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Rapid evidence review: pathways focused on the dying phase in end of life care and their key components

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RAPID EVIDENCE REVIEW:

PATHWAYS FOCUSED ON THE DYING PHASE IN END OF LIFE CARE AND THEIR KEY COMPONENTS

INDEX

Introduction	page 2
In brief: Key messages	page 4
In detail: background, evidence and key messages:	
• Impacts of care pathways	page 10
• Impacts of pathways for the dying phase	page 12
• Diagnosing imminent death	page 16
• Communication	page 18
• Clinically-assisted nutrition & hydration	page 21
• Sedation	page 24
Research in progress	page 28
Research implications	page 29
References	page 31

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WHAT IS THE EVIDENCE ABOUT THE IMPACTS OF PATHWAYS FOCUSED ON THE DYING PHASE IN END OF LIFE CARE, AND THEIR KEY COMPONENTS?

INTRODUCTION

This report presents a rapid review of published peer reviewed research about end of life care pathways focused on the dying phase. In particular it examines evidence in relation to use of such pathways in hospitals. Our intention is to provide clear information for stakeholders charged with considering whether any change in current policy and practice is required.

The review questions were developed through consultation with the National End of Life Care Programme and its clinical networks.

REVIEW QUESTIONS

What is known about the following:

1. The impacts of integrated care pathways?
2. The impacts of pathways for the management of the dying phase in end of life care?
3. The practice and effects of:
 - a. Predicting imminent dying in people nearing the end of life?
 - b. Communication amongst family members, patients, and staff in the last few days and hours of life?
 - c. Clinically-assisted nutrition and clinically-assisted hydration in the last few days and hours of life?
 - d. Sedation in the last few days and hours of life?

TYPES OF EVIDENCE REVIEWED

The summary draws on a wide variety of types of published peer-reviewed research. As is usual practice, we treated the evidence produced by different types of research as varying in their strength. We ranked strength of evidence¹ as follows:

- Strong
 - Systematic reviews of previously published peer reviewed research where the reviewers deem the evidence reviewed as strong
 - Well-designed controlled studies which compare pathway-based care (or components thereof) with other forms of care, where there are: multiple sites; contemporaneous data collection; appropriate statistical analyses; and where the comparator is a reasonable one
 - Qualitative research studies which include multiple sites, contemporaneous data collection, and that address questions which cannot be answered through well-designed controlled quantitative studies
- Moderate
 - Accumulated findings from multiple smaller-scale qualitative research studies
- Weak
 - Qualitative research studies involving observations or interviews from one or two sites
 - Retrospective case-note review studies, and other forms of research comparing practice and/or outcomes before and after the introduction of pathway-based care or its components²

In terms of the strength of evidence, it is important to note here that the nature of end of life care makes it very difficult to generate strong evidence as defined above. End of life care presents multiple challenges in relation to conducting research, including: making contact, involving and recruiting people who are dying and those who care for them; designing and implementing comparison interventions; collecting data and conducting various testing procedures; and attaining institutional bodies' permissions to conduct such research. Later in this review, in the section 'Research Implications', we discuss some of these challenges further, and comment on some strategies for dealing with them.

¹ We drew on the Cochrane Effective Practice and Organisation of Care group's guidance (Cochrane Effective Practice and Organisation of Care Review Group 2002).

² Comparisons that collect data before and after pathway implementation are open to bias because other changes often co-occur, both unconnected and connected to pathway implementation (e.g. staffing changes, policy changes, media coverage and debates, etc.). This means one cannot be certain whether or not it was the implementation of pathway-based care that led to any positive or negative effects. This is why simultaneous comparison with other forms of care is so important.

IN BRIEF: KEY MESSAGES

We summarise here the key messages from the published peer reviewed evidence that we found in relation to each of the review questions. We propose a limited number of associated implications; undoubtedly, these will need to be carefully considered alongside implications arising from other forms of available evidence. In subsequent sections of this document, we describe the evidence in each of these areas and present these key messages in more detail and with citations to specific publications.

1. WHAT IS KNOWN ABOUT THE IMPACTS OF INTEGRATED CARE PATHWAYS?

State of the evidence:

- Effectiveness: The strongest available evidence indicates that for some clinical problems or interventions (e.g. gastro-intestinal surgery) there is evidence of overall benefit; but that for others (e.g. in-hospital stroke care pathways) there may be an overall adverse effect.

Implications:

- It is not possible to use evidence about pathways in other areas to predict potential benefits and adverse effects of pathways for managing the dying phase in end of life care.
- The term 'care pathway' may be unhelpful because it is currently used to describe a very broad range of service initiatives. While these various initiatives are often underpinned by similar principles to pathways for the dying phase in end of life care, they involve very different procedures and have very different aims and outcomes³.

2. WHAT IS KNOWN ABOUT POTENTIAL IMPACTS, BENEFITS, AND ADVERSE EFFECTS OF PATHWAYS FOR MANAGING THE DYING PHASE IN END OF LIFE CARE?

State of the evidence:

- Context: Like the majority of non-pharmacological healthcare interventions and initiatives, the potential benefits and adverse effects of pathways for the dying phase in end of life care have not been robustly compared⁴ with those of alternative forms of care. Furthermore, hospital-based care of dying people in the past cannot be compared with care delivered in the current environment.
- Overall: There is no strong evidence on potential benefits or on potential adverse effects and risks of pathways for managing the dying phase in end of life care. That is, there is no research that has produced evidence by robustly comparing these pathways with other form(s) of care.

³ For instance, pathways outside end of life care very often target reduced length of hospital stay, reduced mortality, and reduced morbidity.

⁴ By robust comparison, we mean here research where there is: contemporaneous data collection rather than recall or *post hoc* review of case-notes; comparison against a fair and appropriate control; inclusion of multiple sites and of adequate numbers of patients and family members for appropriate statistical analysis and for robust qualitative analysis.

- Possible benefits: There is moderate, weak, and indirect evidence from multiple studies of professionals' views, and less often family members' views⁵, and from case-note reviews. This suggests pathways for managing the dying phase in end of life care *may* improve: symptom management; prescription of medicines appropriate for end of life care; documentation, discussion and referrals relating to bereavement and family members' support needs; the severity of their bereavement experiences reported by family members; professionals' ratings of care quality and communication - but *not* family members' ratings; and professionals' confidence.
- Possible risks and adverse effects: The current research-base provides no evidence about risks and adverse effects resulting from use of pathways for managing the dying phase in end of life care, and no evidence about economic aspects of such pathway-based care. (There is moderate evidence that healthcare conversations take longer where they include talk about sensitive and emotional matters, as required by properly implemented pathway-based care. This *could* potentially result in increased costs of pathway-based care because of an increase in staff-time required for communication but could also improve the quality of the experience of end of life care).
- Implementation: Moderate research evidence indicates that care pathways for the dying phase are not always implemented adequately.

Implications:

- Despite reports that pathways for managing the dying phase in end of life care result in staff feeling more competent in delivering effective symptom control, this confidence seems not necessarily to translate into effective communication about dying as perceived by family members.
- Better knowledge about potential benefits and adverse effects of pathways for managing the dying phase and of its key components would require robust, multi-centre, expensive studies (quantitative and qualitative) that compare pathways with other forms of care.
- The lack of evidence makes it particularly difficult to identify whether negative consequences suggested to be associated with pathways for managing the dying phase in end of life care are directly associated with (a) actual pathway-based care, (b) poor implementation of pathway-based care, and/or (c) emotional consequences of illness, death and bereavement.

3A. WHAT IS KNOWN ABOUT PREDICTING DEATH IN THE NEXT FEW DAYS OR HOURS?

State of the evidence:

- Overall: There is very limited evidence on how accurately staff can diagnose imminent dying – i.e. dying within days or hours. Studies involving patients who survive for months or weeks suggest clinicians become more accurate in their predictions as life-span shortens, but these studies do not provide specific information about prediction accuracy for patients who are days or hours from dying.
- Misdiagnosing dying: There is no evidence describing or analysing instances where patients predicted as imminently dying have not died within that care episode.
- Factors making diagnosis difficult: An accumulation of moderate and weak evidence suggests organisational, personal and social factors as well as clinical ones often work against the formal diagnosis of imminent dying; also that accurate prediction in non-cancer patients is particularly difficult.

⁵ Throughout the review we use the term 'family members' to refer to associates of the patient; these include non-professional carers, family members, close companions, and close friends.

Implications:

- Implementation of pathway-based care for the dying phase in end of life care, and associated communications, should take place against a backdrop of acknowledgement that in many cases it is not realistic to expect to be able to diagnose dying with complete accuracy.
- It seems clear that no matter what new evidence is produced, there will always be situations where it is not possible to be certain about the imminence of an individual's death. One way to deal with the limitations on accurate prediction would be for teams to be advised to consider symptom control and planning for possible death whilst also undertaking active medical management aimed at improvement of the patient's current status (which might involve: antibiotics, cardiac or diabetic medications). This strategy would be in line with current recommendations for palliative care and with the principles of the Amber Care Bundle – a tool which aims to improve quality of care of patients who are at risk of dying but may still be receiving active treatment (Modernisation Initiative 2010). This is also in line with General Medical Council guidance (2010) and the Mental Capacity Act which state that care and related decisions should be based on the changing needs of patients. It is relevant to note here that multiple decisions are often needed in end of life care management, and according to the GMC and Mental Capacity Act guidance, each should be carefully and individually considered to weigh benefits, burdens and risks.

3B. WHAT IS KNOWN ABOUT COMMUNICATION AMONGST PATIENT, FAMILY MEMBERS, AND PROFESSIONAL STAFF IN THE LAST FEW DAYS AND HOURS?

State of the evidence:

- Overall: There is very little evidence specific to interpersonal communication in the last few days or hours of life between the triad of patient, family members, and staff. The evidence that exists is weak because it relies on retrospective recall and *post hoc* case-note review - these are known to correlate poorly with actual events. There is a somewhat larger body of research about communication in palliative care more broadly; whilst this does not specifically focus on communication challenges and practices in the last few days and hours of life, it provides some useful indications.
- Effects of communication: Moderate evidence, extrapolated from systematic reviews about palliative care communication over longer periods than the last days or hours, indicates:
 - Healthcare conversation length increases when end of life and associated emotional issues are addressed
 - Increasing participation in decision-making increases satisfaction but does not necessarily reduce distress
 - Discussing life expectancy and prognosis reduces patients' and families' anxiety
 - Professionals underestimate patients' information needs, and over-estimate patients' understanding and awareness of prognosis and end of life issues
 - Doctors tend to focus on medical and technological rather than emotional and quality of life issues
 - Satisfaction amongst patient and family members is associated with supportive doctor behaviours such as explicit commitments to continue to support the patient and ensure their comfort, and explicit support of families' decisions
 - The style and content of professionals' communication affects patients' ability to participate in decision-making
 - The presence of family members influences the quality of care, and this is thought to be because of their communication with the team on behalf of the patient
 - Good and bad communication experiences have a lasting effect on bereaved relatives

- Preferences about communication: Moderate and weak evidence from reports rather than direct observations of communication indicates that patients and family members prefer:
 - Gentle, unambiguous information provision followed by opportunity to discuss it
 - To discuss end of life with a professional who is trusted, and with whom there is an established relationship
 - Professionals communicating in a way that conveys empathy, compassion, and honesty balanced with hope
 - Opportunities to ask about and/or discuss concerns and sensitive issues, and professionals encouraging them to ask questions
 - Professionals checking patients' and family members' understanding of information that has been provided
 - Health professionals preparing family members when death is likely to be imminent
 - The research also indicates that patients and family members differ in their preferences for the amount of information that is provided to them about end of life
- Actual communication practices that are used: There is no observational evidence describing and analysing the specific practices that staff can use to achieve these communication features and actions, nor is there direct observational research that compares effects of different practices.

Implications:

- Interpersonal communication between patients, family members and professionals is generally regarded as very important to the quality of end of life care. Communication is a highly 'active ingredient' of care.
- There is moderate and weak evidence that both good and bad communication occur in end of life care, and that both are very influential on care decisions and on perceived care quality.
- Whilst there is evidence about what patients and family members prefer in terms of the characteristics of professionals' communication (e.g. empathic, trustworthy, gentle, balancing honesty with hope), it is hard to provide evidence-based training and guidance to professionals about exactly how to maximise these characteristics in their communication, because there is little evidence characterising the communication practices involved.

3C. WHAT IS KNOWN ABOUT CLINICALLY-ASSISTED NUTRITION AND CLINICALLY-ASSISTED HYDRATION IN THE LAST FEW DAYS AND HOURS OF LIFE?

State of the evidence:

- Perceptions that clinically-assisted hydration is beneficial: Moderate evidence from many studies indicates that patients, family members and many staff perceive clinically-assisted hydration to be beneficial in terms of comfort and quality of life, and extending life. It is also relevant to note with regards *oral intake*, moderate evidence indicates that reduced oral intake in the dying phase is seen by many patients and family members, especially in Western cultures, as harmful and as shortening life.
- Clinical effects of clinically-assisted hydration: There is moderate evidence that clinically-assisted nutrition and hydration have benefits in some patients, adverse effects in others, and no effect in others. There is strong evidence that clinically-assisted hydration at 1 litre (subcutaneously) per day versus a placebo dose of 100ml (subcutaneously) per day does not improve symptoms, quality of life, or length of survival.

Implications:

- There is little evidence on the frequency of and balance between benefits and adverse effects of clinically-assisted nutrition and hydration. Evidence is not sufficient to inform specific recommendations to use or not to use clinically-assisted nutrition and/or hydration.
- This suggests that healthcare professionals need to make judgements in individual cases on the potential harms or benefits of clinically-assisted hydration and/or nutrition. Judgements should be made in the knowledge that research on clinical consequences does not currently provide clear evidence for or against, and that many patients and families perceive it to be beneficial.

3D. WHAT IS KNOWN ABOUT SEDATION IN THE LAST FEW DAYS AND HOURS OF LIFE?

State of the evidence:

- Overall: No randomised controlled studies have been conducted, and it would be ethically and clinically impossible to conduct the kind of controlled trials that would produce what is conventionally thought of as strong evidence.
- Evidence of effectiveness: The moderate strength evidence that exists indicates that sedation in the last days and hours of life is effective in relieving refractory symptoms. (Refractory symptoms are those which cause great suffering and for which there is a lack of other methods for palliation within an acceptable time frame and without unacceptable adverse effects).
- Evidence with regards risks: The moderate strength evidence that exists indicates that when sedation use is titrated and proportionate to the symptoms it does not hasten an already expected death.

Implications:

These implications summarise comprehensive guidance produced by the European Association for Palliative Care (Cherny, Radbruch et al. 2009) through processes of systematic review and expert consensus

- Advance discussion: Careful discussion, if possible in advance of the last days and hours of life, is needed in relation to decision-making about sedation at the end of life, and should include the multidisciplinary team, patient and family members.
- Evaluation by experts before and during sedation:
 - Patients should be evaluated before and during sedation by a senior physician with experience in palliative care, a palliative medicine expert, or a palliative care team.
 - Evaluation should include refractoriness of symptoms, the patient's capacity to make decisions, and an estimation of anticipated remaining lifespan
 - In the case of existential or psychological distress, clinicians skilled in psychological care should be involved in evaluation; decisions should be made in multidisciplinary case conferences; and respite rather than continuous sedation should be the first option
- Careful documentation:
 - Decisions about sedation should be carefully documented
 - Refractory symptoms for which sedation is used should be carefully documented
- Dosage: sedation should be titrated and proportionate, i.e. at the lowest level necessary to provide adequate relieve of suffering.
 - Apart from in emergencies, the first attempt should be at intermittent or mild sedation
 - Deeper sedation should be used when mild sedation has been ineffective, but might be selected first in cases including where suffering is intense and death is anticipated within hours or a few days
 - For patients viewed as imminently dying, downward titration of drug doses should not be used

- Initiating sedation: medications should ideally be started by a physician and a nurse together, and there should be assessment at least once every twenty minutes until adequate sedation is achieved, and subsequently at least three times per day.
- Care during sedation:
 - Where the goal of care is to ensure comfort until death for an imminently dying patient, the only critical observations made should be those pertaining to comfort (and not heart rate, blood pressure and temperature)
 - Medications for symptom palliation used before sedation should be continued unless they are ineffective or have distressing side effects
 - Decisions about clinically-assisted hydration and nutrition should be treated as independent of the decision about sedation itself
 - Dignity and basic care should be maintained. Oral care, eye care, toilet, hygiene and pressure wound care should be provided on the basis of the patient's wishes and the estimated risks or harms
- Supportive care of family members and effective communication with them: the team must recognise that family members can find the sedation of their relative profoundly distressing. The team must provide supportive care including regular informational and supportive communication. Hospital staff should make every effort possible to provide people with privacy for emotional and physical intimacy. These efforts should include: minimising restriction of visiting, availability of basic supports including tissues, chairs, water, access to a telephone, and opportunity to sleep in the room or nearby.
- After death: family members should be given an opportunity to talk with care providers after their relative's death.

IN DETAIL: Background, evidence, and key messages

1. WHAT IS KNOWN ABOUT THE IMPACTS OF INTEGRATED CARE PATHWAYS IN GENERAL?

Background

Pathways are multi-component complex interventions intended to facilitate decision-making and organization of care for a well-defined group of patients over a well-defined period (European Pathway Association 2007). They involve:

- Explicit goals and care elements based on evidence, best practice, and patients' characteristics and expectations
- Incorporation of these into a structured multidisciplinary plan of care which includes time-frames or criteria-based steps
- Defined roles and activity sequences
- An intention to standardise care for a particular clinical problem, procedure, or episode of care

(Rotter, Kinsman et al. 2010; Vanhaecht, Ovretveit et al. 2012)

Numerous alternative terms are used for integrated care pathways, including: critical pathways, clinical pathways, and case management plans. Furthermore, they encompass a very wide variety of procedures used to try to improve care. They originated in the USA in the 1980's alongside a diagnosis-based finance system and were intended to cut costs whilst maintaining or improving care quality. Their adoption spread through the UK in the 1990's, and they began to be directed not only at increased efficiency but also at increasing the application of clinical guidelines within everyday practice (Vanhaecht, Ovretveit et al. 2012). Pathways now take many forms. They are used in many different clinical conditions, interventions and environments, and in many countries worldwide.

Pathways promise a logical way to both standardise and improve patient care and service delivery. However, like any intervention based on logical premises, fulfilment of this promise should not be assumed when pathways are applied in the complicated, social world of healthcare practice where people must work together in the face of distressing and complex human problems.

Evidence in detail

We draw here on four systematic reviews. These incorporated evidence from more than thirty publications spanning research in Europe, Asia, Australasia, and North America. A high quality, Cochrane review (Rotter, Kinsman et al. 2010) examined the effects of hospital-based clinical pathways on professional practice, patient outcomes, length of stay and hospital costs. The reviewers combined findings from evaluations of a very wide range of pathways, only one of which was in end of life care. Qualitative evaluations were excluded. The reviewers concluded that pathways are associated with reduced in-hospital complications and improved documentation, without negatively impacting on length of stay and hospital costs. The review's overall focus had little relevance to the kinds of outcomes that are intended in end of life care pathways for the dying phase (i.e. perceptions and indicators of care quality). A more inclusive systematic review (Deneckere, Van Herck et al. 2012) included both qualitative and quantitative evaluations of care pathways' effects on teamwork. It

found relatively strong evidence that pathways can: improve professional documentation; improve care continuity; and increase workload. The most frequently found adverse effect was the emergence of team conflicts.

A systematic review with a specific focus on gastrointestinal surgery pathways (Lemmens, Van Zelm et al. 2008) found evidence that these can enhance care efficiency without adverse effects on outcome. A Cochrane review examining research on pathway-based in-hospital stroke care (Kwan and Sandercock 2005) found no differences in terms of death, dependency or discharge destination, or length of stay. However, the review also found some evidence that in-hospital pathway-based care for stroke reduced patient satisfaction and quality of life in comparison to other forms of care; the reasons for this were not clear. It could thus be concluded that clinical pathways are beneficial for managing some clinical problems, but not all (Chan and Webster 2010).

Key messages in detail

State of the evidence:

- A very wide group of practice initiatives fall into the category 'care pathways'.
- A small body of rigorous, comparative research provides strong evidence that pathways have benefits in some conditions and procedures (e.g. gastro-intestinal surgery) and moderate evidence that they have adverse effects in others (e.g. in-hospital management of stroke) (Rotter, Kinsman et al. 2010).
- There is moderate evidence that pathways increase workload, improve documentation, and improve continuity of care (Deneckere, Van Herck et al. 2012).
- There is some limited evidence that team conflict can result from implementation of pathways (Deneckere, Van Herck et al. 2012).

Implications:

- It is not reasonable to assume that because pathways improve outcomes in some settings that they will do so in end of life care for the dying phase.
- The term 'care pathway' may be unhelpful because it is used to mean a very broad range of service initiatives. While these various initiatives are often underpinned by similar principles to pathways for the dying phase in end of life care, they involve very different procedures and practices, and have very different aims and intended outcomes⁶.

⁶ For instance, pathways outside end of life care often target reduced length of hospital stay, reduced mortality, and reduced morbidity. (Rotter, Kinsman et al. 2010)

2. WHAT IS KNOWN ABOUT THE IMPACTS OF END OF LIFE CARE PATHWAYS FOCUSED ON THE DYING PHASE IN END OF LIFE CARE?

Background

End of life care pathways for the dying phase are now used in many countries and settings; the large majority of these entail use or adaptation of the Liverpool Care Pathway for the Dying Patient (Ellershaw 2002; Ellershaw and Wilkinson 2011). Pathways for managing the dying phase in end of life care were developed just over a decade ago in the face of growing consensus that care for people at the end of life, and for their families, was sub-optimal, particularly in acute care settings, and that those dying in hospices received better care (Watts 2012a). They also developed in a context of developments in effective care for the distressing symptoms of end-stage cancer. Pathways for the dying phase are directed at: enhancing care (Watts 2012b); ensuring that the most appropriate management occurs at the most appropriate time; and that it is provided by the most appropriate health professional (Chan and Webster 2010).

Pathways for the dying phase in end of life care take physical form in a structured, multidisciplinary, evidence-based document that maps and guides vital care interventions for individuals and their families in the last days and hours of life and the immediate bereavement period. The Liverpool Care Pathway for the Dying Patient is intended to be initiated when there is consensus that the person has entered the dying phase. It is intended to replace all other documentation including medical and nursing notes. It is designed to prompt and guide healthcare decisions and interventions, and communications with family members and the patient (Ellershaw and Ward 2003).

Evidence in detail

We reviewed three recent systematic reviews of end of life care pathways for the dying phase⁷ (Chan and Webster 2010; Phillips, Halcomb et al. 2011; Watts 2012). A large proportion of the evidence reviewed by these concerned the Liverpool Care Pathway. We also sought empirical research published after the reviews' cut-off dates, and found some case-note reviews and qualitative studies, but no large scale trials. In addition, we sought information on large-scale studies currently in progress (these are listed later in the section 'Research in progress', page 28). A Cochrane review of end of life care pathways for the dying phase (Chan and Webster 2010) set out to review studies comparing effects of pathway-based care with other forms of care. The reviewers aimed to include only studies where effects were quantitatively measured and statistically analysed, and they imposed strict and established criteria for judging the quality of studies, with an aim of limiting bias as much as is possible⁸. They found no studies that met these criteria. However, the reviewers summarised the findings of the studies they excluded whilst also stressing that these must be treated with great caution because the evidence is unacceptably open to bias – i.e. factors other than use of the care pathway may have caused the effects found. The excluded studies suggested that pathway-care *may* have the potential to improve: symptom management; prescription of medicines appropriate for end of life care; clinical documentation and assessment; and family-members' retrospective ratings of their level of bereavement distress. A more inclusive review (Phillips, Halcomb et al. 2011) aimed to provide a wider overview in terms of whether there is evidence to support use of pathways for the dying phase in acute and/or hospice care, and

⁷ Where studies were specifically focused on end of life care pathways for the dying phase in residential or home-based care settings, we did not include them. We did so because of the review's primary focus on evidence and implications for end of life care in hospitals, also because in residential and home care settings, some key outcomes (e.g. avoidance of acute hospital admission) are not relevant to hospital-based care.

⁸ They aimed only to include randomised controlled trials, and high quality controlled before and after studies.

sought to identify evidence about key elements for effective implementation of these pathways. Twenty-six studies were included, including quantitative evaluations, case-note reviews (also known as chart audits), and qualitative evaluations. The majority (15/26) were set in the UK, the rest were from the Netherlands, US, Australia, Ireland and China. This relatively inclusive review concluded that there is only low level evidence available to support use of the pathways, and that this weak evidence suggested pathway-based care for the dying phase promotes good practice; increases accessibility of palliative care; structures care; and promotes proactive management of patient comfort⁹. This review also identified a very small body of evidence on what makes for best implementation: the most frequent finding was that implementation is better where an experienced professional is appointed as a pathway facilitator. A review examining nurses' perceptions of care pathways for the dying phase in end of life care (Watts 2012) concluded that nurses consistently viewed the pathway-based care as improving: care quality and consistency; interprofessional relationships; communication; confidence; and documentation.

The current research-base provides no evidence about adverse effects resulting from use of pathways in end of life care, and no evidence about economic aspects of pathway-based care (Chan and Webster 2010).

Problems of implementation and barriers to the use of pathways for the dying phase in end of life care were examined in detail in the review that included a broad range of evidence (Phillips, Halcomb et al. 2011). This review identified problems including the: absence of rigorous randomised controlled trial evidence; need for modification given the pathways' basis in cancer care; dependence on timely and confident recognition and diagnosis of dying; difficulties of implementation in environments where the focus is on attempts to cure; substantial resource requirements for implementation – including managerial and senior clinical leadership and support; the need for expert pathway facilitators; time for education and establishment of the pathway and for ongoing monitoring.

We found three studies involving evaluation of pathways published after the cut-off dates of the three systematic reviews discussed above. A questionnaire survey surveyed people at least three months after their relative's death (Lokker, van Zuylen et al. 2012) and covered a period both before and after introduction of a pathway for the dying phase, it found that the number of patients reported to have been aware of the imminence of death before and after introduction of the pathway did not change. A case-note review (Johnstone, Jones et al. 2012) across multiple settings indicated a very strong association between pathway-based care and documentation that families' bereavement and spiritual support needs had been attended to. An interview study focusing in depth upon specific cases at a single site (Freemantle and Seymour 2012) investigated factors influencing whether or not patients dying of cancer are cared for using the Liverpool Care Pathway. It found that not instigating pathway-care was due to lack of access to senior review. This was due primarily to senior staff's reduced availability out-of-hours (weekends, evenings), also to prioritisation of patients receiving curative care. The study made some preliminary observations on areas which have been little explored elsewhere. This included doctors' and nurses' reports of instances where patients were taken off the pathway when their condition improved; staff treated these as positive events (rather than threatening to their expertise). The nurses and doctors reported problems arising when senior staff did not 'believe in' pathway care. They also reported relying on senior staff to communicate clearly and unambiguously with patients and family members before other staff felt able to do so, and they reported that not all senior staff communicated in this way. 'Going on the pathway' was reported to be used at times as a euphemism for dying. The authors note that despite pathway-care being reported to result in staff feeling more competent in delivering effective symptom control, this confidence seems not to necessarily translate into effective communication about dying as perceived by patients.

⁹ An interview study published after the review, and specific to acute hospital settings (Clark, Sheward et al. 2012) reported similar findings amongst acute care nurses.

Key messages in detail

State of the evidence:

- Like the majority of non-pharmacological healthcare interventions and initiatives, the potential benefits and adverse effects of end of life care pathways for the dying phase have not been robustly compared¹⁰ with those of alternative forms of care.
- There is no strong evidence involving comparison of the care of dying people in the past with care delivered in the current environment (and it is not possible to go back and collect robust data on practice and outcomes in the past).
- There is no strong evidence on potential benefits and adverse effects and risks of pathways for the dying phase in end of life care. That is, there is no research that has produced evidence by robustly comparing these pathways with other form(s) of care. Other types of research study have suggested a number of benefits of pathway-based care, but it is not possible to be certain whether the effects reported are due to the use of the pathway or to other factors.
- There is moderate, weak, and indirect evidence from multiple studies of staff views, and less often family members' views, and from case-note reviews. However, this may be biased and could in the future be proved incorrect because influences other than introduction of a pathway¹¹ could have caused the effects reported and/or because effects were specific to one particular team or site.
- The moderate, weak and indirect evidence suggests pathways for managing the dying phase in end of life care *may* improve:
 - proactive symptom management
 - prescription of medicines appropriate for end of life care
 - documentation, discussion and referrals relating to bereavement and family members' support needs
 - the severity of their bereavement experiences reported by family members
 - professionals' ratings of care quality and communication - but *not* family members' ratings
 - professionals' confidence in relation to end of life care(Chan and Webster 2010; Phillips, Halcomb et al. 2011; Watts 2012).
- The current research-base provides no evidence of adverse effects resulting from use of pathways for managing the dying phase in end of life care, including evidence that compares with alternative forms of care.
- The current research-base provides no evidence about economic aspects of pathway-based care. There is moderate evidence that healthcare conversations take longer where they include talk about sensitive and

¹⁰ By robust research, we mean here research where there is contemporaneous data collection rather than recall or *post hoc* notes review, comparison against a fair and appropriate control, and inclusion of multiple sites and adequate numbers of patients and family members for appropriate statistical analysis.

¹¹ In studies that collect and compare data before and then after a pathway has been introduced, other influences on any changes seen could include: changes in staff leading to changes in expertise skills and preferences; how well the team is working together; changes in local management or in government health policy; changes in behaviours of staff or families associated – for instance - with media coverage

emotional matters, as required by properly implemented pathway-based care (Fine, Carrington Reid et al. 2010) .This *could* potentially result in increased costs of pathway-based care because of an increase in staff-time required for communication and also in improved quality of care, but this hypothesis would need testing in practice.

- Moderate evidence indicates that care pathways for the dying phase are not always implemented adequately (Phillips, Halcomb et al. 2011; Freemantle and Seymour 2012).

Implications:

- Despite reports that pathways for managing the dying phase in end of life care result in staff feeling more competent in delivering effective symptom control, this confidence seems not to necessarily translate into effective communication about dying as perceived by family members.
- The international diffusion of EOLC pathways has occurred in the absence of compelling evidence of their impact on patients, families and professional practice (Watts 2012a & b; Chan and Webster 2010).
- Developing a more robust evidence base about potential benefits and adverse effects of pathways for managing the dying phase and of its key components would require multiple well-designed and thus relatively expensive studies, using a range of methodologies (including: quantitative and qualitative, controlled comparisons, in depth case studies, and investigations relating to pathways' implementation in practice).
- The lack of evidence makes it particularly difficult to identify whether negative consequences suggested to be associated with pathways for managing the dying phase in end of life care are directly associated with (a) actual pathway-based care, (b) poor implementation of pathway-based care, and/or (c) emotional consequences of illness, death and bereavement.
- There is little knowledge about whether certain elements of pathway care are more important than others, generating such knowledge is always a challenge in complex interventions.

3A WHAT IS KNOWN ABOUT THE RECOGNISING IMMINENT DEATH – A KEY COMPONENT OF ICPS IN END OF LIFE CARE

Background

The clinical decision to use an end of life care pathway for the dying phase to care for an individual patient is dependent on the recognition and diagnosis that the patient is in the last few days and hours of life. If patients who *are dying* are not diagnosed as such, they may be subjected to interventions that are not in their best interests. If patients who are *not dying* are diagnosed as dying, they may not receive the interventions that are needed to maximise the chances of improvement in their condition.

Evidence details

There is a body of literature, including several systematic reviews (Glare, Virik et al. 2003; Coventry, Grande et al. 2005; Trajkovic-Vidakovic, de Graeff et al. 2012; Yourman, Lee et al. 2012), on recognising and diagnosing dying. These include studies on the accuracy of clinicians' predictions (Glare, Virik et al. 2003; Trajkovic-Vidakovic, de Graeff et al. 2012), the accuracy and use of various prediction tools, i.e. models, equations, or checklists (Coventry, Grande et al. 2005; Yourman, Lee et al. 2012), and observational studies on signs and symptoms amongst patients nearing death (Kehl and Kowalkowski 2012). Studies involving patients who survive for months or weeks suggest that clinicians become more accurate in their predictions as death approaches, but these studies do not provide specific information about prediction of dying in days or hours.

We found no evaluations of the accuracy of clinicians' predictions of death in the next few hours/days. Nor could we find systematic reviews relevant to recognition and diagnosis of imminent dying. So we sought recent empirical evidence, and found two relevant studies. A consensus study (Domeisen, Ostgathe et al. 2012) entailing an international Delphi survey of palliative care experts' views on phenomena that indicate the last hours and (up to seven) days of life. It identified a number of domains they considered highly relevant in identifying and predicting imminent death. One factor rated as important was 'intuition' – the authors note that exactly what this means is little understood and needs further investigation. Similar findings were made by a smaller-scale focus group study which gathered the views of experienced nurses in one hospital (van der Werff, Paans et al. 2012). Although subject to limited empirical research, we note here that researchers and research participants often comment on the difficulties of diagnosing death (Raijmakers, van Zuylen et al. 2011), and that these difficulties relate not only to the variability and range of signs and symptoms amongst dying people and the fact there is no single clear sign or cluster of signs (van der Werff, Paans et al. 2012), but also to organisational, social and personal factors that play an important part in people and teams finding it difficult to make an explicit diagnosis of dying (Gibbins, McCoubrie et al. 2009; Chapman and Ellershaw 2011).

Key messages in detail

State of the evidence:

- There is very limited evidence on how accurately staff can diagnose imminent dying – i.e. dying within days or hours. Studies involving patients who survive for months or weeks suggest clinicians become more accurate in their predictions as life-span shortens (Glare, Virik et al. 2003; Trajkovic-Vidakovic, de Graeff et al. 2012), but these studies do not provide specific information about prediction accuracy for patients who are days or hours from dying.

- There is no evidence describing or developing understandings about instances where patients predicted as imminently dying have not gone on to die within that care episode.
- Some studies have documented factors that experienced doctors, nurses and others report they use in diagnosing imminent dying (Glare, Virik et al. 2003; Trajkovic-Vidakovic, de Graeff et al. 2012; Domeisen, Ostgathe et al. 2012). These include various signs and symptoms, but also a little understood factor: intuition. A limitation of these studies is that none have gathered data contemporaneously with dying episodes: they have only gathered data in retrospect, and sometimes in the abstract.
- Knowledge about how experienced clinicians diagnose imminent dying could underpin development of diagnostic checklists or models. However, it is by no means clear whether even the most expert clinician or the most robustly researched checklist/model could ever diagnose imminent dying with consistent accuracy. Besides social, personal and organisational factors making diagnosis difficult, there are important clinical issues: for the majority of people, the trajectory towards dying is unclear, rather than a predictable steady decline. This is increasingly so in societies where medical technology is advanced, and more people survive to very old age.
- Factors making diagnosis difficult: An accumulation of moderate and weak evidence suggests organisational, personal and social factors as well as clinical ones often work against the formal diagnosis of imminent dying.
- An accumulation of moderate and weak evidence indicates that accurate prediction in non-cancer patients is particularly difficult (Gibbins, McCoubrie et al. 2009; Chapman and Ellershaw 2011).

Implications:

- Implementation of pathway-based care for the dying phase in end of life care, and associated communications, should take place against a backdrop of acknowledgement that in many cases it is not realistic to expect to be able to diagnose dying with complete accuracy.
- More knowledge is needed about how professionals predict imminent dying (in the next few days/hours) and about how accurate their predictions are.
- It seems clear that no matter what new evidence is produced, there will always be situations where it is not possible to be certain about the imminence of an individual's death. One way to deal with the limitations on accurate prediction would be for teams to be advised to consider symptom control and planning for possible death whilst also undertaking active medical management aimed at improvement of the patient's current status (which might involve: antibiotics, cardiac or diabetic medications) (see (Gibbins, McCoubrie et al. 2009). This is in line with current recommendations for palliative care (World Health Organisation 2011; Smith, Temin et al. 2012) and with the principles of the Amber Care Bundle – a tool which aims to improve quality of care of patients who are at risk of dying but may still be receiving active treatment (Modernisation Initiative 2010). This proposal is also in line General Medical Council guidance (2010) and the Mental Capacity Act (Department for Constitutional Affairs 2005) which state that care and related decisions should be based on the changing needs of patients. It is relevant to note here that multiple decisions are often needed in end of life care management, and according to the GMC and Mental Capacity Act guidance, each should be carefully and individually considered to weigh benefits, burdens and risks. Where patients lack capacity for relevant decisions, these should be made in their best interests using principles articulated in guidance including that from the General Medical Council (2010) and in the Mental Capacity Act (Department for Constitutional Affairs 2005).

3B. WHAT IS KNOWN ABOUT THE PRACTICES AND EFFECTS OF COMMUNICATION AMONGST PATIENT, FAMILY MEMBERS, AND PROFESSIONALS IN THE LAST FEW DAYS OR HOURS OF LIFE?

Background

Communication is the fundamental mechanism through which most healthcare practice is delivered. Numerous studies of palliative and end of life care document the importance of communication in terms of perceptions of care quality, and long-term sequelae for bereaved relatives. Evidence from numerous studies of healthcare communication indicates that differences in the style and content of communication influence patient and family members' health-related behaviours, care outcomes, and their perceptions of care quality (Stewart 1995; Brown, Stewart et al. 2003).

Evidence details

We found no systematic reviews, and only two recent empirical studies (Jackson, Purkis et al. 2010; Bailey, Williams et al. 2012; Lokker, van Zuylen et al. 2012) which included some focus on interpersonal communication within the triad of patient, family members and staff specifically in the last few days and hours of life. A survey (Lokker, van Zuylen et al. 2012) in the Netherlands that included gathering relatives' reports on individual patients three months or more after death found that patients who were reported by family members to be aware of the imminence of their deaths were also more often reported to have been at peace with dying and to have felt that life had been worth living. A retrospective interview study in the UK (Jackson, Purkis et al. 2010) showed that communication has lasting effects: relatives reported and remembered failures in communication 12 months after the death of patients; they also reported positive memories of small gestures, such as the offer of a cup of tea or of some private space. There is indirect evidence from a detailed and carefully designed case note review (Bailey, Williams et al. 2012) that communication between family members and staff may improve symptom management.

Given the dearth of research directly focused upon communication in the last days and hours of life, we sought and drew upon systematic reviews examining evidence about communication in palliative care and cancer care. These reviews included examinations of: communication with patients with advanced, life-limiting cancer (Back, Anderson et al. 2008); communication with patients with life-limiting illness of all types (Parker, Clayton et al. 2007); doctors' communication with cancer patients at critical points in their course of care (Rodin, Mackay et al. 2009); directly observed palliative and end of life doctor-patient discussions (Fine, Carrington Reid et al. 2010); communication about prognosis and end of life issues with family members and patients with life-limiting conditions (Hancock, Clayton et al. 2007); and shared decision making in palliative care (Frank 2009). We summarise relevant findings from these below.

Key messages in detail

State of the evidence:

- There is very little evidence specific to interpersonal communication in the last few days or hours of life between the triad of patient, family members, and staff.
- The evidence that exists is weak because it relies on retrospective recall and *post hoc* case-note review, these are known to often correlate poorly with actual events (Webb and Stimson 1976; Addington-Hall and McPherson 2001; Rethans, Martin et al. 1994).

- No research has used direct observation comprising recordings of actual interactions during the last few days and hours of life.
- This weak evidence specific to the last few days and hours suggests:
 - Healthcare professionals' skills and willingness to share information and communicate are linked to patients' ability to participate in decision making (Frank 2009)
 - People reporting their deceased relative was aware of imminent death report a more peaceful end of life (Lokker, van Zuylen et al. 2012)
 - When families are present, opioids are more likely to have been ordered and given (Bailey, Williams et al. 2012)
 - At least twelve months after death, relatives remember small gestures, such as offering drinks or private space positively, and they remember perceived failures of communication with distress (Jackson, Purkis et al. 2010)
- Moderate evidence on the *effects of communication* - involving extrapolating from systematic reviews about palliative care communication over longer periods than the last days or hours – indicates:
 - Addressing sensitive topics including end of life, emotions and quality of life issues in healthcare conversations increases the length of those conversations (Back, Anderson et al. 2008; Fine, Carrington Reid et al. 2010)
 - Ability to participate in decision-making is linked to healthcare professionals' communication skills and willingness to share information and engage in communication (Frank 2009)
 - Interventions to increase participation in decision-making are associated with greater satisfaction but do not necessarily reduce distress (Rodin, Mackay et al. 2009)
 - Discussion of life expectancy and prognosis reduces anxiety in patients and family members (Rodin, Mackay et al. 2009)
 - Health professionals underestimate patients' need for information and over-estimate their understanding and awareness of their prognosis and of end of life issues (Hancock, Clayton et al. 2007)
 - Style of communication is at least as important to patients and family members as its content (Parker, Clayton et al. 2007)
- Systematic reviews of communication in palliative care and in life-limiting cancer indicate moderate and weak evidence on patients' and family members' preferences for *communication practices* entailing:
 - Gentle and unambiguous information provision followed by opportunity to talk about it (Frank 2009)
 - Discussion of end of life with a health professional who is trusted and has an established relationship with the patient and family (Back, Anderson et al. 2008) (Parker, Clayton et al. 2007)
 - Conveying empathy, compassion, and honesty balanced with hope (Parker, Clayton et al. 2007) (Frank 2009)
 - Doctors asking about concerns and related to disease progression or dying (Back, Anderson et al. 2008) (Parker, Clayton et al. 2007)
 - Doctors offering to talk about end of life and to discuss components of a good death (Back, Anderson et al. 2008)
 - Health professionals preparing family members when death is imminent (Back, Anderson et al. 2008)
 - Encouraging patients and family members to ask questions (Back, Anderson et al. 2008) (Parker, Clayton et al. 2007)
 - Checking patients' and family members' understanding of information provided (Parker, Clayton et al. 2007)

- Also, research indicates that preferences for amount of information differ between patients and family caregivers with patients wanting less and family members more as illness progresses (Hancock, Clayton et al. 2007; Frank 2009)
- Slightly stronger evidence, in that it has been generated from direct observation of palliative and end of life care communication indicates the following (Fine, Carrington Reid et al. 2010):
 - Doctors tend to focus on medical and technological rather than emotional and quality of life issues
 - Doctors talk more than patients and caregivers within consultations
 - Patient and family member satisfaction is associated with supportive doctor behaviours such as explicit commitments to continue to support the patient and ensure their comfort, and explicit support of families' decisions
- There is moderate and weak evidence that both good and bad communication occur in end of life care, and that both are very influential on care decisions, and on perceived care quality (Jackson, Purkis et al. 2010).

Implications:

- Interpersonal communication between patients, family members and professionals is generally regarded as very important to the quality of end of life care. Communication is a highly 'active ingredient' of care.
- Whilst there is evidence about what patients and family members prefer in terms of the characteristics of professionals' communication (e.g. empathic, trustworthy, gentle, balancing honesty with hope), it is very difficult to provide evidence-based training and advice to professionals about how to achieve these characteristics within their consultations and conversations. This is because there is little evidence about the communication practices that professionals, patients and family members use in the last days and hours of life, and about how such communication practices relate to people's expressed preferences. (Fine, Carrington Reid et al. 2010).

3C. WHAT IS KNOWN ABOUT CLINICALLY-ASSISTED NUTRITION AND HYDRATION IN THE LAST FEW DAYS OR HOURS OF LIFE?

Background

Nutrition and hydration requirements slowly decline during the advance of terminal illness. When oral ingestion is reduced, decision-making about instigating clinically-assisted nutrition¹² and clinically-assisted hydration¹³ may become relevant. Two broad domains of knowledge are relevant. One concerns what is known of people's views and understandings about clinically-assisted hydration and nutrition in terms of both its symbolism and perceived physical effects. The other concerns what is known about bodily responses to clinically-assisted hydration and nutrition. Ethical, emotional, and cultural aspects are known to heavily influence views and decisions about clinically-assisted nutrition and hydration (Río, Shand et al. 2012).

Evidence in detail

We examined the following: an inclusive review of the evidence on perceptions and influences on decision-making in relation to both oral and clinically-assisted nutrition and hydration (Río, Shand et al. 2012); two Cochrane reviews: one on clinically-assisted nutrition (Good, Cavenagh et al. 2008a) and one on clinically-assisted hydration (Good, Cavenagh et al. 2008b), and a recently reported large scale cluster randomised controlled trial examining clinically-assisted hydration (Bruera, Hui et al. 2013).

A broad and inclusive review (Río, Shand et al. 2012) incorporating quantitative and qualitative research examined evidence about: (1) the emotional impact that the *reduction* in oral intake in a terminally ill patient generates in patients, family members, and healthcare staff, (2) people's perceptions of the effects of clinically-assisted nutrition and hydration, and (3) influences on decisions made about initiating clinically-assisted nutrition and hydration. It found that the majority of patients, family members and healthcare staff see food and liquid as staving off physical deterioration in people who are in the dying phase. Cultural differences with regards the effects and appropriateness of reduced intake at the end of life exist, with the idea that reducing ingestion accelerates death most prevalent in Western cultures. Another finding concerned different families' coping styles: families that pressured or forced their loved ones to eat were less accepting and aware of impending death, and families that were more accepting of the patient's reducing oral intake were better able to put their time, energy and focus on other care-giving activities. It also found that families sometimes perceive staff's prioritisation of symptoms other than anorexia as signalling negligence. A further important finding was that staff experienced in palliative and hospice care viewed artificial nutrition and hydration less positively than other healthcare professionals, who are more likely to see it as an inherent aspect of basic care. The review also concluded that lack of information and misperceptions of clinically-assisted nutrition and hydration can play a predominant role in the decision to begin or suspend clinically-assisted nutrition or hydration.

¹² Clinically-assisted nutrition is defined in the Cochrane review of Good et al (2008a) as entailing "administration of nutritional liquid via a central or peripheral venous catheter, that does not directly enter the gastrointestinal system" and/or "through a tube via the gastrointestinal system (nasogastric tube, jejunostomy, gastrostomy)" (p3)

¹³ Clinically-assisted hydration is defined in Good et al's Cochrane review (2008b) as the "administration of non-nutritional fluids, administered via the subcutaneous tissue, venous system or enterally (nasogastric tube, jejunostomy, gastrostomy)" (p3).

Cochrane reviews have examined evidence on the effects of clinically-assisted nutrition (Good, Cavenagh et al. 2008a) and clinically-assisted hydration (Good, Cavenagh et al. 2008b) upon the quality and survival length of palliative care patients. Being Cochrane reviews of quantitative evidence, these included only research highly ranked in terms of evidence quality. For clinically-assisted nutrition (Good, Cavenagh et al. 2008a), the reviewers found no studies that met their quality standard and so no recommendations for practice were proposed. For clinically-assisted hydration (Good, Cavenagh et al. 2008b), five studies were found that met the criteria: three found no difference in outcomes; one found better sedation and less involuntary contractions in those receiving clinically-assisted hydration, and another found that those receiving clinically-assisted hydration had less dehydration but also more symptoms of fluid retention such as pleural effusion and swelling of the limbs and abdomen.

Subsequent to these Cochrane reviews, the findings of a large-scale, multicentre cluster randomised controlled trial have been published (Bruera, Hui et al. 2013). The trial compared use of clinically-assisted hydration with a placebo. Dying patients were randomised to receive either one litre of saline per day via subcutaneous infusion, or a placebo dose of 100 ml per day via subcutaneous infusion. The infusions continued until coma or death, and the patients survived an average of 17 days. No overall differences were found between the groups in terms of: fatigue, involuntary muscle spasms, sedation and hallucination, nor in overall length of survival¹⁴. In discussion, the researchers noted that certain groups (e.g. patients with delirium) might be particularly likely to benefit from clinically-assisted hydration. They argued there is a need for studies focusing on specific patient/symptom groups. Importantly, in a connected study (Cohen, Torres-Vigil et al. 2012) of patients' and families' views on clinically-assisted hydration, the overwhelming majority of dying patients and families perceived that clinically-assisted subcutaneous hydration was clinically useful and helped to enhance comfort, dignity, and quality of life.

Key messages in detail

State of the evidence:

- A large accumulation of moderate evidence indicates that patients, family members and many staff perceive clinically-assisted hydration to be beneficial in terms of comfort and quality of life, and extending life (Cohen, Torres-Vigil et al. 2012; Río, Shand et al. 2012).
- There is moderate evidence that clinically-assisted nutrition and clinically-assisted hydration have both benefits in some patients, adverse effects in others, and no effect in others (Good, Good, Cavenagh et al. 2008a & b).
- There is strong evidence from one study (Bruera, Hui et al. 2013) that clinically-assisted hydration (delivered subcutaneously) at one litre per day when compared with a placebo dose of 100ml per day does not have a positive impact on symptoms, quality of life, nor length of survival in patients who are in the last three weeks of life. A qualitative study with the same group of patients and their families (Cohen, Torres-Vigil et al. 2012) found however that the overwhelming majority of dying patients and families

¹⁴ The effects of clinically-assisted hydration upon survival length are relevant to debates about what is known as 'double effect'. This is a doctrine or argument that "is used as an ethical justification for the specific risk of foreseeable life shortening as a result of a medical treatment" (Sykes and Thorns 2003 p317, see also George and Regnard 2007). In relation to clinically-assisted hydration, the concern is that withholding or withdrawing clinically-assisted hydration may hasten death, even if the primary intent is to reduce the burden of a futile intervention. We refer to 'double effect' again in the section on sedation.

perceived that clinically-assisted subcutaneous hydration was clinically useful and helped to enhance comfort, dignity, and quality of life.

- It is also relevant to note with regards *oral intake*: that moderate evidence indicates that reduced *oral* intake in the dying phase is seen by many patients and family members, especially in Western cultures, as harmful and as shortening life (Río, Shand et al. 2012).

Implications:

- More evidence is needed, particularly in relation to effects of clinically-assisted hydration in patients suffering symptoms that might be particularly strongly influenced by hydration or dehydration (e.g. delirium, and symptoms of fluid overload).
- The current research evidence base is not sufficient to inform specific recommendations to use or not to use clinically-assisted nutrition and/or hydration.
- This suggests that healthcare professionals need to make judgements in individual cases on the potential harms or benefits of clinically-assisted hydration and/or nutrition. Judgements should be made in the knowledge that research on clinical consequences does not currently provide clear evidence for or against, and that many patients and families perceive it to be beneficial.
- Decisions on whether to institute clinically-assisted hydration should take into account the evidence that many patients and families perceive clinically-assisted hydration to be beneficial, and the lack of clear evidence of its harms.

3D WHAT IS KNOWN ABOUT PRACTICES AND EFFECTS OF SEDATION IN THE LAST DAYS AND HOURS OF LIFE

Background

This section differs somewhat from others because we are able to draw heavily here on a set of recommendations derived from extensive literature review and expert peer review, this being the framework of the European Association for Palliative Care for the use of sedation in palliative care (Cherny, Radbruch et al. 2009). The framework is particularly useful given the many different terms used in association with this intervention (Seymour, Rietjens et al. 2011), the different indications for sedation applied in clinical practice, and the different depths of sedation that can be used (Cherny, Radbruch et al. 2009).

The framework defines therapeutic or palliative sedation in the context of palliative care as “the monitored use of medications intended to induce a state of decreased or absent awareness (unconsciousness) in order to relieve the burden of otherwise intractable suffering in a manner that is ethically acceptable to the patient, family and health-care providers.” (Cherny, Radbruch et al. 2009, p581). The situations in which such sedation is used include: management of refractory physical symptoms at the end of life, suddenly arising catastrophic events such as massive bleeding at the end of life, and management of refractory psychological or existential suffering. Refractory physical symptoms are those for which there is a lack of other methods for palliation within an acceptable time frame and without unacceptable adverse effects. It is more difficult to establish whether psychological symptoms and existential distress are truly refractory (associated special guidance is provided in the framework document).

Sedation is considered by experienced clinicians and professional bodies to be “an important and necessary therapy in the care of selected palliative care patients with otherwise refractory distress” (Cherny, Radbruch et al. 2009, p581). Prudent use, due caution and good practice are needed – it “is a treatment of last resort because of its anticipated adverse outcomes and potential risks” (Cherny, Radbruch et al. 2009, p581). Despite these potential problems, it is important for teams, families and patients to engage in discussions and decision-making regarding administration of sedation because avoiding the issue can ultimately result in increased patient distress, and failure to compassionately use all means available to reduce patients’ suffering where their symptoms are refractory.

Evidence in detail

For the reasons noted above, we rely primarily on the review and recommendations produced by the European Association for Palliative Care (EAPC) (Cherny, Radbruch et al. 2009). Our key messages are largely drawn from this framework. In addition, we draw on two systematic reviews published since the EAPC framework: one which focuses on evidence about sedation and its effects on length of survival compared with non-sedation and which also reports on evidence about the prevalence of sedation and reasons for its use (Maltoni, Scarpi et al. 2012); and one which focuses on the experiences of family members in relation to sedation (Bruinsma, Rietjens et al. 2012). We also draw on one section of a review of interventions for cancer-related shortness of breath this section examined evidence in relation to benzodiazepines - a class of drugs commonly used for sedation (Ben-Aharon, Gafter-Gvili et al. 2008).

Controlled comparisons and randomised trials (which can generate what is classed as ‘strong’ evidence) have not been performed in relation to sedation at the end of life. They would be ethically implausible (Maltoni,

Scarpi et al. 2012) and furthermore, there is enough alternative evidence to indicate that sedation has positive effects – so it would be inappropriate to randomise patients not to receive sedation. Most evidence comes from observational studies, the majority of them quantitative, these track and compare dying patients who have and have not received sedation as part of the natural course of their care. The prospective studies are stronger because data are not affected by limitations of memory and of clinical notes.

There are multiple reports indicating that settings and countries vary in the number of patients who are prescribed sedation at the end of life. The most recent review (Maltoni, Scarpi et al. 2012) found that studies following cohorts of patients at the end of their lives report between 15 and 67% of them receive sedation; this large range probably reflects differences in terminology and definitions used in different studies. Delirium, shortness of breath and pain are the most commonly reported indications for using sedation, but again, studies report considerable variation. In particular, whilst most studies report use of sedation for relief of psychological distress, there are some studies that do not mention it at all (Maltoni, Scarpi et al. 2012). The most commonly used family of drugs are benzodiazepines; psychotropic drugs are also frequently used (Maltoni, Scarpi et al. 2012). This is consistent with the European guidance and evidence indicating these drugs are effective in relieving symptoms (Cherny, Radbruch et al. 2009).

Potential adverse outcomes associated with sedation at the end of life include impairment or loss of the patient's ability to interact, distress amongst family members, and distress amongst members of the care team. A recent review sought empirical studies of sedation at the end of life that included evidence about family members' experiences (Bruinsma, Rietjens et al. 2012). They found that the majority of evidence is indirect, that is, the data on family perspectives largely consist of reports by professional caregivers rather than being gathered directly. Also, the data are often gathered retrospectively via case-note review. Thus, the evidence is weak to moderate. The review found family members were reported to be involved in decision-making in 69-100% of cases. The majority of family members were reported to be comfortable with the use of palliative sedation, but several studies found that relatives were distressed by its use: the reviewers note: "On the one hand, relatives want the patients' suffering to end; on the other hand, they expressed concerns regarding the aim of sedation, the patients' well-being, and their own well-being" (Bruinsma, Rietjens et al. 2012, p441-2).

Potential risks of sedation at the end of life include agitation (as a paradoxical effect of the medications) and hastening death. The systematic review and expert consultation by Cherny et al (2009) which examined multiple sources of evidence, concluded that use of sedation at end of life does not hasten the death of patients overall. Similarly, Sykes and Thorns' review (2003) concluded that "most of the evidence suggests that in the context of specialist palliative care [sedation] is not associated with shortening of life." P317. There have been reports of small numbers of patients (less than 4%) being judged by doctors as having death hastened by sedation administered within research trials (Morita, Chinone et al. 2005; Sykes and Thorns (2003). Sykes and Thorns (2003, p317) report one of their own studies in a specialist palliative care unit of 238 patients, of whom 48% were treated with sedatives. They judged that in only two cases was the doctrine of double effect possibly relevant to patients who were treated with sedatives. As we noted earlier (Footnote 13) the double effect doctrine or argument "is used as an ethical justification for the specific risk of foreseeable life shortening as a result of a medical treatment." (Sykes and Thorns 2003, p317; see also George and Regnard 2007). In the two cases Sykes and Thorns report, the condition of each patient was rapidly deteriorating and they were very disturbed. In relation to the double effect doctrine (see footnote 14) and its relevance to sedation, Sykes and Thorne conclude that "although the doctrine is a valid ethical device, it is, for the most part, irrelevant to symptom control at the end of life. To exaggerate its involvement perpetuates a myth that satisfactory symptom control at the end of life is inevitably associated with hastening death. The result can be a reluctance to use medication to secure comfort and a failure to provide adequate relief to a very vulnerable group of patients" (Sykes and Thorns 2003, p317).

In terms of concurrent use of other pharmacological treatments, one well-designed randomised trial found midazolam – a benzodiazepine frequently used in sedation - enhanced the effectiveness of opioids in the treatment of dyspnoea at the end of life (Ben-Aharon, Gafter-Gvili et al. 2008). More broadly, the EAPC framework guidance states that “Medications for symptom palliation used before sedation should be continued, unless they are ineffective or have distressing side effects. Medications that are either inconsistent with or, irrelevant to, the goal of patient comfort may be withdrawn generally.” (Cherny, Radbruch et al. 2009, p 587).

Key messages in detail

State of the evidence:

- Overall: No randomised controlled studies have been conducted, and it would be ethically and clinically impossible to conduct the kind of controlled trials that would produce what is conventionally thought of as strong evidence (Maltoni, Scarpi et al. 2012).
- Evidence of effectiveness The moderate strength evidence that exists indicates that sedation in the last days and hours of life is effective in relieving refractory symptoms, and that when its use is proportionate to these symptoms it does not hasten an already expected death (Cherny, Radbruch et al. 2009; Sykes and Thorns 2003).

Implications:

These comprise a brief summary the EAPC’s ten item framework (Cherny, Radbruch et al. 2009). For further detail, the full document should be consulted.

- Advance discussion: Careful discussion, if possible in advance of the last days and hours of life is needed in relation to decision-making about sedation at the end of life, and should include the multidisciplinary team, patient and family members.
- Evaluation by experts before and during sedation:
 - Patients should be evaluated before and during sedation by a senior physician with experience in palliative care, a palliative medicine expert, or a palliative care team
 - Evaluation should include refractoriness of symptoms, the patient’s capacity to make decisions, and an estimation of anticipated remaining lifespan
 - In the case of existential or psychological distress: clinicians skilled in psychological care should be involved in evaluation; decisions should be made in multidisciplinary case conferences; and respite rather than continuous sedation should be the first option
- Careful documentation:
 - Decisions about sedation should be carefully documented
 - Refractory symptoms for which sedation is being used should be carefully specified and documented
- Dosage: sedation should be titrated and proportionate, i.e. it should be at the lowest level necessary to provide adequate relieve of suffering.
 - Apart from in emergency situations, the first attempt should be at intermittent or mild sedation
 - Deeper sedation should be used when mild sedation has been ineffective, but might be selected first in cases including where suffering is intense and death is anticipated within hours or a few days
 - For patients viewed as imminently dying, downward titration of drug doses should not be used as this places the patient at risk of recurrent distress

- Initiating sedation: medications should ideally be started by a physician and a nurse together, with patient initially being assessed at least once every twenty minutes until adequate sedation is achieved, and subsequently at least three times per day.
- Care during sedation:
 - Evaluation of sedation and other observations: evaluation by staff with expertise in palliative and end of life care should continue – see above. However, where the goal of care is to ensure comfort until death for an imminently dying patient, the only critical observations should be those pertaining to comfort (and not heart rate, blood pressure and temperature)
 - Medications for symptom palliation used before sedation should be continued unless they are ineffective or have distressing side effects
 - Clinically-assisted hydration and clinically-assisted nutrition: decisions about clinically-assisted hydration and nutrition should be treated as independent of the decision about sedation itself
 - Dignity and basic care should be maintained: the care team must always maintain the same level of humane dignified treatment as before sedation; oral care, eye care, toilet, hygiene and pressure wound care should be provided on the basis of the patient's wishes and the estimated risks or harms in relation to goals of care
- Supportive care of family members and effective communication with them: the team must recognise that family members can find the sedation of their relative profoundly distressing. The team must provide supportive care including regular informational and supportive communication, and in hospitalised patients staff should make every effort possible to provide people with privacy for emotional and physical intimacy. These efforts should include: minimising restriction of visiting, availability of basic supports including tissues, chairs, water, access to a telephone, and opportunity to sleep in the room or nearby.
- After death: family members should be provided with the opportunity to talk with care providers after their relative's death.

RESEARCH IN PROGRESS

We are aware of a number of research studies in progress that are highly relevant to the review questions considered in this report. In particular, a number of studies in progress are examining the impacts of the Liverpool Care Pathway for the dying phase or adaptations thereof; these include large scale, multicentre, and controlled comparative studies.

Integrated care pathways for management of the dying phase in end of life care

1. A cluster randomised controlled trial of the effects of the Liverpool Care Pathway in acute hospitals in Italy (Costantini, Ottonelli et al. 2011)
2. A randomised controlled trial of use of the Liverpool Care Pathway in residential care homes (Brännström and Lindqvist 2011)
3. A matched case study of the impact and economics of the Liverpool Care Pathway in residential care and intensive care units (Ellershaw, Haycox et al. 2010)
4. A before and after study on the impact of introducing a brief end of life tool which uses the same principles as the Liverpool care pathway, but is condensed into a more brief format (Reid, Gibbins et al. 2013)
5. A qualitative observational and interview study examining care of people with dementia dying in hospitals and of their family members (Pollock, Porock et al. 2010) includes evidence on the use and implementation of care pathways for the dying phase in end of life care for people with dementia
6. A mixed methods study examining outcomes of a dying care pathway in four stroke units in Scotland from the perspective of care quality, family members' perspectives, and staff perspectives (Cowey et al. 2011)
7. A realist evaluation of integrated care pathways in palliative care (Dalkin, Jones et al. 2012)
8. A European Commission funded four-year programme: 'InSup-C: Patient-centred integrated palliative care in advanced cancer and chronic disease' began in November 2012. It will investigate the use of integrated care pathways for palliative care and make recommendations (Hasselaar and Payne 2012)

Sedation:

1. A Cochrane review is underway in relation to the evidence on the effects of pharmacological palliative sedation on quality of life and on specific refractory symptoms (Beller, van Driel et al. 2012). It is expected to report its findings in 2013 (Beller, Personal communication)
2. A multicentre, cross-European qualitative study on the perspectives of clinical staff and bereaved family members on the use of continuous sedation until death for cancer patients (Seymour, Rietjens et al. 2011) will report its findings in 2013 (Seymour, Personal communication)

IMPLICATIONS FOR RESEARCH

Background

We list below a number of recommendations for research that arise from our analysis of key evidence gaps. These recommendations were generated through discussion within the review team and with the End of Life Care programme and its networks. First though, we provide some background on the kinds of research needed and the challenges of conducting it.

The published evidence examined in this report indicates the value of research which includes a variety of methods both qualitative and quantitative, i.e. mixed methods projects. For instance, in relation to clinically-assisted hydration, we noted that the findings of a multicentre randomised controlled trial (Bruera, Hui et al. 2013) and those of a related qualitative interview study of the views and understandings of patients and family members (Cohen, Torres-Vigil et al. 2012) provided important and somewhat contrastive findings. As we explained, both elements of this evidence are highly relevant in informing the decisions that have to be made by clinicians, patients and family members about clinically-assisted hydration in practice.

As we noted earlier, the conduct of research into dying and end of life care entails management of difficult challenges including sensitively making contact and effectively involving and recruiting people who are dying and those who care for them; designing and implementing appropriate comparison interventions; collecting data including through conducting testing procedures. Fortunately, novel methods of engaging participants in end of life research are being developed: recent studies have reported innovative strategies for recruitment, consent, and collaborative multicentre research (Addington-Hall and McPherson 2001; Sigurdardottir, Haugen et al. 2010; Wilson, Pollock et al. 2010; Payne, Seymour et al. 2011; Gibbins, Bloor et al. 2012; Gibbins, Reid et al. 2012; Reid, Gibbins et al. 2013). However, solutions are yet to emerge in relation to the considerable challenges associated with current institutional barriers and the environment of the NHS. Attaining institutional bodies' permissions to conduct research into dying and end of life care, and to conduct mixed methods research, is challenging. Great sensitivity is required in undertaking research into death and dying and it is right to subject this to rigorous scrutiny and appraisal¹⁵. However, the intrinsic difficulty of conducting research into dying and end of life care is compounded by some of the features of current research governance structures (Pollock 2012). Regulatory structures can be ill-fitted to the emergent and negotiated processes involved in mixed methods and end of life care research. Regulatory shortcomings result in costly delays and difficulties in recruitment (Fudge, Redfern et al. 2010; Thompson and France 2010) which undermine the success and quality of research and consequently, the capacity of findings to be applied directly for patient benefit. The Health Research Authority was established in 2011 with a remit to support and promote a robust and efficient regulatory and governance framework. Mixed methods, qualitative, and end of life care research would benefit from increased efficiencies in terms of the framework for gaining access and permissions, but it is not yet clear what the work of the Health Research Authority will be in this regard.

¹⁵ It is worth noting that participants in qualitative studies - including studies about end of life - report their participation to be a positive experience even when it involves discussion of topics and experiences which they anticipate to be emotionally challenging and distressing (Lowe et al, 2006; Pesson, 2008).

Research priorities

In light of the evidence reviewed, and of research we know that is already in progress, we propose the following to be research priorities.

- An overall prioritisation of research on:
 - end of life in non-cancer patients
 - quality of life and quality of care from the perspective of patients and family members
 - psychological effects and sequelae for family members
 - UK based research: given wide cultural differences in attitudes, communication, and clinical practice in relation to end of life care, is important in order to inform UK policy and practice
 - research in relation to end of life and end of life care for cultural and ethnic minority groups is needed for similar reasons
- Prioritisation of studies and research programmes that entail mixed methods. These are required in order to generate knowledge and understanding of multiple perspectives, as is required to inform real life decision making (as illustrated in our discussion above on the different forms of evidence about clinically-assisted hydration).
- Use of the criteria proposed by the Cochrane Effective Practice and Organisation of Care Group (2002) for the design of rigorous studies, but adaptation of these so as to encompass qualitative data collection and analyses. Commissioners should recognise that studies designed in this way are expensive.
- Specific research on areas including:
 - Collating currently available guidance, expert practice and recently reported innovations for recruiting and conducting research with patients who are or may be in the dying phase
 - Studies using the insights of implementation science to examine fidelity of implementation pathways for the dying phase in end of life care with actual recommendations and formal policies, and to examine barriers and facilitators to implementation in acute hospital care
 - Description and analysis of episodes where people are predicted to die, and are placed on pathway-based care, but do not go on to die in that care episode
 - Research on how experienced clinicians diagnose dying within days or hours, and how accurate their diagnoses are. This should be based on collection of data during actual episodes of care (i.e. contemporaneously) rather than using retrospective review
 - Research on decision-making and communication in relation to end of life care, and comparison of practice with professional guidance (General Medical Council 2010) and the law – particularly the Mental Capacity Act (Department for Constitutional Affairs 2005)
 - Direct observational research using recordings of end of life care conversations between patients, family members and experienced staff to provide knowledge about how experienced end of life care practitioners communicate, and about the effects of those practices
 - Research on clinically-assisted hydration in relation to subgroups of patients who have symptoms that are particularly sensitive to hydration levels

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