

1

PRC

International multicentre studies - challenges and solutions

Stein Kaasa
Head of Department and Professor
Dept. of Oncology Oslo University Hospital and University of Oslo, Norway
Leader PRC NTNU Trondheim, Norway



www.ntnu.no/prc European Palliative Care Research Centre (PRC)

2

The research processes

- Why do we need multicentre studies?
- How to conduct them?
 - The initial phase
 - The planning phase
 - The protocol writing phase
 - The funding phase
 - The running (of the trial) phase
 - The analysis and writing up phase

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

3

Lessons learned

- Thinks takes time
- Leadership is needed at all sites
- Large variations in ability to conduct research
 - Infrastructure

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

4

“Leadership is needed “

www.ntnu.no/prc European Palliative Care Research Centre (PRC)



7

The potential positive outcomes of international collaboration

- Sample size
- Representativity (external validity)
- More collaboration
- Exchange of ideas and knowledge

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

8

“In hospice care we are not doing research-it is unethical”

- Some of the history of palliative care research
- Does it still apply?

www.ntnu.no/prc European Palliative Care Research Centre (PRC)



11

The potential negative outcomes of international collaboration

- Costs
- Selection bias
- Monitoring - cannot do it
- Time
- Net outcome for each centre
 - Publication
 - PhDs
 - Postdocs

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

12

Do we need multicentre studies and international collaboration?

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

13

Methodological challenges

Anno Aachen 2005

- Most studies have been small
- Some suffer from a substantial attrition rate
- Even for pain intensity no consensus on how to measure
- Example...several recent Cochran rew.
- Lack of information on differences expected to be detected

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

14

The approach to systematic symptom assessment in palliative care – PAT-C

Hjermstad MJ, Loge JH, Kaasa S on behalf of the PAT-C working group

Background

- Palliative care patients have high levels of various subjective symptoms
- Low consistency on how to assess these systematically
- Subjective symptoms are the main targets for:
 - Clinical interventions
 - Palliative care research
- A valid, international tool for symptom assessment will yield evidence-based knowledge for clinic and research

Overall PAT-C aims

To develop a comprehensive symptom assessment tool by the use of item response theory (IRT) and bedside computer adaptive technology (CAT).

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

15

EAPC Cross Sectional Survey

Anno Lyon 2002

Protocol writing Committee

- Stein Kaasa
- Geoff Hanks
- Karin Torvik
- Nathan Cherny
- Franco de Conno

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

16

Main objectives

- Establish a network for future prospective studies
- Identify patients using specialist palliative care
- Provide detailed information on the use of strong opioids

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

17

“What is your Centre based upon?”

(%)	No of patients (%)	No of Centres
Hospice	1143 (38)	36 (26)
General Hospitals	813 (27)	47 (33)
Home care	458 (16)	24 (17)
Cancer Hospital	229 (8)	12 (9)

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

18

Time since referral to the palliative care program

Time	%
<6 months	75
1/2 year - 2 years	22
> 2 years	3

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

- 19
- ### Place of care
- #### Are there any variations?
- Anticipated life expectancy
- www.ntnu.no/prc European Palliative Care Research Centre (PRC)

- 20
- ### Expectations - Place of palliative care delivery
- “Hospice is to be expected to care for the imminently dying”
 - “A more mixed population is expected in general hospitals”
- www.ntnu.no/prc European Palliative Care Research Centre (PRC)

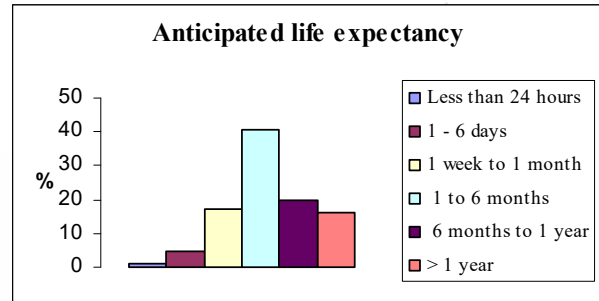
21

Anticipated life expectancy

- Less than 24 hours
- 1 - 6 days
- 1 week to 1 month
- 1 to 6 months
- 6 months to 1 year
- \geq 1 year

22

Anticipated life expectancy



23

Place of palliative care delivery versus anticipated life expectancy

	General hospital	Hospice	Homecare (spec. adv. Service)
1-6 days	7	7	3
1 week to 1 month	18	22	10
1 to 6 months	42	39	45
6 months to 1 year	21	17	24
\geq 1 year	12	15	18

24

Use of opioids by Country (%)

Type of opioids	Belgium	UK	Greece	Norway	Spain
Morphine SR	7	17	3	29	16
Morphine parenteral	1	0	3	2	0
Fentanyl TD	26	9	42	13	10
Tramadol PO	6	4	0	1	10
Codeine comb.	2	9	22	10	1

25

Comments - opioids by country

- There are major variations between countries with respect to the use of opioids.
 - Morphine SR 3% to 43% of the sample
 - Fentanyl TD 0% to 50% of the sample

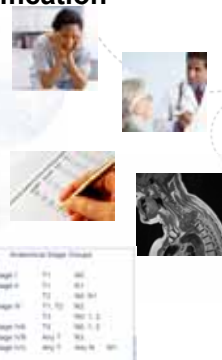
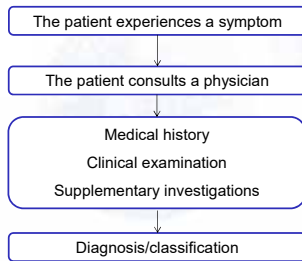
26

The heterogeneity of palliative care

- At centre level – staff and place in the healthcare system
- Patient population
- Treatments
- And much more.....
- Were we and are we in trouble?
 - Understanding the data from studies?
 - In conducting multicentre studies?

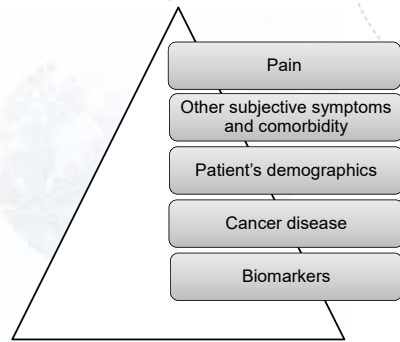
27

The diagnostic process 'It is all about classification'



28

Content of an ideal classification system



Cancer pain classification International agreement on including:

- Pain intensity



- Breakthrough pain



- Neuropathic pain



- Psychological distress



EAPC basic dataset pilot study

- Recruiting centers
 - Norway (starts Spring 2015)
 - Canada
 - Portugal
 - Italy
 - More centres are welcome

Sigurdardottir KR et al. The European Association for Palliative Care basic dataset to describe a palliative care cancer population: Results from an international Delphi process. *Palliat Med.* 2014

Implementation of new knowledge Are we good enough?

- SCP – a method for implementation?
- Are we “cutting waste”?

THE LANCET Oncology

Definition and classification of cancer cachexia: an international consensus

Kenneth Fearon*, Florian Strasser*, Stefan D Anker, Ingvar Bosaeus, Eduardo Bruera, Robin L Fainsinger, Aminah Jatoi, Charles Loprinzi, Neil MacDonald, Giovanni Mantovani, Mellar Davis, Maurizio Muscaritoli, Faith Ottery, Lukas Radbruch, Paula Ravasco, Dedan Walsh, Andrew Wilcock, Stein Kaasa, Vickie E Baracos

33

THE LANCET Oncology
Volume 375, Number 2, February 2012, Pages 205-206



Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC

Augusto Caraceni*, Geoffrey Hanks*, Stein Kaasa*, Michael J Bennett, Cinzia Brunelli, Nathan Cherny, Ola Dale, Franco De Conno, Marie Fallon, Magdi Hanna, Dagny Foksvåg Haugen, Gitte Juhl, Samuel King, Pål Klepstad, Eivor A Lougansel, Marco Maltoni, Sebastiano Mercadante, Maria Nabal, Alessandra Pigni, Lukas Radbruch, Colette Reid, Per Sjogren, Patrick C Stone, Davide Tassinari, Giovambattista Zeppetella, for the European Palliative Care Research Collaborative (EPCRC), on behalf of the European Association for Palliative Care (EAPC)

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

34

Is it applied?

- No and yes ?
- Why?
- Lack of implementation power?
- Lack of interest in common standards?
 - More important “me and my patients”?
- And many other explanations?

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

35

The future

- Plan A: Conduct large enough international intervention studies which answer clinical relevant research questions
 - “Keep it simple-stupid”
- Plan B: Think big
 - Need to understand the entire patient population
 - And in that sample conduct intervention studies

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

36

Plan B: Think big
An example – we are planning

- How to treat , care for and organize
- Patients with brain metastasis
- And how does it affect the family?
- Few studies
- Heterogeneous population
- Fragmented RCTs

www.ntnu.no/prc European Palliative Care Research Centre (PRC)

37

Plan B: Think big An example – Brain metastasis

- All patients in a defined region or country in a prospective registry-with a prospective design based upon Standardized Care Pathways
 - Clinical data
 - Place and type of care
 - PROMs
- Conduct several RCTs in the cohort
 - Surgery
 - Radiotherapy
 - Chemotherapy
 - “Best supportive and palliative care”
 - Family care

38

Plan B: Think big An example – net benefits

- Total insight in to a very heterogeneous population with large degree of morbidity
- Understanding of the effects of the treatment in and outside RCTs at all levels of care
- Understand the effects at health care provider level
- Have an unique system to fast and effective start new intervention studies
- A system for prospective evaluation of the effects of the SCP



40



41



www.ntnu.no/prc

42



www.ntnu.no/prc

European Palliative Care Research Centre (PRC)