at the Health Care Inspectorate, Ministry of Health, the Netherlands. From 2014 till 2018, she was posted in Geneva at the World Health Organisation (WHO), where was responsible for the development of 'iSupport': WHO's extensive online training and support program for caregivers of people with dementia. Anne Margriet Pot is also endowed professor at the Vrije Universiteit Amsterdam, extraordinary professor at Optentia, North West University, Johannesburg, South Africa and honorary professor at the University of Queensland, Australia.

We are working closely with the World Health Organisation who are providing expertise and input regarding 'iSupport'. We are also working closely with the Pan-American Health Organisation who are developing the 'iSupport' online platform for our trial and feasibility study.

21. Protocol amendments

21.1 Current version of the protocol

Version 3 dated 01/11/2022.

21.2 Amendments

Pg/section	Changes to protocol since v2
Pg.1	Protocol version and date updated; New sentence to add "IRAS ID: 311565"; Sponsor Representative name and email changed. Previous representative has left Bangor University.
Pg.2	Co-investigator Paul Brocklehurst removed. He has taken up a new post elsewhere and is unable to continue with the study.
Contents	Minor changes to include addition of new section 17 and subsequent amendments for subsequent section numbers.
10.4	Minor change to change responsibility from Algar-Skaife to Masterson-Algar.
17.	New section to include Definition of end of study.
18.	Amendment from section number 17 to 18.
19.	Amendment from section number 18 to 19; Minor change from "FI" to "RI, FAI"; Minor change from "DP" to "SK"; Minor change to remove PB who has left the study, and amend the health economist to include initials for BA.
20	Amendment from section number 19 to 20.
21	Amendment from section number 20 to 21.
21.1	Minor change to update protocol version and date.
Footer	Protocol version and date updated.

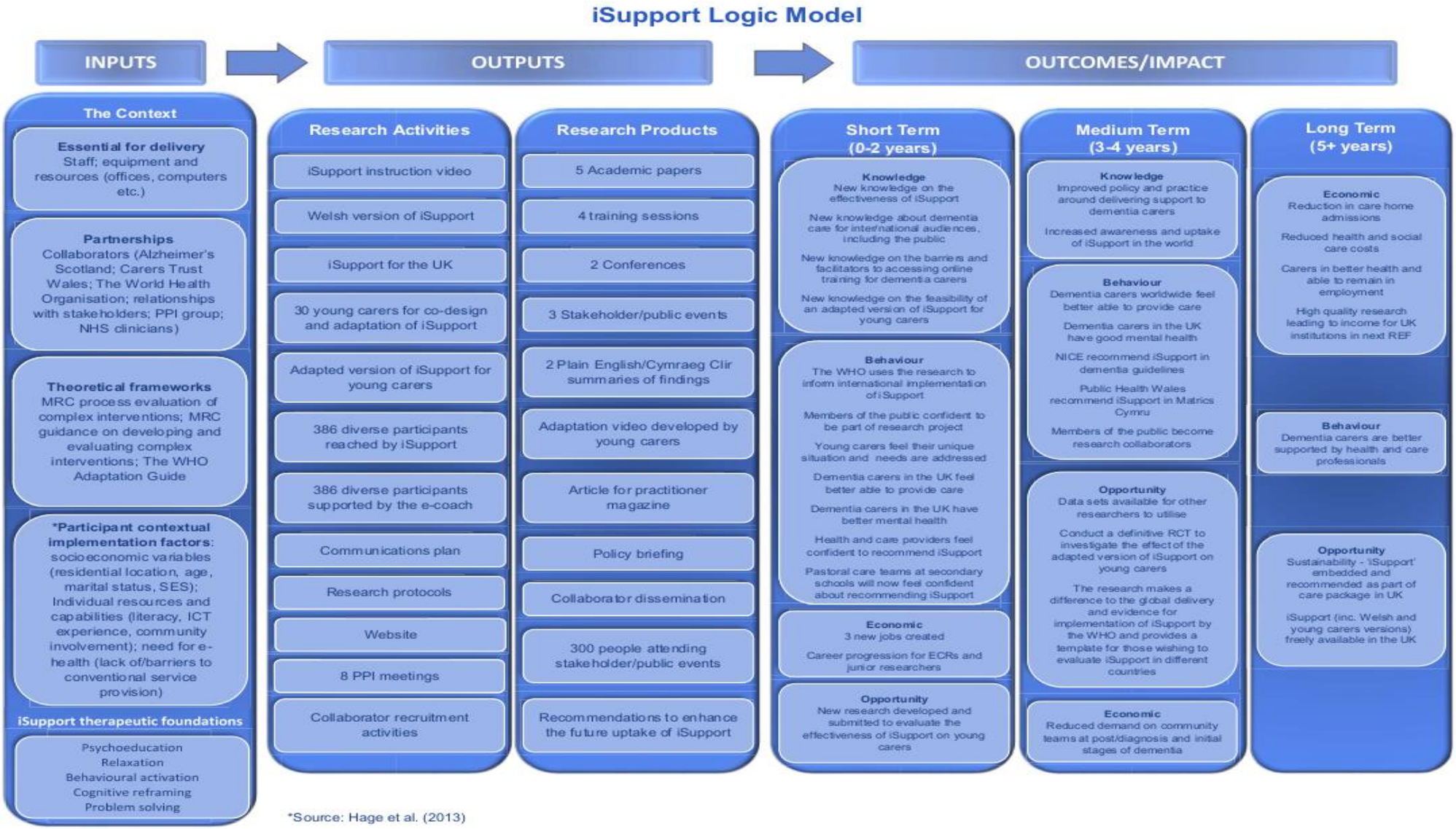
Pg/section	Changes to protocol since v1
Pg.1	Protocol version and date updated;
Pg.2	Co-investigator Kat Algar-Skaife removed. She has taken up a new post elsewhere and is unable to continue with the study. Patricia Masterson-Algar is now leading the process evaluation (changes agreed by the NIHR). Contact email for GH updated.
2.1	Minor change to bullet points order to match section 2.2.
4.3.1	New section to describe research sites.
4.3.2	New section for organogram of research sites and study reporting.
4.5	Minor change to remove "competence" (see section 4.5.4 below).
4.5.1	Minor changes to make clear individual criteria to be considered in the context of the whole study, as recommended by the IDMC and recorded in meeting minutes from 25/05/2021.
4.5.4	Minor change to remove information about the Short Sense of Competence Questionnaire (SSCQ), as it was agreed with NIHR to remove from the case report form (CRF) due to overlap with other measures.

4.7	Minor changes to remove reference to some health economics questions which were removed from the CRF, following initial piloting on the CRF.
4.7.1	Minor changes to remove reference to some health economics questions which were removed from the CRF, following initial piloting.
11.	Minor change to make clear the research ethics committee.
18.	Minor changes to content for PMA, JS, GH, and "FI, JC and DP". Minor changes to remove 2 researchers previously listed who have left the study, and add a sentence to capture health economist post.
19.	Minor change to remove reference to Faaiza Bashir, as she has left the Carers Trust (who are still named collaborators).
20.1	Minor change to update protocol version and date.
22.	References removed for SSCQ, as above for section 4.5.4.
Footer	Protocol version and date updated.

21. Appendices

Appendix 1: 'iSupport' logic model 41

Appendix 1: 'iSupport' logic model



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