What are the most important questions for palliative care from the health services point of view?

Irene J Higginson
Cicely Saunders Institute
Department of Palliative Care, Policy & Rehabilitation
King’s College London
www.csi.kcl.ac.uk
Thank you for inviting me

Outline

<table>
<thead>
<tr>
<th>New era of society and health care: new landscapes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Five key health services research questions</td>
</tr>
<tr>
<td>Transformative research</td>
</tr>
<tr>
<td>Methods to evaluate complex interventions</td>
</tr>
</tbody>
</table>
Disclosures

• Have developed and evaluated some models of palliative care services that are available freely
• Have developed measurement tools that are available freely
• No pharmaceutical/tobacco etc funding
• No spin out company or shares
New era, new landscapes

• Ageing
• Numbers affected by cancer increasing
• New treatments
• Patients living longer
• More co-morbidity
What percent of our GDP is spent on health care?

Source: King’s Fund (OECD) 2013 figures
Figure 1: Total health care spending (public and private) as a proportion of GDP

Denmark: 10.1% EU-14

8.5% UK

Data source: OECD
1. Ageing: worldwide 2000 and 2050

2. Increased cancer survival

3. Increased awareness, screening and treatment

Cancer worldwide. Now v 2025

Incidence

- World
  - All cancers excl. non-melanoma skin cancer
  - Number of new cancers in 2025 (all ages)

- Male
  - Incidence in 2012: 4,500,000
  - Demographic effect: 5,900,000
  - Total: 10,438,997

- Female
  - Incidence in 2012: 4,400,000
  - Demographic effect: 5,100,000
  - Total: 8,572,065

Mortality

- World
  - All cancers excl. non-melanoma skin cancer
  - Number of cancer deaths in 2025 (all ages)

- Male
  - Mortality in 2012: 3,500,000
  - Demographic effect: 3,000,000
  - Total: 6,597,817

- Female
  - Mortality in 2012: 2,900,000
  - Demographic effect: 2,000,000
  - Total: 4,945,055

GLOBOCAN 2012 (IARC) (3.12.2014)
Given this can we afford palliative care?

Now?

In the future?
The future, UK trends and projections 1951-2074

By 2030, 44% of deaths will be in those over 85 years

Where we will die in 2030
If current trends are projected forward

Numbers of home and institutional deaths, E&W 1999 - 2030

Home deaths fall by 40%, > 1/10 die at home

20% more beds

The ‘new’ era of patient and family needs has implications for palliative care

- Ageing, more oldest old
- More multi-morbidity
- More fluctuant trajectories of illness
- Treating later into course of illness

- More deaths in Europe (due to post war boom in birth-rate and ageing)
- In older people physical illness has a greater social, functional and psychological effect
- MORE UNCERTAINTY – services and treatments need to respond to this
May 2014 – World Health Assembly resolution on palliative care, to be integrated into health systems – UICC said – essential health care service for people with chronic and life limiting illness

67th World Health Assembly

Rolling summary of events surrounding the 67th WHA. For immediate updates please follow @UICC @NCDAlliance #WHA67 on Twitter.

23 May 2014: 20h00 | Today, Ministers of Health gave their support to a groundbreaking resolution on palliative care that will help drive national action to reduce barriers to the accessibility and availability of palliative care.

UICC delivered a joint statement (click here to read in full) supported by the European Society for Medical Oncology, the NCD Alliance and a coalition of palliative care and health advocacy groups welcoming the adoption of a comprehensive resolution. In particular, we highlighted the critical importance of:

- Developing palliative care standards and policies, integrating them into health systems, at all levels, across the life course, and embedding them in national NCD plans;
- Offering on-going basic, intermediate and specialist training and education in palliative care – that can be built on existing curricula adapted to local settings;
- Reviewing legislation and policy for controlled medicines (including formulary and patient restrictions, supplementary prescribers, prescription limits, and emergency prescriptions) to improve access and rational use
We need new ways of approaching palliative care for future

• Is model of providing palliative care constantly from initial referral feasible or desirable?
  – Resources and workforce in palliative care
  – Is it right for patients and families
  – Role of short term palliative care?

• Challenge of limited access for many people
  – How to decide and provide? How to measure quality?
  – Role for tools used by generalists (but beware if they don’t have training and context (e.g. hospital) different
Palliative care has moved from rectangles to triangles

Modern concept of palliative care
Palliative care for the 21st century, bow-ties
(Hawley PH, J Pain & Sympt Manage 2014; 47 (1): e2-e5)

Modern Definitions of Palliative Care –
• an approach applying to life-threatening illness and applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life (WHO)

• provides an extra layer of support with relief from the symptoms, pain, and stress of a serious illness (Meier, D)
Deterioration: possible models for some different disease trajectories

- Old Cancer
- Organ Failure, e.g. renal, lung,
- sudden death
- dementia / frailty
- disability threshold
- death

Quality of life vs. Time
Car journeys? The problem of no integration
Car(e) journeys? The problem of no integration
Transformative health services research for the new era of palliative care?

<table>
<thead>
<tr>
<th>Five key questions:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. What are the most effective models/services for palliative care for the new multimorbid populations (e.g. respiratory plus cancer) and their families and who benefits most?</td>
</tr>
<tr>
<td>2. What are the most cost-effective models, especially focussed on home / community care?</td>
</tr>
<tr>
<td>3. How do we ensure safety and quality of palliative care services, including consistent outcomes?</td>
</tr>
<tr>
<td>4. How much should palliative care provide and how much should it educate/train/support?</td>
</tr>
<tr>
<td>5. How do we identify those in need, or should it be a standard for all?</td>
</tr>
</tbody>
</table>
James Lind Alliance – top 10 research questions developed by patients and families – 9/10 top questions were on health services

1. Best ways of providing palliative care outside of working hours?
2. Ways to improve access to palliative care services?
3. What are the benefits of Advance Care Planning?
4. What information and training do carers and families need?
5. How to ensure that staff, including healthcare assistants, are adequately trained to deliver palliative care?
6. Best ways to determine a person’s palliative care needs, then initiate and deliver this care in non-cancer diseases (e.g. chronic obstructive pulmonary disease (COPD), heart failure, motor neurone disease (MND), AIDS, multiple sclerosis, Crohn’s disease, Parkinson’s disease, dementia)?
7. Core palliative care services provided no matter what the diagnoses?
8. What are benefits, and best ways, of providing care in the patient’s home?
9. Best ways to ensure continuity for patients at the end of life. Can palliative care improve this?
10. Best ways to assess and treat pain and discomfort at the end of life in people with communication and/or cognitive difficulties?

But: palliative care has a good track record of innovating new services and a poor record of evaluating them

- Difficulties include:
  - General problems of palliative care research: recruitment, ill population, bias, ethics, measurement of effects/outcomes, attitudes to research
  - Specific issues of evaluating services: Incomplete record of what service is and does, varied implementation, effect of therapist, timing, service developed before evaluation, service IS COMPLEX

- Before we can start to answer the questions about the best models of care we need to know how to do this research
Need transformative health and social care research for complex interventions and complex situations

And new clinical services (and those funding them) need to be willing to ensure that this research is done EARLY in development, as well as continued
Themes in the Cicely Saunders Institute: integrating research, clinical, education, plus patient, family and public engagement:

- **Evaluating and improving care**
  - Cancer
  - Complex disability
  - Neurological
  - HIV/AIDS
  - Renal failure
  - Organ failure
  - Multimorbidity

- **Person centred outcome and assessment measures**
  - Palliative care
  - Outcome Scale (POS)
  - Goal attainment scales
  - Rehabilitation scales
  - Complexity & costs

- **Focused clinical research on symptoms**
  - Breathlessness
  - Depression
  - Pain
  - Spasticity

- **Living and dying in society**
  - Ageing
  - Caregivers
  - Preferences / choice
  - Place of care and death
  - Ethnicity & culture
  - Global health
  - Spirituality

- **Methodological development**
  - Policy and Guidance

- **Collaboration**
  - Dissemination

- **Education**
What is a complex intervention?

an intervention (e.g. treatment, service) with several interacting components

• Components may act both independently and interdependently

• Can be difficult to know which are the “active ingredients”

• Often highly context specific

• Often have multiple outcomes (intended and unintended)
What is a complex intervention in palliative care?

- Service
- Education programme
- Tool used by non palliativists
- Integrated care
- Care pathway

Box 2 What makes an intervention complex?

Some dimensions of complexity

- Number of and interactions between components within the experimental and control interventions
- Number and difficulty of behaviours required by those delivering or receiving the intervention
- Number of groups or organisational levels targeted by the intervention
- Number and variability of outcomes
- Degree of flexibility or tailoring of the intervention permitted

Source: BMJ. 2008 Sep 29;337:a1655. doi: 10.1136/bmj.a1655
Why does it matter?

additional problems for evaluators, over and above usual practical and methodological difficulties, E.g.

- difficulty standardising the design and delivery of the interventions (e.g. treatment, service, pathway)
- and of the control group
- sensitivity to features of the local context, may not be replicated
- organisational and logistical difficulty of applying experimental methods to service or policy change
- length and complexity of the causal chains that link intervention with outcome
Why does it matter?

Consequences of failing to recognise you are dealing with complex interventions:

• Failed studies – when the intervention has an effect
• Positive studies – but no one knows what the active ingredients are – ‘evaluating a ‘black box’
• Results which don’t apply to anywhere else
• Results which can’t be implemented
• Dangerous implementation, failing to recognise key components that are needed, and missing them
• Cutting costs by policy makers to implement without key ingredients, because not shown they are important
MRC guidance on developing and evaluating complex interventions (need all these)

Feasibility/piloting
1 Testing procedures
2 Estimating recruitment /retention
3 Determining sample size

Development
1 Identifying the evidence base
2 Identifying/developing theory
3 Modelling process and outcomes

Palliative care researchers and clinicians can address any of these components

Evaluation
1 Assessing effectiveness
2 Understanding change process
3 Assessing cost-effectiveness

Implementation
1 Dissemination
2 Surveillance and monitoring
3 Long term follow-up

Craig et al 2008, MRC, and in BMJ. 2008 Sep 29;337:a1655. doi: 10.1136/bmj.a1655
Applying the MRC guidance in palliative care in practice

• Define and describe the context
• Define and describe the intervention and the control
• Define and describe theoretical basis and proposed mechanism of action
• Consider active ingredients
• Match research methods to questions, consider mixed methodologies
• Consider impact on different stakeholders
Development for palliative care: Methods Of Researching interventions and services in palliative and End of life Care (MORECare)

- Palliative and End of Life Care research presents its own unique problems
- MRC made a call through the Methodological Research Programme to evaluate this
- Collaboration between King’s College London, University of Manchester, University of Edinburgh and University of Aberdeen with international Delphi exercises and consultation

For all results see: www.csi.kcl.ac.uk/morecare.html
Evaluating Complex Interventions in palliative and end of life care: MORECare focussed on these topics in research

Statistical Analysis

Health economic assessment

Ethics

Mixed Methods Research

Outcome measurement

MORECare trying to make it more manageable

Twitter @CSI_KCL
Three systematic reviews


MORECare Transparent Expert Consultation (TEC)

**Who were the experts?**

Expert panel and other experts identified in literature to agreed focus, scope literature and identify topic experts and appropriate multiagency and discipline mix (from health care and clinical research, not only palliative care) for summit meeting.

We aimed always to include experts in the methods external to palliative and end of life care, researchers, clinicians and service developers in palliative care, patients, consumers and few policy makers.
Evaluating complex interventions in End of Life Care: the MORECare Statement on good practice generated by a synthesis of transparent expert consultations and systematic reviews

Irene J Higginson, Catherine J Evans, Gunn Grande, Nancy Preston, Myfanwy Morgan, Paul McCrone, Penney Lewis, Peter Fayers, Richard Harding, Matthew Hotopf, Scott A Murray, Hamid Benalia, Marjolein Gysels, Morag Farquhar, Chris Todd and on behalf of MORECare

Main guidance, plus 4 papers and an abstract from the TEC

 Mostly open access
Patient, caregiver, health professional and researcher views and experiences of participating in research at the end of life: a critical interpretive synthesis of the literature

Marjolein H Gysels*, Catherine Evans and Irene J Higginson

Results: Of a total of 239 identified studies, 20 studies met the inclusion criteria, from: the US (11), the UK (6) and Australia (3). Most focused on patients with cancer (12) and were conducted in hospices (9) or hospitals (7). Studies enquired about issues related to: EoL care research in general (5), specific research methods (13), and trial research (2). The studies evaluating willingness to participate in EoL care research showed positive outcomes across the different parties involved in research. Factors influencing willingness were mainly physical and cognitive impairment. Participating in research was a positive experience for most patients and carers but a minority experienced distress. This was related to: characteristics of the participants; the type of research; or the way it was conducted. Participatory study designs were found particularly suitable for enabling the inclusion of a wide range of participants.

Conclusion: The evidence explored within this study demonstrates that the ethical concerns regarding patient participation in EoL care research are often unjustified. However, research studies in EoL care require careful design and execution that incorporates sensitivity to participants’ needs and concerns to enable their participation. An innovative conceptual model for research participation relevant for potentially vulnerable people was developed.
Results from Evans, C et al, *Palliat Med.* 2013 Dec;27(10):885-98 most studies were feasibility context of MRC Framework

Craig et al 2008, MRC
MORECARE recommendations, studies must move from

- Theory, development and modelling – try to understand mechanism of intervention
  
  If successful

- Feasibility of intervention AND study design and mechanism / active ingredients
  
  If successful

- Evaluation-with comparison- use randomised trial or appropriate alternative. Assess outcomes and intervention processes
  
  If successful

- Rollout and monitor results of wide implementation

Feedback and revisions

Consider implementation implications at each step
In evaluation for complex interventions need to optimise intervention and methods of evaluation at same time.

Campbell, N. C et al. BMJ 2007;334:455-459
## MORECARE STATEMENT: 36 points

<table>
<thead>
<tr>
<th><strong>Recommendations</strong></th>
<th></th>
</tr>
</thead>
</table>
| **Introduction/ background** | 1. Present theoretical framework for the intervention and levels of need established  
2. Present objectives appropriate to the level of intervention development |
| **Design** | 3. Indicate and justify stage in MRC guidance for development and evaluation of complex interventions, e.g. feasibility, preliminary evaluation, efficacy / cost effectiveness and wider effectiveness  
4. Feasibility stages should test both feasibility of the intervention and of methods of evaluation, including outcome measurement  
5. Justify methods, considering appropriate use of existing data sets and secondary analysis as these may produce rapid information  
6. Justify methods of empirical studies considering mixed methods, observational studies and randomised trials |
| **Study team** | 7. Ensure involvement from: (i) consumers, patients and caregivers; (ii) relevant clinicians; (iii) relevant methodologists to develop study questions, questionnaires and procedures; and (iv) researchers familiar with the challenges in EoLC studies  
8. Ideally involvement should be well established and continuing, beyond a specific study, with joint meetings or rotations between clinical and research staff |
Ethics

- It is **ethically desirable** to undertake research into palliative and end of life care and **can be unethical not too**.

- **Collaborate with patient and caregivers** in the design of the study and any ethical aspects to incorporate their comments.

- **Attend** the ethics committee meeting **with a caregiver or patient**, as a means to help the committee better understand the patient point of view.

- Ensure **proportionality** in patient and caregiver **information sheets**, appropriate to the study design and level of risk, as excessive information in itself can be tiring/distressing for very ill individuals.

- Allow **for reflection and comment** in the questionnaires?

- Create a **Research Ethics Network** for Palliative and End of Life care to further and disseminate best practice.

- **Train those working in on ethics and governance** committees in the specific issues and wishes of patients in palliative and end of life care and their families.

- **Review and amend the law** regarding consent so that **advance consent** for studies other than clinical trials of medicinal products applies.

Outcome measurements

When should the primary outcome or end point be measured? A trade off between attrition and time for the intervention to have an effect.

Choose an outcome measure that is validated in one setting or several?

Some challenges

Should I use staff, patient, observer, or proxy/caregiver reported measures

Twitter @CSI_KCL
# Outcomes – top recommendations

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Median (1&lt;sup&gt;st&lt;/sup&gt; - 3&lt;sup&gt;rd&lt;/sup&gt; quartile)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Measurement properties</strong></td>
<td></td>
</tr>
<tr>
<td>...easy to administer and interpret (e.g. short and low level of complexity)</td>
<td>8 (7-9)</td>
</tr>
<tr>
<td>... applicable across care settings to capture change in outcomes by location</td>
<td>8 (7-9)</td>
</tr>
<tr>
<td>... responsive to change over time and capture clinically important data</td>
<td>8 (7.8-8)</td>
</tr>
<tr>
<td><strong>Timing</strong></td>
<td></td>
</tr>
<tr>
<td>Time points require clear identification to establish a baseline</td>
<td>7 (6-9)</td>
</tr>
<tr>
<td>Time points need to be established before conducting the evaluation.</td>
<td>7 (5-8)</td>
</tr>
<tr>
<td>when prospective measurement is used, end points should correspond to when the effect of the intervention is expected to take place.</td>
<td>7 (6-8)</td>
</tr>
<tr>
<td><strong>Other properties</strong></td>
<td></td>
</tr>
<tr>
<td>...Valid and reliable in the relevant population</td>
<td>8 (7-9)</td>
</tr>
<tr>
<td>... Use a measure that can be integrated into clinical care</td>
<td>8 (7-9)</td>
</tr>
<tr>
<td>... Data from patients and proxy measures should be differentiated in the dataset.</td>
<td>8 (7-9)</td>
</tr>
</tbody>
</table>

Palliative care Outcome Scale (POS) and Edmonton Symptom Assessment System both meet these criteria.
Palliative care Outcome Scale (POS) and Edmonton Symptom Assessment System both meet these criteria
Attrition is to be expected and if you don’t have attrition you may have the wrong population in the study

Define and report different types of attrition, consider how timing of data collection effects attrition.

**Taxonomy of missing data to understand different types** –
- ADD – attrition due to death;
- ADI – attrition due to illness;
- AaR – attrition at random

Investigate patterns of missing data and/or the conduct of the study to identify the cause of missing data, to inform choice of imputation method.

A clear statistical analysis plan required that identifies how to deal with missing data

• ensure appropriate multi-disciplinary skills mix or training of team define the theoretical paradigm, method of integrating results and safeguards to ensure rigor at the outset

• plan investigation carefully to avoid undue burden of qualitative and quantitative questionnaires – perhaps dividing data collection or selecting questions and/or samples appropriately

• take into account any potential therapeutic effect of qualitative interviews where participants can express their feelings, if these are similar to components of the intervention

• ensure research nurses or those collecting data are appropriately trained in qualitative data collection

HEALTH ECONOMICS

Much disagreement – but some areas of health economic agreement

- Assess costs from a SOCIETAL perspective

- Need to understand more about preferences

- Develop choice approaches and palliative care measures in QALYS
### MORECARE: other recommendations

<table>
<thead>
<tr>
<th><strong>Recommendation</strong></th>
<th></th>
</tr>
</thead>
</table>
| **Clinician / researcher collaboration** | 4. Increase collaboration and understanding between clinicians and researchers in EoLC through rotations, joint departments and exchanges  
5. EoLC organisations to create a research-aware culture for practitioners by informing practitioners and patients on admission to a service that the organisation is actively involved in research  
6. Develop specific training for practitioners in palliative and end of life care about research practice, its value and how to recruit  
7. Introduce screening questions about patient/family willingness to be approached for research (as a general principle) in routine initial assessments on entry to palliative care services |
| **Funders** | 8. Develop collaboration to ensure that funding supports advancement in knowledge, where one study builds from the finding of another and there is progression to multicentre studies, full evaluations and cost effectiveness studies  
9. Assess study proposals against the MORECare statement |
| **National bodies/strategy** | 10. Develop repositories of routine data and from specific studies which can be used for secondary analysis to quickly answer current questions  
11. Develop collaboration to take forward the MORECare statement |
| **Journal editors** | 12. Statistical – next presentation  
13. Use MORECare statement when assessing studies, alongside other established criteria, e.g. STROBE, CONSORT |
Effectiveness of early integration of palliative care: randomised trial evidence, UK evidence, NIHR funded

- 105 patients randomised to early palliative care integrated with respiratory services
  - Cancer, COPD, ILD

- Significant benefit in primary outcome, a component of quality of life, 16% better in early palliative care group
  - Significant survival benefit
  - No difference in costs

Source: Higginson et al Lancet Respiratory Medicine, Dec 2014; 2(12): 979-987 DOI:10.1016/S2213-2600(14)70226-7
Illustrative quotes about valued interventions and approach of the Breathlessness Support Service, 2014

‘It’s improved my ability to cope with it better; my breathlessness has improved [...]. Going to the clinic has done that because before I would get into a panic when I was breathless, but now I can sit down use my fan, wet my face, read my laminate (breathlessness poem) and I calm down pretty quick so, that’s is um, it’s funny how a laminate (breathlessness poem) could be so helpful (laughs). It’s embarrassing to know that just that, that writing, to be able to read it it calms me down so well.’  (Female, COPD)

“The advice they gave me which improved me mentally and my walking stick that helped me physically. It’s overall, its good overall, I’m happy. I’m glad. I’m glad I did come.’  (Male, Cancer)

Source: Higginson et al Lancet Respiratory Medicine, Dec 2014; 2(12): 979-987
DOI:10.1016/S2213-2600(14)70226-7
Non-experimental designs can answer important questions about access, outcomes, differences.

- **Experimental designs**
  - Randomized controlled trial

- **Non-experimental designs** (observational designs)
  - (A) Population level data
    - Ecological study
  - (B) Individual level data
    - Case report/series
    - Cross-sectional study
    - Case-control study
    - Cohort study (prospective/retrospective)
E.g. National routinely collected data has been used to explore effects of Strategies over time

Reversal of the British trends in place of death: Time series analysis 2004–2010


- Reversal linked to strategies and support

- But in non cancer, children, small or no effect

- New paper coming out in BMC Medicine 1 Feb….
Explore regional differences in ecological studies
Variation in place of death - 2006-2010

At home

In hospital

Source: Guidecare project, Cicely Saunders Institute, Higginson, Ho, Wei. Supported by NIHR.
• Longitudinal study has challenged ‘single trajectory per condition’ model. It is more complex than this.
• Within one condition different trajectories are encountered.
• Many patients also have multiple co-morbidities
• Individual patients often have more fluctuating trajectories

Bausewein et al Pall Med 2010; 24: 777
Can use cross sectional data to explore levels of concern at different stage of illness – e.g. psychological concerns

Clinical audit / clinical databases, descriptive studies and surveys

• Collect data on a more representative group of patients - show effects in real world
  – Can identify strengths and weaknesses
  – Cannot test ‘cause and effect’ but can often highlight areas for further research, and data can be modelled to explore associations, differences and ‘cause’

Danish Palliative Care Database (DPD) – excellent example of what can be achieved….

• Need collaboration and similar measures
What should we do?

• Ensure more and more research is multicentre
• Conduct studies into new models of care and treatments — so our teams can provide the best — but not only through randomised trials
• Build better evidence understanding and skills into our education — so we can develop evidence based practice
• Use a few standard outcome measures in clinical practice — so that clinical data sets could be pooled and comparison is easier
<table>
<thead>
<tr>
<th>Take home thoughts</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New era of palliative care: new landscapes</strong></td>
</tr>
<tr>
<td><strong>Transformative models of care and treatment</strong></td>
</tr>
<tr>
<td><strong>Transformative research Methods to evaluate complex interventions</strong></td>
</tr>
</tbody>
</table>
Acknowledgements

• Colleagues and collaborators, patients and families
• Funders, National Institutes for Health Research (NIHR) and Cicely Saunders International
• For resources go to :
  • www.csi.kcl.ac.uk
  • www.pos-pal.org