Research Protocol (**version 4.0, 26th July 2013**)

DRIE (Dehydration Recognition In our Elders)

Development of a simple tool for diagnosis of water-loss dehydration: a diagnostic accuracy and cohort study.

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Funder: NIHR (Career Development Fellowship, NIHR-CDF-2011-04-025), contact Karen Fernando, Programme Manager, Karen.fernando@nihrtcc.org.uk

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Research sites: the research will be carried out within care homes in Norfolk and London, UK

Samples will be analysed in the pathology laboratory of the Norfolk and Norwich University Hospital, Norwich Research Park, Norwich NR4 7UY, Norfolk, England, UK, contact Sue Kerry (01603 646545).

Ethics Committee: NRES Committee London – East, REC Offices, Room 10, 4th Floor West, Charing Cross Hospital, Fulham Palace Road, London W6 8RF. 020 331 10100. 11/LO/1997, Full approval granted 25th January 2012.Steering Committee:

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DRIE website: the DRIE study website provides further information on the study, including information on the steering committee and participating care homes. See http://driestudy.appspot.com/homes.html.

Study summary

Dehydration in older people is associated with risk of poor health outcomes such as falls, heart disease, confusion, pressure ulcers, poor wound healing, infections, drug toxicity, and poor quality of life. Early identification, prevention and treatment of dehydration in the community would be good for older people and reduce NHS costs. As assessment of blood osmolality (a good measure of hydration) is not commonly available in residential care, a simple tool (a short decision tree of tests) that could be carried out day to day by older people or their carers, that accurately indicates hydration status, is desirable.

This research aims to improve health and wellbeing of older people in the community through:
1. identifying a tool that can be used in residential care to identify early dehydration, so that prevention and treatment strategies can be rapidly mobilised, and
2. clarifying associations between dehydration and health, functional status and quality of life in frail older adults.

We will recruit 200 older people living in residential care (where dehydration is common). At baseline we will assess for water-loss dehydration (through blood osmolality) and measure promising markers of dehydration (such as dry mouth, tongue furrows, cognitive status, body temperature, dry under-arm, urine colour and specific gravity, feeling tired, headachy or thirsty, missing drinks, body temperature, cognition, pulse, orthostatic hypotension, fingernail capillary refill and foot vein filling) as well as collecting health and demographic information. We will use baseline data to assess diagnostic accuracy of each marker, then consider markers collectively to develop a decision tree to diagnose or rule out dehydration, while minimising testing.

We will also collect data on mortality, quality of life and functional status at 1 and 2 years. This will allow us to clarify the predictive value of dehydration in longer term health in older people.

Background

The study purpose is to develop and optimise a tool to diagnose impending or current water-loss dehydration in older people

Justification:
Dehydration in older people is associated with high levels of risk of adverse health outcomes and death (1;2), and contributes to many major causes of death and morbidity, including falls, heart disease, confusion, constipation, renal failure, pressure ulcers, poor wound healing, infections, drug toxicity, and poor quality of life (3-10). John Reid, Secretary of State for Health, stated that high numbers of unplanned hospital admissions in the "at-risk elderly" were for entirely preventable conditions such as dehydration (11). In the US the estimated avoidable cost to the 1999 US healthcare system of older people admitted to hospital with a primary diagnosis of dehydration was $1.1 to $1.4 billion annually, and hospitalisation rates appear to be rising (12) with estimated costs in 2004 at $5.5 billion (13). Early identification, prevention and treatment of dehydration in the community would be good for older people and reduce NHS costs.

Dehydration is a complex condition resulting in a reduction in total body water (6), including water loss dehydration (due to water deficit, which can be hypernatraemic or hyponatraemic in the presence of hyperglycaemia) and salt loss dehydration (due to salt and water deficit, generally hyponatraemic, rarely isotonic). The reference standard for water loss dehydration is debated. While serum osmolality is a strong contender, disadvantages include slow response to dehydration and rehydration (14), but these are outweighed by its advantages. Advantages include that it can be measured at a single assessment (change in weight over a short period signals change in hydration but requires assessment over several days), is associated with health outcomes, and directly measures amounts of effective solute in plasma - as these solutes are impermeable to cell membranes they influence cell volume via their osmotic force on cells. Abnormally raised osmolarity implies dysregulation in multiple organ systems, and cell dehydration as intracellular fluid moves to extracellular space to reduce the osmolarity, shrinking the cells (15). Community dwelling elders with serum osmolality ≥300mOsmol/L had a 40% increased risk of 8 year mortality (RR 1.4, 95% CI 1.0 to 1.9, multivariate adjustment), and greater risk of new disability over 4 years (RR 2.1, 95%CI 1.2 to 3.6, multivariate adjustment) compared to those with normal osmolality (16). Salt loss and isotonic dehydration are also important, but differ from water-loss dehydration, requiring distinct treatment (with isotonic fluids). Hyponatraemia is less common and less predictive of outcome than increased osmolarity in older people (associated with 25% increase in 5-year mortality (2)), so needs to be studied separately (6).

Effective osmolality is a function of sodium, potassium and glucose, and either serum sodium or glucose levels will be raised in water loss dehydration. Current dehydration (serum osmolality >300 mOsmol/kg), which develops following impending dehydration (295-300 mOsmol/kg), can be a medical emergency and 17% of those admitted to hospital with a main diagnosis of dehydration die within 30 days (2). If we can diagnose impending dehydration and prevent current dehydration this may improve life for older people and reduce health costs. Impending dehydration may cause poor health in its own right, so diagnosis of impending dehydration may improve health and quality of life for older people, but this will not be clear until we can diagnose and address impending dehydration. For these reasons this research will focus on water-loss dehydration, with serum osmolality as reference standard

Dehydration prevalence in frail older people varies by setting, level of care required, social deprivation and how hydration status is assessed. 4% of the growing number of older people in the UK live in a care home or long-stay hospital (rising to 21% of those aged 85+) – this is an extremely frail population (17). In Norfolk care homes we found that on a single assessment 30%

of 56 residents living in six care homes were dehydrated (with a furrowed tongue) (18), while a Californian nursing home study found 31% dehydrated at some point over 6 months (19).

Dehydration is more common as we age as our thirst response (20) and total body water (TBW) both reduce (10;21), and medications and increased dependence on carers increase dehydration risk (7). Contributors to low fluid intakes include clinical (dysphagia, functional impairment, dementia, and pain), social (lack of attention to drink preferences, inability of residents to communicate with staff, and lack of social support) and institutional factors (untrained and unsupervised staff). Water-loss dehydration, like falls or anaemia where identified, needs to be investigated to assess its causes, before addressing underlying problems. Where reduced fluid intake or increased losses are indicated, suggested interventions to prevent or reverse dehydration in older adults living in care homes include education and involvement of care staff, use of social times, drinks carts and water jugs, encouraging relatives to drink with residents, monitoring urine colour, and supporting those with swallowing problems (3;7).

To protect the health of care home residents, and prevent emergency hospital admissions, older people themselves and/or care staff must recognise and treat impending water-loss dehydration. Serum osmolality, though the best indicator of water-loss dehydration, is too invasive for day to day monitoring in residential care, and in current dehydration emergency action has to be taken - there is no time to wait for lab results (22). Clinical signs are commonly used to diagnose dehydration, but there is doubt about the diagnostic accuracy of many commonly used signs in older people (though effective in children and younger adults). A systematic review of the diagnostic accuracy of physical signs of hypovolaemia, which included studies published up to late 1997, found that in the few relevant studies there was limited evidence that in older people with vomiting, diarrhoea or reduced fluid intake that dry axilla supported the diagnosis of hypovolaemia, while moist mucous membranes or a tongue without furrows supported lack of hypovolaemia. Capillary refill time and poor skin turgor were not diagnostic in older people (23). An Australian cohort found that orthostatic blood pressure drop, sternal skin turgor, tongue dryness and body mass index were good indicators of early dehydration, but assessed against a reference standard of physician diagnosis (made using the very signs being tested (index tests), so were potentially biased) (24).

We have an accepted protocol for a diagnostic accuracy review to assess clinical and physical signs for diagnosis of dehydration in older people to the Cochrane Renal group and will complete this review in late 2011 (25). As only 1 relevant paper has been fully published (assessing the relationship we are interested in, and providing a 2x2 table needed to run our analyses) we have collected data sets with the required data and re-analysed them to provide the information we need. We have collected 18 full data sets, including data on well over 2000 older people aged 65+. No single sign appears to have good enough sensitivity and specificity to diagnose dehydration alone, but several signs show promising discriminatory ability (positive likelihood ratio >2 or negative likelihood ratio <0.5). These include dry mouth and tongue furrows, cognition, body temperature, urine colour and specific gravity, bio-electrical impedance, feeling tired, underarm sweating, missing drinks between meals, capillary refill and enjoyment of food. Additionally several authors of studies published in the past (where the datasets are no longer accessible) have suggested that foot vein filling and headaches may be good measures to try. These measures from the systematic review, as well as measures from existing tools for diagnosing dehydration in children (26) and measures used by healthcare professions but not formally tested previously will be tested within this primary study.

It is likely that a short decision tree of tests will be needed to accurately diagnose impending or current water-loss dehydration in residential care (27) (a simple tool was recently published but was validated against physician assessment (28)).

Currently available evidence on dehydration in older people is patchy. It is vital for the health and wellbeing of older people, and to reduce unplanned emergency hospital admissions, that we identify impending dehydration in the community and residential care, and learn to prevent current dehydration. Our approach to develop the research base for water-loss dehydration will be to validate a short decision tree of clinical and/or physical signs of impending dehydration for use by older people and/or their carers. Validation will be both essentialist (against the best reference standard of water-loss dehydration, serum osmolality), and consequentialist (assessing the utility of this panel in predicting mortality, functional status and QoL) (29). This will prepare for future randomised trials of screening and intervention to prevent or redress impending water-loss dehydration on important health outcomes in older people.

Primary Aim:

The principal research objective is to identify a tool (a short decision tree of clinical and physical signs) that will identify water-loss dehydration in frail older people.

Secondary aims:

Additional objectives include:

1. Quantify diagnostic accuracy (sensitivity/specificity) of each clinical or physical sign
2. Quantify the incidence of dehydration in older people living in residential care
3. To understand the relationship between hydration status at baseline and mortality, quality of life and functional status 1 and 2 years later.
4. To understand the relationship between sudden weight changes over 1 year (indicating change in fluid status) and mortality, quality of life and functional status at 1 and 2 years.

Study design

This will be a cohort study (researchers will be blind to reference standard results when assessing index tests). The design of this research incorporates understanding gained from the current literature on dehydration (summarised above), advice from members of PPIRes, discussions and debates with research mentors and steering group, results from (and debates during development the protocol for) our current systematic review of diagnostic accuracy of clinical and physical signs of water-loss dehydration in older people (which includes many current researchers in dehydration within the author group (25)), advice from the NIHR interview panel (who will be funding this research) and our ethics committee, discussions with care home managers and staff during the process of recruiting homes interested in participating in this research.

We will carry out primary research to improve identification of dehydration in residential care, assessing the diagnostic accuracy of clinical or physical signs that appeared promising in the diagnostic systematic review (25). Serum osmolality will be the reference standard for water-loss dehydration (295-300mOsmol/kg impending, >300mOsmol/kg current dehydration). As serum osmolality is not commonly available in residential care, a simple decision tree of tests to be carried out day to day by older people or their carers would be desirable.

Sample size: we will recruit 200 participants. Using the Kappa statistic as a measure of diagnostic accuracy and assuming a dehydration prevalence (current or pending categorised together) of approximately 40%, a sample size of 180 would ensure a standard error of no more than 0.05 for Kappa values in excess of 0.75. 200 participants recruited would allow for 10% to

terminate assessment before all signs are assessed or to provide unreadable blood samples. For values of at least 0.6, the standard error would be no more than 0.06. Thus, this sample size should provide an estimate of diagnostic accuracy with a precision to allow an assessment of the practical utility of the identified signs. Our previous experience of approaching 6 care homes with 213 residents recruited 50 participants to provide blood samples. Our potential set of participants for this study will be smaller as we will exclude those with diagnosed heart failure or renal failure, suggesting that approaching ~50 care homes will provide enough participants.

Inclusion criteria: People aged 65+ living in residential care (care homes, nursing homes and mixed homes) in Norfolk (or on the Norfolk lists, this includes a few homes situated near the border in Suffolk). Inclusion of care homes will not be based on the star rating system (formerly conducted by the Care Quality Commission or CQC) as the rating system ceased in mid 2010.

We will include participants regardless of their capacity to provide informed consent, although the study is designed to protect all participants and include them only if they find the research acceptable. Inclusion of those with dementia was strongly encouraged by the NIHR interview panel that awarded the funding for this research, as those with dementia are at greatly increased risk of dehydration, so it is vital that the tool developed is applicable to those with dementia as well as those without. This decision has been strongly supported by care home managers and staff in my recent discussions with them over their involvement in this study. We will only include adults who can provide their own informed and signed consent OR whose consultee has provided signed consent that they believe that the resident would have consented if they were able to make the decision themselves.

We do not plan to stratify inclusion by age group (as most of those living in residential care will be either physically or mentally frail, all will be at some increased risk of dehydration), or by gender (although the samples are likely to be weighted towards women, as more care home residents are women). While we are aiming for a representative sample of care home residents, we will not exclude any interested participants on this basis.

Exclusion criteria: we will exclude those who the care home manager is aware has been diagnosed with renal failure or heart failure, as fluid physiology changes with these conditions (and fluid retention is more likely). Those in receipt of palliative care, or with illnesses that suggest they are unlikely to survive for at least 3 months will not be recruited. Additionally we will not seek to recruit people who are unable to provide their own consent, and are known to be frightened of, or upset by, needles or blood tests as we will assume that the process of the interview and blood sample will be upsetting to them.

Recruitment: the chief investigator (CI) contacts care home managers in Norfolk (NOT residents or relatives) to discuss the participation of new care homes in the study. Contact has been made through an article in the Eastern Daily Press on the study, another in Norfolk Care News, via a radio interview about the study, through recommendation from one care home to another or from care home management to several of their homes, and through letters sent to 100 Norfolk care homes, followed by phone calls to arrange a visit by the CI and research assistant (RA). Now that ethical approval has been gained the participating care homes have been sent information (as leaflets and small posters) that they can use to distribute information about the study well ahead of time to staff, residents and relatives. We have been phoning care homes to agree when we will visit, recruit and carry out the research, and the process of care home recruitment will continue again in the summer as we begin to know how many care homes need to be recruited. Additionally, as we work in care homes we will ask that they provide information on the research to new residents, so that we may potentially include some further residents in the study at 6 or 12 months after first visiting.

Older people living in care homes are potentially liable to undue persuasion to participate, but this will be carefully avoided regardless of capacity to consent. We will offer time and opportunity for potential participants to discuss their participation (or lack of it) with ourselves, their relatives, care home staff and management, ensuring that they understand that participation is totally voluntary and that no loss of care or support will result from a decision not to participate. They also need to know that if they participate there will be a blood test and that this may cause some pain and has the potential to cause some bruising or bleeding (though this will be minimised).

We will be including some participants who are able to give their own informed consent, and some who are unable to consent on their own behalf. The principles behind this process (described below) are that if a resident can give their own consent (or decline consent) then this will be accepted regardless of the opinions of relatives. However, if a resident is unable to consent on their own behalf we will ask the responsible consultee to consider providing consent on behalf of the resident on the basis that they feel the study is useful and appropriate, and that they believe that the resident would give their own consent to participation if they were able to do so. Any participant may withdraw consent, without providing reasons, at any point – verbally or through their behaviour.

Recruitment of participants (residents) will occur in several stages. For each home:

Visit 1. We will visit the home, having sent invitations to staff, residents and relatives (individually or via a newsletter), to discuss the study with staff (we may need several meetings to include different shifts), relatives (we will offer a time during the day and also an evening meeting time) and residents (as appropriate within the home, we may speak to small groups of residents, or residents individually, after introduction by home staff). We will not recruit on this day, but encourage interested residents to discuss the study with their friends, relatives and staff.

On this day we will also ask the home manager to complete a list of residents (not named, but coded by room number) with their age, gender, months living at the home, weight, height and MUST score. For each resident we will also ask them to indicate any reasons for not including the resident – including that they are aged <65, have diagnosed heart failure or renal failure or have a short life expectancy. For residents whom the home believes fulfil our inclusion criteria we aks that they provide the residents name so that we can ask the resident if they would like to participate in DRIE. This list will be collected on the day of visit 2. It provides the study with anonymous data on the full care home population (to allow assessment of how typical our participants are) without collecting data that would impinge on the rights of those who decline to participate or who are not eligible.

Visit 2 (approximately 1 week after visit 1). Following an introduction by care home staff, we will ask the residents on the list provided by the manager individually if they would be interested in participating in the study (having repeated the basic information on the study as many may not remember clearly). We will briefly describe the study using a participant information leaflet with large print and pictures to help depict it clearly. The potential participant will retain the leaflet.

1. If the participant seems interested in participating we will ask them some questions. Being able to answer suggests that they have capacity to give their own consent as they are able to retain information long enough to make an effective decision, are capable of making this decision at this time, and are able to make a free choice. As part of this we will ask the resident to tell us

a. what the study is trying to do ("can you tell us what the study is about?" - expected answer is anything to do with drinking or hydration, which indicates that they understand the purpose of the research),
b. what they will be asked to do with us ("if you take part in the study, what will happen to you?" - expected answer is to have a blood test, to answer some questions and have some simple physical tests, suggesting that they understand the nature of the research, and the potential burden and risks),
c. who will know the results of the blood and urine tests, blood pressure, pulse and body temperature ("If you take part in the study, who will we tell the results of the blood & urine & BP tests to?" - expected answer is that care home manager and their GP will be told the results, indicating understanding of the nature of the research and how their information will be used, as well as understanding a potential benefit of the research),
d. Whether they mind if we ask the care home manager about their health, wellbeing and medications now, and how they are in one and two year's time ("if you take part in this study may we ask [the care home manager] about your health, wellbeing and medications now, and in one and two years?" - expected answer would be yes, indicating consent to use their current health information now and also their live status as outcome data even though they will not be able to give consent at that time if they have died), and
e. Whether they know what will happen if they don't participate ("if you decide not to take part in this study, will it cause any problems?" - expected answer that there would be no consequences, their care and support would not alter, showing that they understand that participation is entirely voluntary).

2. If residents can tell us these crucial bits of information about the study we will accept that they have capacity to provide their own informed consent. If they also choose to be involved we will ask them to sign the consent form, including asking whether they would be happy to be weighed over the following year (this is not essential for participation). This form will also be signed by the researcher.
3. If the resident is not able to answer the above questions but has not expressed a desire not to be involved, then we will ask the care home manager if they believe the resident to find blood tests frightening or upsetting. If so, we will not try to encourage participation any further. If not, we will send the responsible relatives (consultee) a letter asking for consent for the resident to participate. Consent will be based on the consultee feeling that the research is worthwhile, and also that they believe that the resident would have wanted to participate in the study if they were still able to make the decision for themselves.

Visit 3 (approximately 2 weeks after visit 2, may take place over several days). At this meeting we will sit with each resident for whom we have consent (their own or via a relative or consultee). We will briefly describe the study again (with pictures), check that they do not object and then move into the research interview. If at any point the resident decides not to participate, or appears uncomfortable or upset, or moves away then we will assume that consent has been withdrawn, whether or not the resident is able to express this verbally. For those residents for whom consent has been provided by a relative we will try again once more at a different time of day (or a different day) when their mood may have altered, but again, only proceed if the resident appears happy to work with us.

Some residents may want their consultee or a member of care home staff with them during the interview. In this case we will aim still to gather answers to all our questions from the resident (participant) rather than the consultee or member of staff. If this proves impossible questions that are answered by anyone other than the resident will be labelled as being answered by their surrogate (with a star).

As the blood test is likely to be the point at which residents decide to withdraw, and also which may lead residents to worry, this will occur 5-10 minutes into the research interview (once formalities have been completed and the resident relaxed in a sitting position) – this will waste less of the residents time if they decide not to have the blood test, and mean that they don't worry about the looming blood test through the remainder of the interview. It also allows us time to keep pressure on the wound and ensure bleeding has ceased, while working through some of the interview questions and tests. If the first attempt at venepuncture fails then we will relax the participant, progress with the interview, then allow one more attempt at venepuncture. If this second attempt succeeds (in that enough blood is collected for assessment of serum osmolality) then data collection will progress as planned, but if it fails the interview will be abandoned (as the remaining data are not interpretable in the absence of serum osmolality readings). Blood for assessment of serum osmolality will always be collected first (before other blood samples) so that if only one reading can be carried out on the blood samples it will be serum osmolality. If 2 attempts at venepuncture fail to collect enough blood to assess serum osmolality we will collect a small finger-prick blood sample (which will only be used to assess serum osmolality).

Visit 4 (approximately 52 weeks after visit 3). At this visit the live status of all participants for whom data was collected in visit 3 will be ascertained from the care home manager or deputy (this outcome data will be used for all participants). Additionally we will ask the manager questions to allow us to assess functional status for all those who remain alive, whether they have experienced an episode of dehydration, the participants use of healthcare in the preceding year, and the positive and negative effects of the DRIE study on the care home over the past year. Those who remain within the care home will be approached, the study re-described and we will ask if the resident would be happy to participate in the follow up meeting. If so, this will take place immediately, participants asked whether they feel that they drink enough to remain healthy, and their quality of life assessed.

At 2 years (approximately 104 weeks after visit 3) the final data collection will be via phone or personal meeting with the care manager (no participant involvement will be required). The participants live status and functional status (Barthel Index) will recorded.

Pilot. The process of visits 1 to 3, and data collection will be piloted at a single care home (Ellacombe, in Norwich during March 2012) before rolling out to further homes, so that if modifications are necessary these can be decided and incorporated in all future data collections.

Methodology

In detail, we will collect only data needed to carry out the research aims. All data collection will be by Lee Hooper (CI) or Diane Bunn (RA) or both.

Resident identification and to allow blood test results to be provided to the care home manager and GP (retained in a separate table within the access database so that the dataset can be easily anonymised at any point by removing this table):

- Resident number
- Resident full name
- Likes to be addressed as
- Resident date of birth
- Care home name
- GP name and address
- NHS number

Within the main electronic dataset we will collect:

- Resident number
- Resident age
- Care home
- Gender

Reference standard data: serum osmolality, serum sodium, serum potassium, serum glucose (random) and serum urea, serum creatinine, liver function tests, haematocrit.

- Blood samples will be identified by study number, date and study name, and analysed at the Norfolk and Norwich University Trust Pathology laboratory
- Results will be returned to the CI
- Serum osmolality information will be interpreted and provided to the care home manager (or deputy) and the resident's general practitioner
- Blood samples will be destroyed after analysis within the laboratory

Index tests (to use as described in original papers in systematic review):
The flow of the tests and questions will be roughly as follows (but we will adapt this to improve the way that the testing works as necessary). Before we interview and test a participant we will make sure that they have had a drink in the last half hour (making them an appropriate drink if not) and we will help them to the toilet (to empty their bladder) on the way to the interview:

1. Start by moving to an appropriate location, ideally the resident's own bedroom, and ensuring that if they would like a care worker or family member with them that this has been organised (and that if they do not want anyone with them this is also ensured).
2. On the way to the participant's room measure height and weight (in care homes chair scales)
   - Resident is settled in a comfortable seat. During this time to have a general friendly chat as appropriate with the participant. Once settled to ask short questions about how the resident is currently feeling (tired, thirsty, out of sorts, has a headache e.g. do you have a headache at the moment?)
   - EuroQoL-5D-3L assessment of quality of life (using EuroQol 5D, simple and fast, permission granted for us to use this free of charge, see http://www.euroqol.org/home.html)
3. Take blood samples (once resident has been sitting for 5- 10 minutes to ensure standardisation) – as above. Label and store all samples, dispose of all sharps as per SOP.
4. Assessment of resident's mouth (timed to ensure the resident has not had a drink for 30 minutes at least)
   - Assess mouth for dry or furrowed tongue, dry inside cheek, dry or cracked lips
   - Ask short questions about favourite drinks, whether the participant ever misses drinks at any meal, ever misses drinks between meals, are they looking forward to their next meal, do they ever feel thirsty?
   - Measure body temperature (using an ear device)
   - Assess foot vein filling and finger capillary refill (base of middle finger, dominant side) times
   - Check for dry skin on calf, cheeks, inner arm, and check for presence of tears in eyes.
5. Once participant has been sitting comfortably for at 5-10 minutes check for orthostatic hypotension:
   - Assess pulse rate and blood pressure while still lying down.
   - Help resident to stand in front of stable chair (using usual aids, help support them in case of dizziness), then measure BP after standing for 30 seconds and 3 minutes. After the 30 second measure ask if they feel dizzy (help them to a sitting position of any problems)
   - While standing assess whether breathing is normal, deep or deep and rapid
6. After the OH assessment :
   - Visual (Snellen) test
   - Mini-mental state exam (MMSE (31;32))

- Brief questions on sleep and continence (do you sleep well? How many hours do you sleep each night? Do you go to the toilet in the night? Do you feel tired when you get up in the morning? Do you ever worry you won't be able to reach the toilet to pass urine in time? Ever drink less in the evening so won't need to get up in the night?
- Brief questions on exercise (have you been outside in the past week? do you ever walk around with no clear purpose? Note use of walking aids within care home)
- Hospital Anxiety and Depression Scale (HADS) questionnaire (questions asked verbally)
- Short series of questions (in food frequency format) on assessment of intake of water, hot drinks, cold drinks and alcoholic drinks (short FFQ based on Nurses' Health Study (30))
- Establish ethnicity

7. Help participant to toilet (if help is needed), ask for a urine sample (collected in disposable "hat" in toilet). Help participant back to their preferred location in the home, make them comfortable with a drink and snack (where appropriate). Return to test urine:
   - Urine colour (against standard chart) and volume
   - Urine specific gravity (using dipstix), other dipstix measures
   - Urine specific gravity using refractometer
   - Urine volume (mls)
   - Weight of continence pad (used and dry)
8. Observation of resident during day (appropriate times for this will be planned, plus we will record any ad hoc observations following informed consent)
   - Length of wait when ask for help to go to toilet (if help needed)
   - Social interaction around drinking between meals (with carer, with visitor, with other resident(s), none)
   - Response to resident when offered a drink (express preference or not, drink immediately/drink over time/not tasted, any of drink left after 30 minutes)

To ask of care home manager for each participating resident:

- History of recent (over past week) vomiting, diarrhoea, cold, urinary tract infection (UTI) and/or fever
- History of recent (over past 2 months) hospital admissions and/or healthcare professional contact
- Current and chronic illness (including Sjogren's syndrome which results in dry eyes and mouth, diabetes which may alter serum osmolality, constipation, delirium, dementia and depression which can increase the risk of dehydration, and swollen ankles to indicate oedema)
- Current medications (and doses)
- Weight history
- Functional status assessment (Barthel Index, well validated, covers crucial areas of functional status for care homes, fast (33;34))
- Recent changes in functional or mental status
- Risk factors for poor food and/or fluid intake or increased fluid requirements
- Measure of social deprivation (based on previous home address (postcode) and occupation of self and spouse)
- Does the resident seem well in themselves today, or out of sorts?
- Establish whether the resident has HIV or infectious hepatitis

Care home data (also to ask of care home manager, but once per home at baseline):

- Care home manager and contact details
- Total number of residents currently, number with dementia, and type of care offered (residential/ nursing/ dementia etc)
- Number of staff in several categories
- Availability of drinks to participants

- Measures the home takes to prevent dehydration in residents
- Standard drinks regime for home
- Presence or not of en-suite bathrooms
- Uptake of recent free training offered on hydration (PHAN)
- Standardising of weight scales
- Temperature of sitting and dining areas of the home, outside temperature (this last will be directly measured by researchers, not asked of manager).

Sequential weight assessment:
If the resident or their relative gives consent for collection of weight data, and the care home is able to, we will ask the home to measure the resident's weight weekly over the year following the initial interview. This will be used to pinpoint cases of dehydration during the year between baseline assessment and the final interview at 1 year (to be used within the cohort analysis).

Phone call at 1 month:
Phone call to home manager to ask whether any action has been taken by the care home and/or GP (or any other health professional) around hydration for those participants with impending or current dehydration.

1 year interview:
At 1 year the care home manager will be asked to report on live status of all baseline participants. For those still alive and living in the care home we will ask for information to complete the Barthel index (from the care manager) and ask residents for permission to re-interview them. If this is acceptable we will re-assess quality of life and ask whether they feel that they drink enough to remain healthy. As the EuroQoL is very brief and non-invasive we will not formally re-assess capacity or formalise consent. For all participants (present and live or not) we will ask the manager whether they have experienced an episode of dehydration, the participants use of healthcare in the preceding year, and we will ask the manager more general questions about the positive and negative effects of the DRIE study on the care home over the past year. Those who remain within the care home will be approached, the study re-described and we will ask if the resident would be happy to participate in the follow up meeting. If so, this will take place immediately, participants, and their quality of life assessed.

2 year data collection:
At 2 years the researchers will contact the care manager to ask about live status of the resident and their functional status. The resident themselves will not be re-interviewed. Consent will be gained for this at baseline.

Data analysis: Data will be entered into an access database to be stored, cleaned and analysed. Assessment of water-loss dehydration will be on the basis of serum osmolality, a binary variable (i.e. hydrated or dehydrated, cut-off at 295mOsm/kg). Initial univariate analyses will be conducted to assess the diagnostic value of each considered factor. Those showing the best diagnostic accuracy will be considered collectively. 'Classification and Regression Trees' (CART (35)) will be used to develop a decision tree to diagnose impending and current water loss dehydration, while minimising the testing load required by residents and staff. The use of CART allows a greater flexibility over, say, logistic regression in which all predictor variables need to be assessed. Using a CART approach, it should be possible to use predictor variables in a more sequential fashion, thus avoiding the necessity of assessing every sign for every individual before a diagnosis can be made. Papers written will conform with STARD reporting standards for diagnostic studies (36).

The cohort data gathered will be used to assess the consequentialist effects of dehydration (assessed by the developed diagnostic tool, and by measured serum osmolality) assessing the relationship between impending or current water-loss dehydration and mortality, change in functional status (Barthel Index) and QoL from baseline to 1 year in older care home residents. To maintain the power of the study we will ascertain mortality and functional status at 1 year (from care staff) of all participants who give informed consent and provide baseline data, even if they withdraw or are unable to provide informed consent for the final assessment. To assess potential confounding multivariate models will be adjusted for baseline age, gender, functional status, BMI, diabetes and other chronic illness, cognitive impairment, creatinine and number of medications. Cox proportional hazards models will be presented using hazard ratios (and 95% CIs). Secondary analyses will be carried out using the 2 year data, in the same way.

Position of this study in the 3-year funded research plan

This study is part (sections 2 and 3 below) of a 3-year NIHR funded research (as a Career Development Fellowship, also including considerable training) which aims to improve the health and wellbeing of older people living in the community through:

1. Systematic review (and summary) of research on prevention and reversal of impending water-loss dehydration, making best evidence accessible to UK health and social care workers,
2. Primary research to identify a simple decision tree of dehydration signs in residential care so that prevention and treatment strategies can be rapidly mobilised,
3. Clarifying associations between dehydration and health, functional status and quality of life in frail older adults,
4. Development and dissemination of an evidence-based statement of appropriate action to be taken when dehydration is identified in older people living in care homes to improve hydration in older people, and
5. A pilot study of the developed dehydration tool (decision tree of clinical signs) to assess its practicality, invasiveness, acceptability, and diagnostic accuracy in a different context,
6. The 3 years will be informed by an expert group of older people living in residential care and care staff, and will result in high quality publications as well as development of expertise, research capacity, collaboration networks and dissemination strategies to ensure future research & health improvements for frail older people.
7. The RA will also plan, develop and carry out a small piece of independent research as part of their PhD work.

	2012				2013				2014			
	Jan-Mar	Apr-Jun	Jul-Sept	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sept	Oct-Dec	Jan-Mar	Apr-Jun	Jul-Sept	Oct-Dec
Expert group meetings, 6												
Systematic reviews (SR), 1												
SR write up & dissem, 1												
Ethics for primary studies	2,3			7	7	5	5					
Cohort recruitment & data collection, 2												
Cohort follow up, 1&2 yrs, 3					1yr	1yr	1yr	1yr	1,2y	2y	2y	2y
Primary analysis-decision tree, 2												
Consensus statement, 4												
Cohort secondary analysis, write up & dissemination, 3												
Pilot of dehydration tool, 5												
RA's PhD project work, 7												
Capacity & network dvpt, 6												

Safety considerations

The risks of participation in the research to residents centre on the blood sample as other tests are simple and non-invasive. The risk from the blood sample includes pain, bruising, infection and excessive bleeding. These risks will be explained to the residents, and the risks minimised by using correct technique (including washing hands, using an alcohol swab), supporting the arm used, using a tourniquet correctly, collecting all materials before the venepuncture is begun, covering the puncture site and applying pressure for 3 minutes after needle withdrawal, check for haematoma and apply an adhesive bandage. Samples will be pre-labelled and transported within a labelled biohazard transport bag, needles disposed of in a sharps box and all other materials discarded appropriately. (For training in phlebotomy see quality assurance section).

There is greater risk of excessive bleeding for those residents on warfarin treatment, so any residents on warfarin will be identified before their interview, and pressure maintained on the puncture for longer, with especial care to ensure bleeding has ceased before the end of the interview. Samples from any residents with HIV or infectious hepatitis will be labelled "Risk of infection".

Balance may be an issue for some residents, so we will collect urine specimens by asking the resident or their carer to place a sterile "hat" within the toilet, rather than needing to hold a container while passing urine. When we ask residents to stand to assess postural changes in blood pressure (orthostatic hypotension) we will encourage them to use any equipment that they would usually use to help with standing and walking, and will also stand with them in physical contact, and provide any necessary support for the 3 minutes of standing. They will stand in front of a solid chair, and so if any resident becomes dizzy or needs to sit down they will be immediately helped back into a safe sitting position.

Additional burdens to participants include the time taken for the interview and anxiety before the blood sample or other tests. In order to ensure that the resident is not anxious we will aim to be friendly and speak quietly with the resident (not between researchers or with care staff) about the resident's family or history or previous job or where they lived before coming to the care home, to help distract them. If the resident is too anxious we will suggest that we discontinue the interview without taking blood. We will try to make the process of the interview interesting and enjoyable, but will allow residents to leave and discontinue if or when they want to.

Benefits to residents include a small token of gratitude (a £10 voucher OR an equivalent value box of chocolates OR attractive bath products OR another token felt appropriate by the care home) for all residents who complete the interview (with a blood test and all relevant clinical and physical tests OR where we try but are unable to take blood from the resident).

The results of all blood and urine tests, blood pressure, heart rate and body temperature, including the blood test on serum osmolality (giving a definitive assessment of whether the resident is hydrated, or has impending or current dehydration) will be provided to the care home manager and the residents GP, helping to optimise their care. This will be the first planned contact of the study with the participant's GP, we will not be pre-notifying GPs of participation in the study. Care home managers and staff will be encouraged to attend Puree, Hydration and Nutrition (PHAN) training in reducing the risks of dehydration and malnutrition, and provided with materials to help them manage any residents that are dehydrated. We hope that residents will also enjoy their time with the researchers.

Where the pathology laboratory is concerned about any of the blood test results they phone through results to the consultant who requested the blood test. When this occurs (the lab has Lee's and Diane's mobile numbers to facilitate this, as we will have requested the tests) we will

phone on the urgent results to both the resident's GP and their care home within 24 hours (much sooner where feasible), following this with the usual letter including all the relevant results.

If the researchers come across any important information such as suspicion of elder abuse such information will be reported to the care home manager, and also to Norfolk Adult Social Services (or the local Adult Social Services team for care homes outside Norfolk).

Quality assurance

Delivery of all the tests will be practiced and standardised by Lee Hooper (CI) and Diane Bunn (RA) so that they flow well, some can be carried out concurrently where this is safe and effective use of time, and they are reproducible. They will carry the tests out on each other using the standard operating procedures for each, based on the suggested methods within our source material for each (referenced where available above). These will be learnt by the 2 researchers practicing on each other and referring frequently back to the standard operating procedures. Once the procedure is clear they will check reproducibility of assessment using kappa statistics on friends and family members. Once the tests are reproducible on adults we will check reproducibility and acceptability of the tests in a small group of older experts (aiming for a kappa of >0.7 for every test) before carrying out any of the tests within the study (to ensure all data are high quality and useful, and we do not waste any participant data).

Lee Hooper and the research assistant will both be trained in phlebotomy. Diane Bunn is a registered nurse and has been taking blood samples for more than 20 years in clinical and research contexts. Lee Hooper has not taken blood samples before. She will undergo training in phlebotomy. The Norfolk and Norwich hospital have a standard 12-hour training package that they run, using the equipment we will be using in care homes, but Lee will gain additional supervised on-ward experience with older patients, and her trainers will test her to ensure that she is appropriately skilled to take blood samples in care homes, with the provision of further sessions if they are needed. This training will be supervised and assessed by Gillian Blythe, Phlebotomy Manager at the Norfolk and Norwich University Hospital. Lee will also use Diane's experience to ensure her own skills are of a high quality. Diane will undergo a "refresher" training with Gillian Blythe to ensure she is using appropriate and up to date local methods.

The process of recruitment, assessment of capacity, and data collection will be piloted at a single care home before rolling out to further homes, so that if modifications are necessary these can be decided and incorporated in all future data collections.

Dissemination of results

We will develop and disseminate an evidence-based consensus statement of appropriate action to be taken when dehydration is identified in older people living in care homes. Lee will hold a development and dissemination workshop, including 12-18 invited participants (2-3 of each of the following: older people and staff from the expert group, care home managers, primary care staff, dietitians, care home researchers and gerontologists). At the workshop we will present data on the optimal tool(s) to assess dehydration in older people living in care homes (data from the systematic reviews and cohort analyses) and work to develop a consensus statement on assessment of dehydration in care homes, and a dissemination plan.

Dissemination is likely to include publication in at least one high quality scientific journal, and writing up the research and guidelines to be accessible to older people, care home staff and members of the public (to consider open access journals, websites, paper and DVD dissemination). Following the workshop we will put the dissemination plan into practice, using our developed collaborations and potential conference presentations. We will present data at the

British Society of Gerontology conference, Nutrition Society Summer meeting, an INVOLVE conference and the American Dietetic Association Conference.

In order to facilitate information within the study participants and care homes we will produce a newsletter towards the end of year 1 (before embarking on follow up interviews) and towards the end of years 2 and 3. This will be distributed in paper copy (in large print and accessible language format) to all the care homes involved in the research and to all individual participants, to keep them up to date with the progress of the research. We will also set up and maintain a study website that will provide information to those who wish to find out more about the study (it will allow access to participant information sheets, researcher and sponsor contact details, the newsletters and summarise and signpost presentations and publications.

Problems anticipated

The recruitment procedure will be time consuming and we may be in danger of low levels of recruitment, however, the care home managers contacted to date have been overwhelmingly positive about their homes participating in this research, and so including as many homes as we need does not appear to be a problem. It will be difficult to tell how enthusiastic residents will be until we begin recruiting. We are lucky in that we have from early February 2012 (or once ethical approval is granted) to the end of March 2013 to complete recruitment, but aim to complete recruitment earlier than this. The slightly complex procedures are necessary to ensure that residents have time and opportunity to discuss their participation with care staff and friends and relatives, which is very important in ensuring that consent is truly informed.

Procedures for recruiting those with dementia who are not competent to provide their own consent are slightly longwinded but again are important to ensure that only those for whom the study is appropriate become participants. The issue of defining capacity to consent has been solved in a practical manner, by devising a core set of information that a participant needs to be conscious of before they are understood to retain capacity to consent. Those able to provide their own consent will do so, the consultees of those who cannot will be asked whether the resident would have chosen to participate if they were still able to make the decision.

Project management

Day to day management will be by the CI, Lee Hooper, with the aid of a detailed Gantt chart and protocol (progress will be formally discussed between Lee and Diane (RA) every fortnight with reference to the Gantt chart, which reflects the protocol).

The steering committee will meet every 6 months and will require an overview of progress and will provide an opportunity to discuss and solve problems. The steering committee will consist of the fellowship mentors, professors Lee Shepstone, John Potter and Paul Hunter, an additional PhD supervisor for Diane Bunn (once she is registered for a PhD), Vicky Cowap (Quality Assurance manager at NorseCare, the group that now run care homes formerly owned and run by Norfolk County Council), Hilary MacDonald and/or Linda Gill of Age UK Norfolk, and Joyce Groves, an elderly member of PPIRes (Patient and Public Involvement in Research). Sue Steel, contracts manger, will also be invited to belong to the steering committee as the representative of the sponsor. The mentors will also be available between meetings for support on specific practical, management or academic issues.

Lee Hooper (CI) will be the first port of call for queries about the study, but if any participants or care homes have worries about the research or its conduct they will be encouraged to contact Sue Steel to discuss them. Lee Hooper will have day-to-day control of the budgets and will review them monthly.

The career development fellowship (funding this research) has funding for training associated with it, and we will use this budget both to build skills in research in the CI and research assistant, but also to ensure that any shortfalls in any aspect of practical training are made good. Proposed training currently includes phlebotomy skills as well as training in research leadership and management; a range of practical, methodological and statistical skills in diagnostic accuracy and cohort planning, recruitment and analysis; systematic review skill development; training in randomised controlled trial methodology (for later studies); expertise in dehydration; working with older people; specific research skills; and Research assistant training.

Ethics

Mental capacity issues

The 5 core principles of the Mental Capacity Act (37) are retained within this research proposal in that:

1. Each resident will be assumed to have capacity to make their own decision about whether to participate in the research unless we establish that they lack capacity
2. We will support each resident to make their own decision by explaining the research to them in simple terms, backing this up with clear pictures (and written material with large text), and asking short simple questions to enable the resident to demonstrate their capacity.
3. Any person who declines or agrees to participate and who has capacity to make that decision will have their decision honoured.
4. Participation of a resident in the research, when decided by a consultee, will be based on the known preferences of the resident for participation in this sort of research when they still had capacity to decide. There are potential benefits of participation, for those who are not unduly upset by having blood tests, in the added information to the care home manager and GP on their blood test results, including their hydration status. Thus the decision can be seen to be made in the best interests of the resident.
5. If we could appropriately assess dehydration status in a way that did not involve a blood test we would use that way, but there is no other good reference standard (see introductory discussions).

Additional to these principles, there are specific rules for research including those lacking capacity (38). We will not approach residents or relatives until ethical approval for the research has been attained. Approval will be accepted from the residents consultee only if they believe that that the resident would have wanted to participate in the research if they still had capacity. If at any time a resident is unhappy with participation in the research, expressing this verbally or physically (for example, by leaving or seeming frightened or worried, or telling us to stop) then we will assume that consent has been withdrawn and the research stopped. As those with dementia can have mood swings, for residents without capacity we will try once again to carry out the research (at a different time, with a gap of at least 2 hours, when the resident appears alert but calm). However, if the resident expresses disinterest or unhappiness with the research at the second attempt, the research will cease and we will not try again, so consent will be assumed permanently withdrawn. This process will be recorded.

Confidentiality

All data collected within this study will be linked to a specific resident. As each resident is recruited we will randomly allocate them a unique 4-digit number. The consent form, and a single isolated table within the access database will link the number with the resident's name, date of birth, GP name and address and care home. The main access database tables will include only the number, not the resident's name, so that once the linking table is removed the electronic

records on their own will not be traceable back to individual residents. However, each test or piece of information will still link with the individual's serum osmolality within the data set (as this is needed to develop the tool).

The only raw data that will be available to anyone other than the CI and the research assistant will be the result of the blood tests, which will be provided, with the resident's name and date of birth, to the care home manager and the resident's GP only. The researcher and the research assistant will both understand that resident data is confidential, and will not be disclosed to anyone except in these circumstances.

All paper data will be stored in locked filing cabinets, within secure offices (restricted access to Norwich Medical School staff only). The electronic data will be password protected according to UEA/ GCP data protection policies.

One potential issue is that those who are confused may wish to have a familiar face with them during the interview, either a member of staff or a family member, and family members may wish to be present. We will aim to include staff or a family member in the interview where this is desired by the resident, but will express the need for confidentiality where a resident is not keen for another person to be present.

Conflict of interest

There is some risk that our reporting cases of dehydration to care home managers will weaken the relationship between baseline hydration status and health outcome. However it would be unethical to not report this information in a timely fashion to both the care home and the GP, as it may facilitate the resident's improved health.

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