

# Quality of life in the end of life phase of high-grade glioma patients

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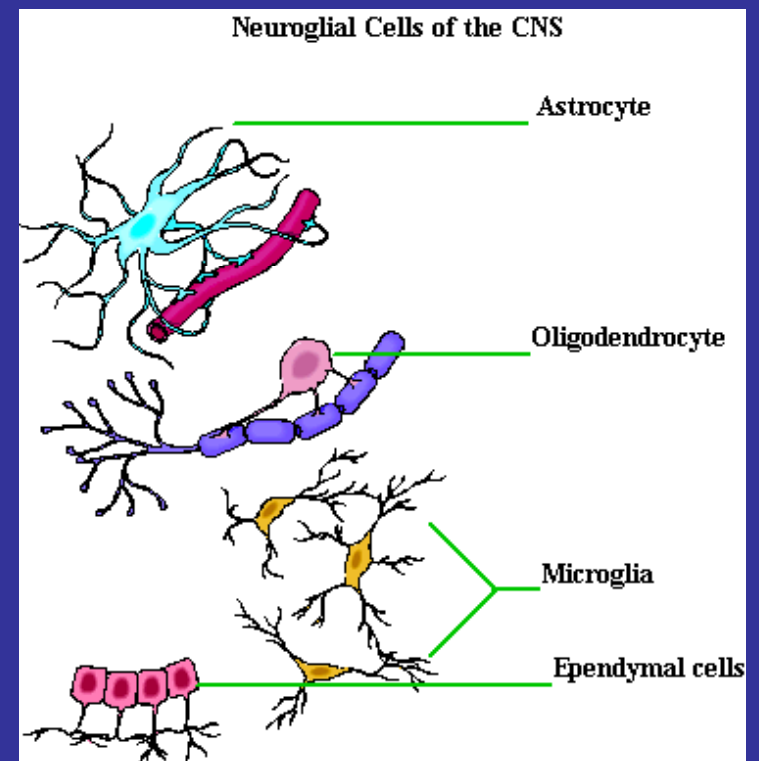
# Outline presentation

- Background high-grade glioma
- Quality of life in high grade glioma patients
- Aims current study
- Methods
- Results
- Conclusion
- Discussion



# Glioma

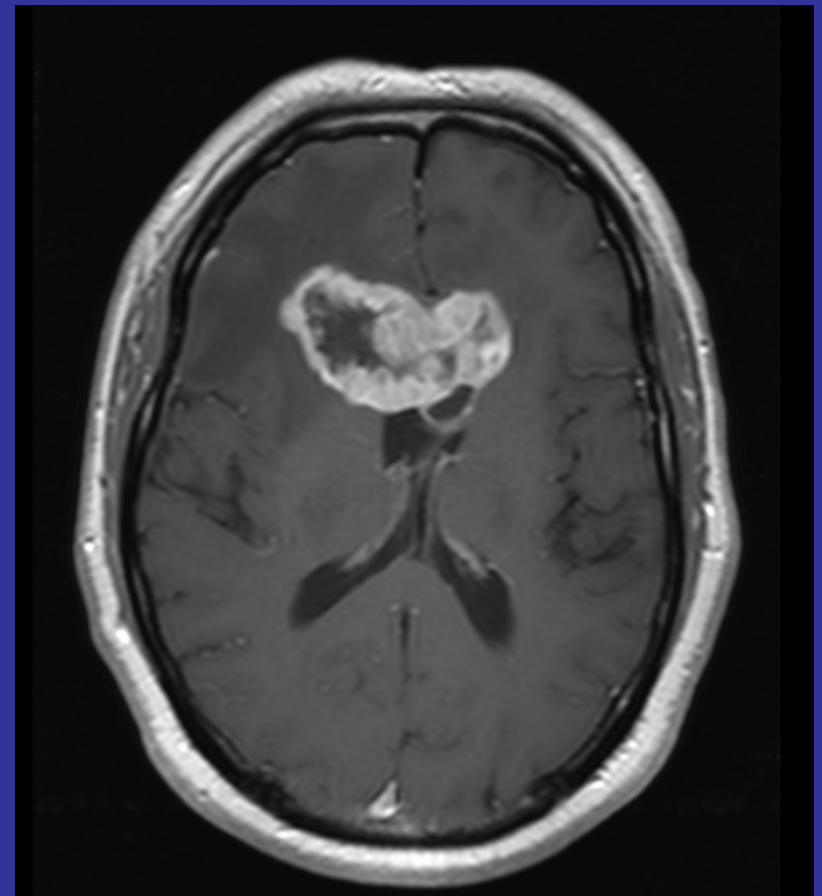
- Primary brain tumour
- Malignant transformation glia cells
- Grading I – IV
  - Low grade: I & II
  - High grade: III & IV



Background

## Diagnosis

- Imaging
  - CT-scan
  - MRI
- Pathological diagnosis
  - Biopsy
  - Resection



## Multimodal treatment

- Surgery
- Radiotherapy
- Chemotherapy
- Chemoradiation



## Prognosis

- Incurable disease
- Median survival
  - Grade III: 1.5- 5 years
  - Grade IV: 12 months
- Maintain quality of life as long as possible is important treatment aim



## Quality of life in HGG patients

- Disease has major negative effect on health-related quality of life (HRQOL)
- HRQOL in HGG patients comparable to HRQOL in lung cancer patients and patients with other neurological diseases
- Treatment may improve HRQOL, but side effects can hamper it



## End-of-life (EOL) phase

- Begins when the condition declines and no further tumour treatment seems realistic
- Only supportive treatment is given
- Disease specific symptoms (e.g. seizures, drowsiness) are more prominent than general symptoms
- Little known about QOL in the end of life phase



## Limitations QOL measurement in the EOL phase

- Subdomains QOL instruments do not capture experiences unique to dying process
- Excessive weight physical domains in QOL assessment
- Spiritual domain rarely covered
- Non-response bias in ill patients



## Background

# QOL in the end of life phase

Domains important in dying patients	Content
Physical comfort	<ul style="list-style-type: none"><li>•Pain</li><li>•General symptoms</li><li>•Disease specific symptoms</li></ul>
Psychological well-being	<ul style="list-style-type: none"><li>•Emotional functioning</li><li>•Dignity</li><li>•Autonomy</li><li>•Resilience</li></ul>
Social functioning and well-being	<ul style="list-style-type: none"><li>•Communication</li><li>•Social connection</li></ul>
Spiritual well-being	<ul style="list-style-type: none"><li>•Spiritual well-being</li><li>•Transcendence</li><li>•Suffering</li></ul>
Physical functioning	<ul style="list-style-type: none"><li>•Independence, mobility</li></ul>
Cognitive functioning	<ul style="list-style-type: none"><li>•Ability to think, mental alertness, comprehension, avoiding confusion</li></ul>
Overall perceived Quality of Life	<ul style="list-style-type: none"><li>•Overall rating quality of life</li></ul>
Overall perceived Quality of Death	<ul style="list-style-type: none"><li>•Overall rating quality of death</li></ul>



## Background

# QOL in the end of life phase

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Physical comfort	<ul style="list-style-type: none"><li>•Pain</li><li>•General symptoms</li><li>•Disease specific symptoms</li></ul>
Psychological well-being	<ul style="list-style-type: none"><li>•Emotional functioning</li><li>•<b>Dignity</b></li><li>•Autonomy</li><li>•Resilience</li></ul>
Social functioning and well-being	<ul style="list-style-type: none"><li>•Communication</li><li>•Social connection</li></ul>
Spiritual well-being	<ul style="list-style-type: none"><li>•Spiritual well-being</li><li>•Transcendence</li><li>•Suffering</li></ul>
Physical functioning	<ul style="list-style-type: none"><li>•Independence, mobility</li></ul>
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Overall perceived Quality of Death	<ul style="list-style-type: none"><li>•Overall rating quality of death</li></ul>



## Dignity

- Dignity is defined as the quality of being worthy of esteem or respect
- Preserving dignity is frequently mentioned by patients when considering the end of life
- Dying with dignity is considered as a goal of palliative care



## **Multi-centre international end of life study**

- Evaluate the end of life decision making process in HGG patients
- Determine quality of life (QOL) of HGG patients and relatives in the end of life phase
- Establish quality of care for HGG patients in the end of life phase
- Compare end of life care in HGG patients among countries and cultures



## Study aims

- Determine QOL
  - Last 3 months
  - Last week
- Identify determinants of QOL in the last 3 months of life
- Identify determinants of dying with dignity
- **Find tools for improvement of QOL in end-of-life phase**



## Study design

- Retrospective approach focused on relatives and physicians
- QOL in EOL phase reported by relative after death of patient
- Dutch cohort HGG patients diagnosed in 2005 and 2006 in 3 hospitals
- Relatives of deceased patients approached in 2009



# Development questionnaire

Domains important in dying patients	Content	EORTC QLQ C30/ BN 20 Scale
Physical comfort	<ul style="list-style-type: none"> <li>•Pain</li> <li>•General symptoms</li> <li>•Disease specific symptoms</li> </ul>	<ul style="list-style-type: none"> <li>•PA, H (1-2 items)</li> <li>•DY, FA, NV (1-2 items)</li> <li>•S, Dr, BC, MD (1-3 items)</li> </ul>
Psychological well-being	<ul style="list-style-type: none"> <li>•Emotional functioning</li> <li>•Autonomy</li> <li>•Resilience</li> </ul>	<ul style="list-style-type: none"> <li>•EF (4 items)</li> <li>•NA</li> <li>•NA</li> </ul>
Social functioning and well-being	<ul style="list-style-type: none"> <li>•Communication</li> <li>•Social connection</li> </ul>	<ul style="list-style-type: none"> <li>•CD (3 items)</li> <li>•SF (2 items)</li> </ul>
Spiritual well-being	<ul style="list-style-type: none"> <li>•Spiritual well-being</li> <li>•Transcendence</li> <li>•Suffering</li> </ul>	<ul style="list-style-type: none"> <li>•NA</li> <li>•NA</li> <li>•NA</li> </ul>
Physical functioning	<ul style="list-style-type: none"> <li>•Independence, mobility</li> </ul>	<ul style="list-style-type: none"> <li>•PF2 (5 items)</li> </ul>
Cognitive functioning	<ul style="list-style-type: none"> <li>•Ability to think, mental alertness, comprehension, avoiding confusion</li> </ul>	<ul style="list-style-type: none"> <li>•CF (2 items)</li> </ul>
Overall perceived Quality of Life	<ul style="list-style-type: none"> <li>•Overall rating quality of life</li> </ul>	<ul style="list-style-type: none"> <li>•QL2 (1 item)</li> </ul>
Dying with dignity	<ul style="list-style-type: none"> <li>•Rating dignified death</li> </ul>	<ul style="list-style-type: none"> <li>•NA</li> </ul>



## Study design

- Questionnaires to relatives of deceased HGG patients derived from:
  - EORTC QLQC-30
  - EORTC BN20
  - MOS SF36
  - questionnaire on advanced directives
  - patient dignity inventory



# Development questionnaire

Domains important in dying patients	Content	VUmc questionnaire for relatives
Physical comfort	<ul style="list-style-type: none"> <li>•Pain</li> <li>•General symptoms</li> <li>•Disease specific symptoms</li> </ul>	<ul style="list-style-type: none"> <li>•PA, H (2x1 item)</li> <li>•DY, FA, N (3x1 item)</li> <li>•DR, BC, MD (3x1 item)</li> </ul>
Psychological well-being	<ul style="list-style-type: none"> <li>•Emotional functioning</li> <li>•Autonomy</li> <li>•Resilience</li> </ul>	<ul style="list-style-type: none"> <li>•EF (3 items)</li> <li>•Q: Able to decide</li> <li>•NA</li> </ul>
Social functioning and well-being	<ul style="list-style-type: none"> <li>•Communication</li> <li>•Social connection</li> </ul>	<ul style="list-style-type: none"> <li>•CD (1 item)</li> <li>•SF, FL (2x1 item)</li> </ul>
Spiritual well-being	<ul style="list-style-type: none"> <li>•Spiritual well-being</li> <li>•Transcendence</li> <li>•Suffering</li> </ul>	<ul style="list-style-type: none"> <li>•Acceptance disease (1 item)</li> <li>•Q: Peaceful death</li> <li>•NA</li> </ul>
Physical functioning	<ul style="list-style-type: none"> <li>•Independence, mobility</li> </ul>	<ul style="list-style-type: none"> <li>•PF (2 items)</li> </ul>
Cognitive functioning	<ul style="list-style-type: none"> <li>•Ability to think, mental alertness, comprehension, avoiding confusion</li> </ul>	<ul style="list-style-type: none"> <li>•CF (5 items)</li> </ul>
Overall perceived Quality of Life	<ul style="list-style-type: none"> <li>•Overall rating quality of life</li> </ul>	<ul style="list-style-type: none"> <li>•QL (1 item)</li> </ul>
Dying with dignity	<ul style="list-style-type: none"> <li>•Rating dignified death</li> </ul>	<ul style="list-style-type: none"> <li>•Dignity (1 item)</li> </ul>



## Pilot questionnaire

- Interviews with 5 relatives along the questionnaire



Difficult/  
confronting



Time  
investment



Redundant  
items



Missing  
items



## Scoring

- All items and/ or scales converted to 0-100 scales using EORTC QLQ-C30 algorithm
- Symptom scales: higher score represents worse QOL
- Functional scales, QOL, dignity scale: higher score represents better QOL
- 2 questions (nominal answers) reported separately



## Reliability scales

	Internal consistency (Cronbach's $\alpha$ )	Correlation between items
CF 3 months before death	0.883	0.476 – 0.732
CF last week before death	0.907	0.392-0.813
PF 3 months before death	0.789	0.692
PF last week before death	0.428	0.309
EF 3 months before death	0.642	0.248-0.448
EF last week before death	0.743	0.396 – 0.651



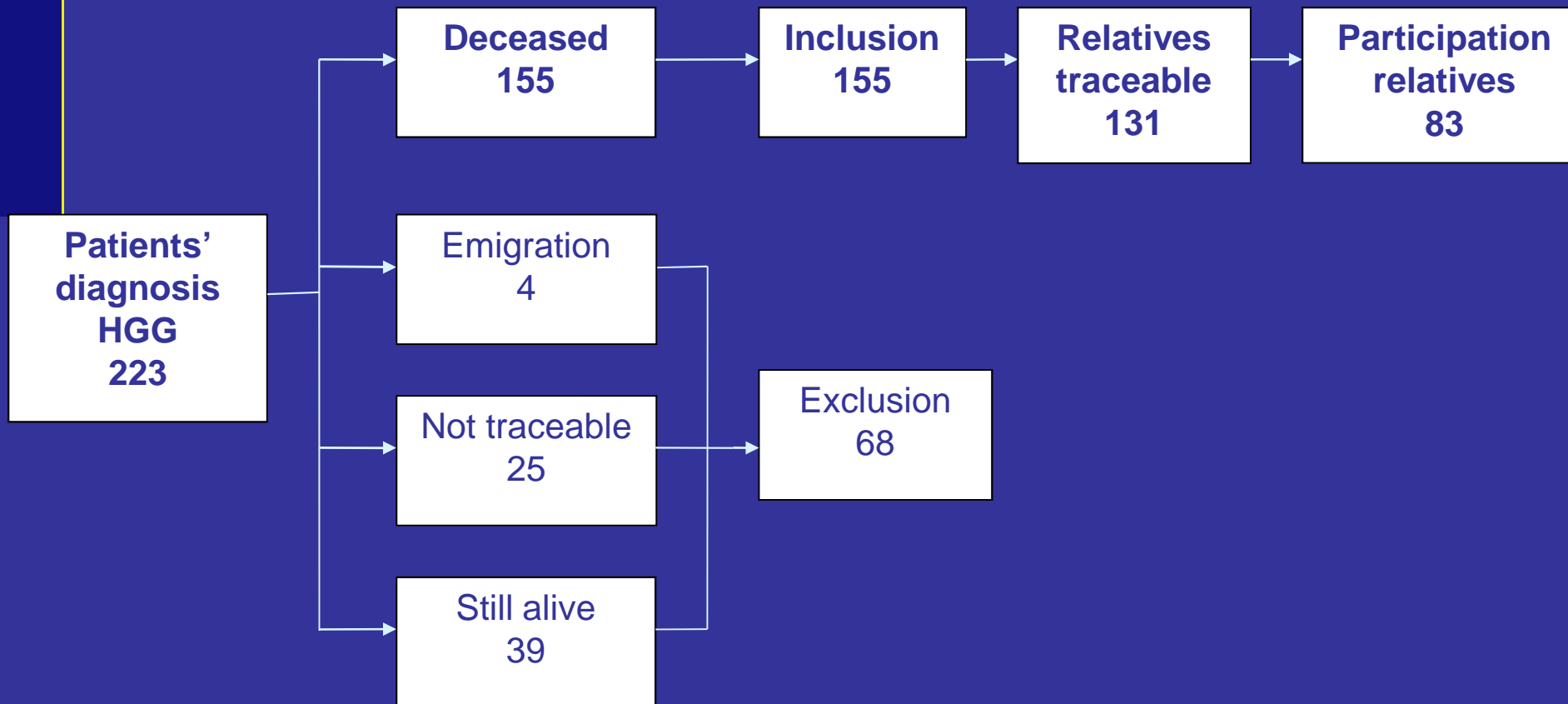
## Data analysis

- Differences between scores last 3 months and last week: wilcoxon rank test
- Correlation between continuous determinants and QOL/ dignity: spearman's rho correlation coefficient
- Correlation between dichotomous determinants and QOL/ dignity: Mann Whitney U test
- Determinants:
  - Patient characteristics
  - Symptom scales
  - Functional and spiritual scales



## Preliminary results

# Patient identification – Dutch cohort



## Results

### Baseline characteristics patient (n =83)

		N (%)
<b>Sex</b>	Male	53 (64%)
	Female	30 (36%)
<b>Age</b>	Median (range)	61 (20-86)
<b>Relationship status</b>	Single	9 (11%)
	With partner	70 (84%)
	Widowed	4 (5%)
<b>Religious</b>	No	45 (55%)
	Yes, not important	13 (15%)
	Yes, important	25 (30%)
<b>Education</b>	Low	37 (45%)
	Intermediate	21 (25%)
	High	25 (30%)
<b>Place of death</b>	At home	50 (60%)
	Nursing home	10 (12%)
	Hospice	8 (10%)
	Hospital	14 (17%)
	Other	1 (1%)



## Results

### Baseline characteristics relatives (n =83)

		N (%)
<b>Sex</b>	Male	30 (36%)
	Female	53 (64%)
<b>Age</b>	Median (range)	58 (30-86)
<b>Relationship to patient</b>	Partner	66 (80%)
	Parent	6 (7%)
	Child	9 (11%)
	Sibling	2 (2%)
<b>Religious</b>	No	45 (55%)
	Yes, not important	8 (10%)
	Yes, important	29 (35%)
<b>Education</b>	Low	31 (37%)
	Intermediate	26 (31%)
	High	26 (31%)



## Results

### Physical comfort and communication

	Last 3 months Mean (SD)*	Last week Mean (SD)*	Wilcoxon rank P
Headache (H)	31 (35)	41 (42)	0.001*
Nausea (N)	20 (27)	62 (37)	0.058
Motor dysfunction (MD)	62 (37)	79 (35)	0.000*
Drowsiness (Dr)	51 (32)	84(27)	0.000*
Fatigue (FA)	72 (27)	89 (21)	0.000*
Pain (PA)	29 (33)	51 (42)	0.000*
Bladder control (BC)	36 (41)	69 (41)	0.000*
Dyspnoea (DY)	17 (25)	44 (41)	0.000*
Communication deficit (CD)	40 (34)	71 (38)	0.000*

\* For illustrative purposes descriptive statistics are presented as if normal distribution



## Results

### Functional, spiritual and QOL scales

	Last 3 months Mean (SD)*	Last week Mean (SD)*	Wilcoxon rank P
Cognitive functioning (CF)	54 (28)	30 (28)	0.000*
Physical functioning (PF)	50 (33)	7 (15)	0.000*
Emotional functioning (EF)	70 (24)	65 (28)	0.021*
Acceptance disease	57 (33)	67 (33)	0.058
Family life	45 (39)	NA	NA
Social functioning	17 (26)	NA	NA
Support	82 (27)	NA	NA
QOL	29 (26)	NA	NA
Dying with dignity	NA	71 (28)	NA

\* For illustrative purposes descriptive statistics are presented as if normal distribution



## Determinants of QOL last 3 months

- Baseline characteristics

- Sex
- Age
- Education
- Religion
- Relationship status
- Place of death

→ **No correlation with QOL**



## Results

### Determinants of QOL last 3 months

	Spearman's Correlation Coefficient	P-value	Bonferroni correction * 9
Headache (H)	- 0.154	0.183	NS
Nausea (N)	- 0.203	0.079	NS
Motor dysfunction (MD)	- 0.155	0.187	NS
Drowsiness (Dr)	- 0.267	0.018*	NS
Fatigue (FA)	- 0.252	0.027*	NS
Pain (PA)	- 0.171	0.161	NS
Bladder control (BC)	- 0.120	0.297	NS
Dyspnoea (DY)	- 0.304	0.009*	NS
Communication Deficit (CD)	- 0.163	0.154	NS



## Results

### Determinants of QOL last 3 months

	Spearman's Correlation coefficient	P-value	Bonferroni correction * 6
Cognitive functioning (CF)	0.261	0.027*	NS
Physical functioning (PF)	0.171	0.152	NS
Emotional functioning (EF)	0.334	0.005*	S
Acceptance disease	0.370	0.002*	S
Family life	0.256	0.024*	NS
Social functioning	0.264	0.019*	NS



## Results

# Determinants of dying with dignity

- Baseline characteristics
  - Sex
  - Age
  - Education
  - Religion
  - Relationship status
  - Place of death

→ **No correlation with dignity**



## Results

### Determinants of dying with dignity

	Spearman's Correlation Coefficient	P-value	Bonferroni correction * 9
Headache (H)	- 0.227	0.065	NS
Nausea (N)	- 0.063	0.605	NS
Motor dysfunction (MD)	- 0.129	0.227	NS
Drowsiness (Dr)	- 0.301	0.007*	NS
Fatigue (FA)	- 0.133	0.256	NS
Pain (PA)	- 0.281	0.028*	NS
Bladder control (BC)	- 0.062	0.588	NS
Dyspnoea (DY)	- 0.107	0.373	NS
Communication Deficit (CD)	- 0.297	0.008*	NS



## Results

# Determinants of dying with dignity

	Spearman's Correlation coefficient	P-value	Bonferroni correction * 4
Cognitive functioning (CF)	0.278	0.028*	NS
Physical functioning (PF)	0.127	0.280	NS
Emotional functioning (EF)	0.231	0.084	NS
Acceptance disease	0.181	0.200	NS



## Results

# Determinants of dying with dignity

Acceptance death, peaceful death	N of patients	Dignity score Mean (SD)	P-value
Yes	27 (33%)	80 (24)	0.016*
No	12 (15 %)	48 (38)	
Unaware	31 (36%)	69 (26)	
Unknown	13 (16%)	NA	



## Conclusions

- QOL is poor in the end of life phase and diminishes towards death in almost all aspects
- Higher levels of fatigue, dyspnoea and drowsiness are associated with poorer overall QOL last 3 months
- Better emotional functioning and better acceptance of disease are significantly associated with better QOL



## Conclusions

- Drowsiness and pain may affect dying with dignity
- Communication deficit and diminished emotional functioning may affect patients' dignity
- Acceptance of death important for dying with dignity



## Shortcomings

- Conceptual framework to be discussed
- Retrospective approach
- Proxy-reported outcomes
- Over-representation of partners compared with siblings etc.
- Response rate 63%
- Other determinants should be examined



## Future prospects

- Relation between quality of end of life care during last week and death with dignity?

→ correlation coefficient 0.452;  $p = 0.000^*$



## Future prospects

- End of life decision-making often hampered because of inability to decide. Relation with dying with dignity?

		N	Dignity score Mean (SD)	P-value
Decision against patient's will	Yes	12	58 (37)	0.206
	No	67	74 (26)	
Decision against relative's will	Yes	10	50 (35)	0.025*
	No	69	74 (25)	



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