

# Colloque Palliative Care CHUV

Lausanne, 20th February 2025

## Soins palliatifs précoces et tardifs en neuro-oncologie

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Universität  
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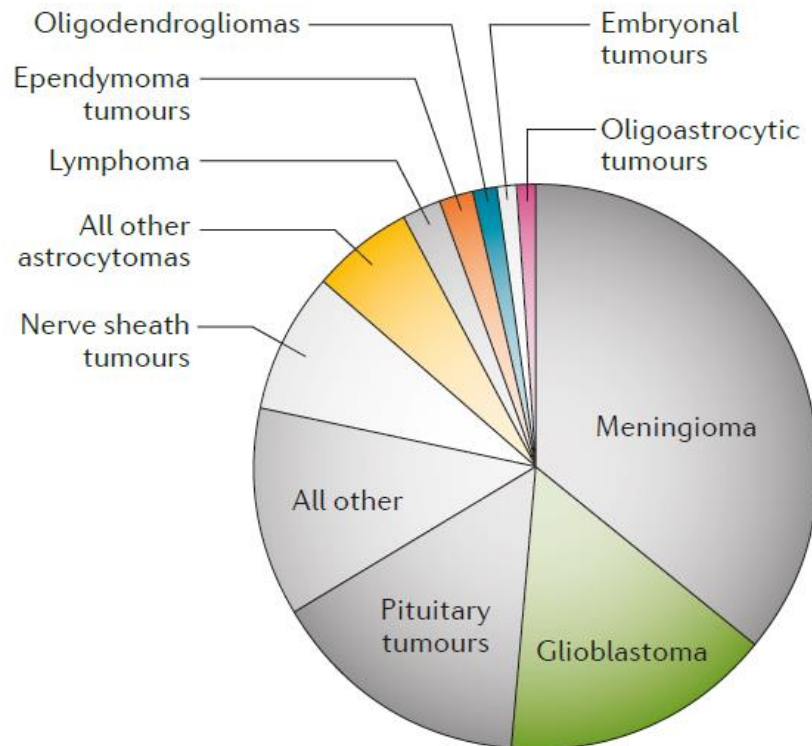


**Brain tumours**  
**KILL MORE**  
**WOMEN**  
**UNDER 35**  
than breast cancer



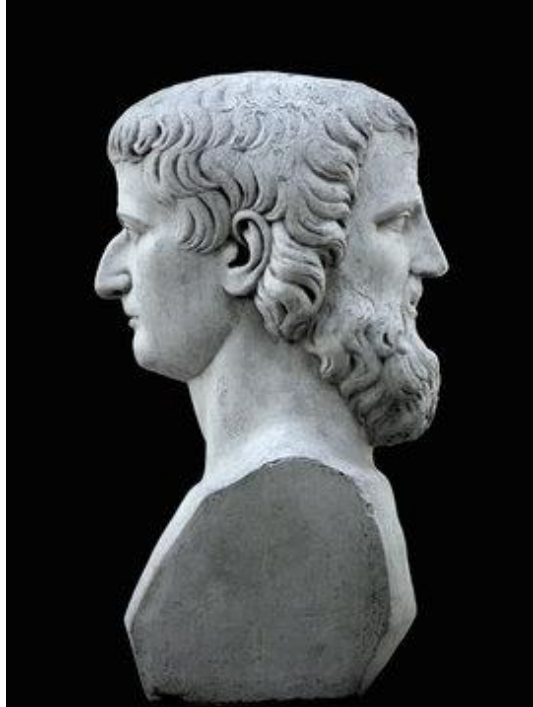
# Primary brain tumors

## Relative frequency of primary brain and central nervous system tumours

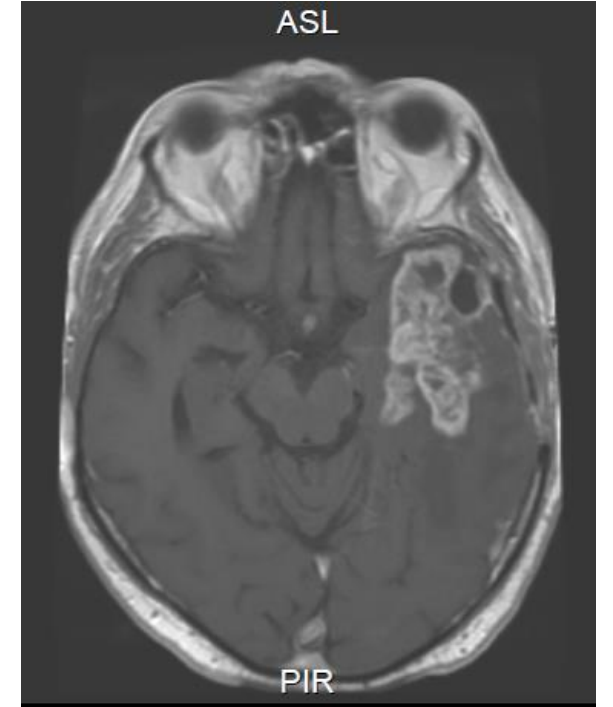


- **Gliomas:**  
28% of all brain tumors and  
80% of all malignant tumors
- **Annual incidence of gliomas:**  
6.6 / 100.000, of which about  
half are glioblastomas  
(CBTRUS; USA)  
3.9 / 100.000 (Kanton of  
Zurich; glioblastoma)
- **Median OS of glioblastoma –  
12-14 months**
- **Long-term survival in  
glioblastoma > 5 years – 5%**

# The issue with brain tumors

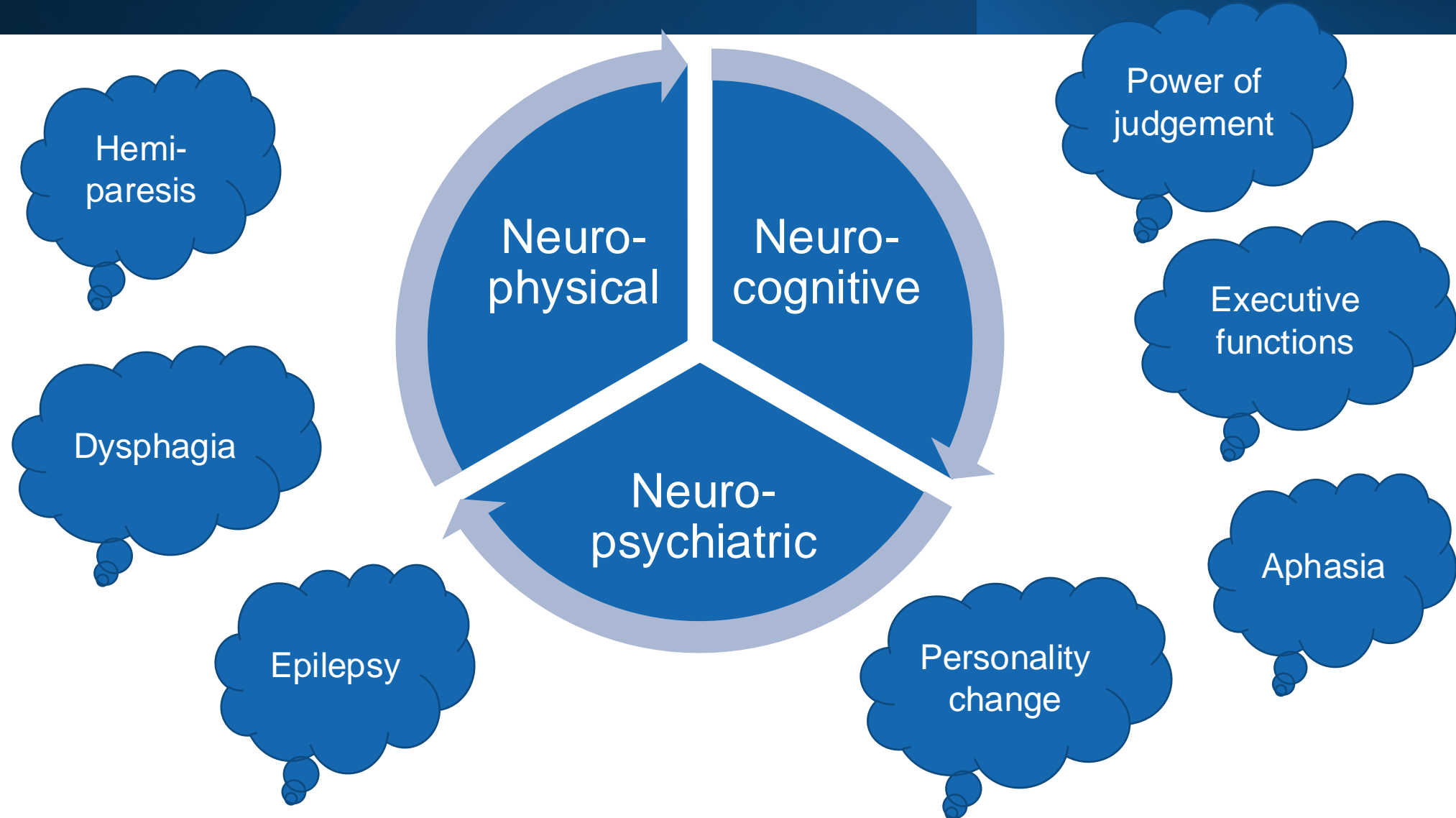


- Usually short disease trajectory and early deterioration
- Usually no curative treatment – palliative from the beginning
- Symptom burden combines oncology and neurology symptoms









# Complex symptoms



Symptom	Recommendation
Epilepsy	LEV as first-line AET Lacosamide and Perampanel as add-on Intranasal midazolam in dysphagia
Fatigue	No pharmacological interventions Non-pharmacological interventions potentially helpful
Headaches	Dexamethasone Bevacizumab as early disease steroid-sparing agent Co-analgetics
Cognition	No pharmacological interventions Neurocognitive rehabilitation with modest effects (in young patients with favorable disease trajectory) Surgical resection of space-occupying lesions Hippocampal avoidance (brain mets)
Psych symptoms	Provoking agents screening Standard pharmacological treatment Non-pharmacological interventions for depression



## Survival of brain tumour patients with epilepsy

 Maximilian Mastall, 
  Fabian Wolpert, Dorothee Gramatzki, Lukas Imbach, Denise Becker, Anton Schmick, Caroline Hertler, Patrick Roth, 
  Michael Weller and 
  Hans-Georg Wirsching

## Seizure reduction is a prognostic marker in low-grade glioma patients treated with temozolomide

Johan A. F. Koekkoek<sup>1,2,3</sup> · Linda Dirven<sup>1,3</sup> · Jan J. Heimans<sup>1</sup> · Tjeerd J. Postma<sup>1</sup> · Maaïke J. Vos<sup>2</sup> · Jaap C. Reijneveld<sup>1</sup> · Martin J. B. Taphoorn<sup>1,2,3</sup>

Low-grade glioma – risk of seizure around 60-85%

High-grade glioma – risk of seizure around 45%

End-of-life seizures – varying between 30-56%

Status epilepticus in brain tumor patients is associated with reduced survival

Seizure reduction is a prognostic marker for survival

### Status epilepticus

Definition:

- > 5mins of tonic-clonic seizures OR 20-30mins of focal seizures OR a series of seizures without clinical/encephalographical remittance between

Treatment:

- Benzodiazepine (e.g. Midazolam 5mg sc/ 3mg iv or clonazepam 1mg iv) up to every 5mins
- AET treatment – LEV OR phenytoin OR VPA

# Management of epilepsy in brain tumor patients

Pim B. van der Meer<sup>a</sup>, Martin J.B. Taphoorn<sup>a,b</sup>, and Johan A.F. Koekkoek<sup>a,b</sup>

- Levetiracetam is the preferred choice for treatment (no drug interactions, favorable efficacy, several application routes available)
- Preferred add-ons are lacosamide, perampanel and VPA
- No survival benefit from AET confirmed
- Treatment of tumor treats seizures

## Improved seizure control in patients with recurrent glioblastoma treated with bevacizumab

Caroline Hertler<sup>a</sup>, Katharina Seystahl, Emilie Le Rhun, Hans-Georg Wirsching, Patrick Roth, Michael Weller<sup>a</sup>, and Dorothee Gramatzki<sup>a</sup>

Department of Neurology, Clinical Neuroscience Center, University Hospital and University of Zurich, Zurich, Switzerland (C.H., K.S., E.L.R., H.-G.W., P.R., M.W., D.G.); Competence Center for Palliative Care, University Hospital Zurich, Zurich, Switzerland (C.H.); Department of Neurosurgery, Clinical Neuroscience Center, University Hospital and University of Zurich, Zurich, Switzerland (E.L.R.)

VOLUME 34 · NUMBER 7 · MARCH 1, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

## Does Valproic Acid or Levetiracetam Improve Survival in Glioblastoma? A Pooled Analysis of Prospective Clinical Trials in Newly Diagnosed Glioblastoma

Caroline Hoppold, Thierry Gorlia, Olivier Chinot, Mark R. Gilbert, L. Burt Nabors, Wolfgang Wick, Stephanie L. Pugh, Monika Hegi, Timothy Cloughesy, Patrick Roth, David A. Reardon, James R. Perry, Minesh P. Mehta, Roger Stupp, and Michael Weller

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Accepted April 29, 2021

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Medicine  
Reports

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CASE DISCUSSIONS IN PALLIATIVE MEDICINE

Open Access

## Subcutaneous Levetiracetam Application Sustains Therapeutic Drug Levels

Sophia Westphal, MD, Caroline Hertler, MD, David Blum, MD, PhD, and Markus Schettler, MD\*



## Depression and anxiety in glioma patients

Pim B. van der Meer<sup>1</sup>, Linda Dirven<sup>2</sup>, Caroline Hertler<sup>3</sup>, Florian W. Boele<sup>4</sup>, Albert Batalla, Tobias Walbert<sup>5</sup>, Alasdair G. Rooney and Johan A.F. Koekkoek

All author affiliations are listed at the end of the article

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Article

<https://doi.org/10.1038/s41591-024-03224-y>

## High-throughput identification of repurposable neuroactive drugs with potent anti-glioblastoma activity

Received: 6 December 2023

Accepted: 31 July 2024

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Check for updates

Sohyon Lee<sup>1,14</sup>, Tobias Weiss<sup>2,14</sup>, Marcel Bühler<sup>2</sup>, Julien Mena<sup>1</sup>, Zuzanna Lottenbach<sup>1</sup>, Rebekka Wegmann<sup>1</sup>, Miaomiao Sun<sup>2</sup>, Michel Bihl<sup>3</sup>, Bartłomiej Augustynek<sup>4,5</sup>, Sven P. Baumann<sup>4</sup>, Sandra Goetze<sup>6,7,8</sup>, Audrey van Droogen<sup>6,7,8</sup>, Patrick G. A. Pedrioli<sup>6,7,8</sup>, David Penton<sup>9</sup>, Yasmin Festl<sup>1</sup>, Alicia Buck<sup>1,2</sup>, Daniel Kirschenbaum<sup>10</sup>, Anna M. Zeitlberger<sup>11</sup>, Marian C. Neidert<sup>11</sup>, Flavio Vasella<sup>12</sup>, Elisabeth J. Rushing<sup>10</sup>, Bernd Wollscheid<sup>6,7,8</sup>, Matthias A. Hediger<sup>4</sup>, Michael Weller<sup>2,13,15</sup> & Berend Snijder<sup>1,7,13,15</sup>

### Prevalence

- 16–41% for depression
- 24–48% for anxiety

### Risk factors

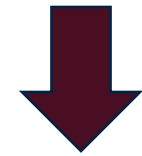
- Low KPS
- Prior history of mood disorders
- Adverse events of medication

### Treatment options (pharmacological)

- SSRI > SNRI > TCA for depression
- SSRI, SNRI and pregabalin for anxiety

### Treatment options (non-pharmacological)

- Possibly psychosocial intervention for depression
- Cognitive behavioral training for anxiety



**Anti-depressant vortioxetine is the strongest preclinical candidate**

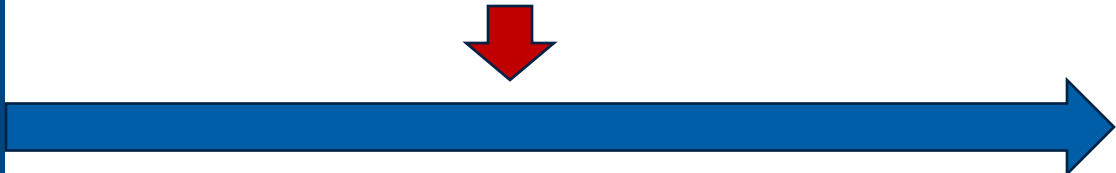
Symptom	Recommendation
Early palliative care	Due to rapid neurocognitive deficits and decline, early implementation of support systems – also for caregivers – and early advance care planning should be initiated
Caregiver needs	Psychoeducation to increase mastery Use of social support relate to better HRQoL
End of life care	Effective symptom control Adherence to the preferred place of death Reduction of aggressive end-of-life treatment

# Case

-

## Mrs. K

## EoL preferences



1/2021 – WHO IV

3-4/2021 – RT


11/2021

- Glioblastoma ED 1/2021
- Recurrence after RT 4/2021
- KPS 90%; Writer and linguistic professor
- Presents with her husband to discuss end-of-life option and to implement support services
  
- Wants to opt for assisted suicide «later when it gets worse»
- Main goal: autonomy and brain functioning
- Monthly appointments to keep up and to avoid missing «external feedback» on cognitive worsening

## Understanding the association between fatigue and neurocognitive functioning in patients with glioma: A cross-sectional multinational study

Jantine G. Röttgering<sup>o</sup>, Jennie W. Taylor, Melissa Brie, Tracy Luks, Shawn L. Hervey-Jumper<sup>o</sup>, Stephanie Phan, Paige M. Bracci, Ellen Smith, Philip C. De Witt Hamer, Linda Douw<sup>o</sup>, Christina Weyer-Jamora, and Martin Klein<sup>o</sup>

## The course of neurocognitive functioning in high-grade glioma patients [Get access >](#)

Ingeborg Bosma , Maaike J. Vos, Jan J. Heimans, Martin J.B. Taphoorn, Neil K. Aaronson, Tjeerd J. Postma, Henk M. van der Ploeg, Martin Muller, W. Peter Vandertop, Ben. J. Slotman ... [Show more](#)

*Neuro-Oncology*, Volume 9, Issue 1, January 2007, Pages 53–62,

THE LANCET

REVIEW · Volume 3, Issue 3, P159-168, March 2004

Neurology

## Cognitive deficits in adult patients with brain tumours

[Dr Martin JB Taphoorn](#) <sup>a</sup>  · [Martin Klein](#)<sup>b</sup>

- Although individual patients might experience both fatigue and neurocognitive impairment, **the relationship between the two is weak**. Consequently, both fatigue and neurocognitive functioning should be independently assessed and treated with targeted therapies.
- Between baseline and eight months, patients deteriorated in information-processing capacity, psychomotor speed, and attentional functioning. Further deterioration was observed between 8 and 16 months.
- Patients with recurrence have lower information-processing capacity, psychomotor speed, and executive functioning; further factors are radiotherapy and AET (EIAED).

## Advance care planning (ACP) in glioblastoma patients: Evaluation of a disease-specific ACP program and impact on outcomes

Lara Fritz<sup>†</sup>, Marthe C. M. Peeters<sup>†</sup>, Hanneke Zwinkels, Johan A. F. Koekkoek, Jaap C. Reijneveld, Maaïke J. Vos, H. Roeline W. Pasman, Linda Dirven<sup>○</sup>, and Martin J. B. Taphoorn

- Increase survival
- Maintain quality of life
- Reduce symptom burden
- Minimize complications of treatment
- Deliver care in line with patient's preferences and goals

**What do we want for our patients?**

Aim is that people receive care that is consistent with their values, goals and preferences during the course of disease



## Advance care planning (ACP) in glioblastoma patients: Evaluation of a disease-specific ACP program and impact on outcomes

Lara Fritz<sup>†</sup>, Marthe C. M. Peeters<sup>†</sup>, Hanneke Zwinkels, Johan A. F. Koekkoek, Jaap C. Reijneveld, Maaïke J. Vos, H. Roeline W. Pasman, Linda Dirven<sup>○</sup>, and Martin J. B. Taphoorn

- Decision-making requires core capacities:
  - understanding
  - appreciation
  - reasoning
  - expression of choice
- Up to 90% of patients suffer from cognitive deficits early
- Up to half of patients have reduced decision-making capacity during treatment phase
- Decrease in neurocognitive functioning over time
- During EOL phase: even higher symptom burden (aphasia, loss of consciousness)

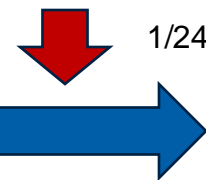
### Why is ACP important in brain tumor patients?

# Case

-

## Mrs. G

## ACP



1/24

8/2020 – WHO IV

9-4/2021 – RT/TMZ

6-2/2022 – CCNU

6/2023 – RT

3/2024

- Glioblastoma ED
- Recurrence after SOC, CCNU and RT
- KPS 80%; travels and lives by herself
- Daughter 16 years; Ex-husband
- Presents with her brother for an ACP – main symptom at progression: aphasia
  
- Start ACP 2/2024
- Second appointment for ACP 7 days later: unable to communicate; unable to care for herself

CLINICAL STUDY

## Symptoms and medication management in the end of life phase of high-grade glioma patients

J. A. F. Koekkoek · L. Dirven · E. M. Sizoo · H. R. W. Pasman · J. J. Heimans · T. J. Postma · L. Deliens · R. Grant · S. McNamara · G. Stockhammer · E. Medicus · M. J. B. Taphoorn · J. C. Reijneveld

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

Eefje M. Sizoo <sup>a,\*</sup>, H. Roeline W. Pasman <sup>b</sup>, Janine Buttolo <sup>a</sup>, Jan J. Heimans <sup>a</sup>, Martin Klein <sup>c</sup>, Luc Deliens <sup>b,d</sup>, Jaap C. Reijneveld <sup>a,e</sup>, Martin J.B. Taphoorn <sup>a,f</sup>

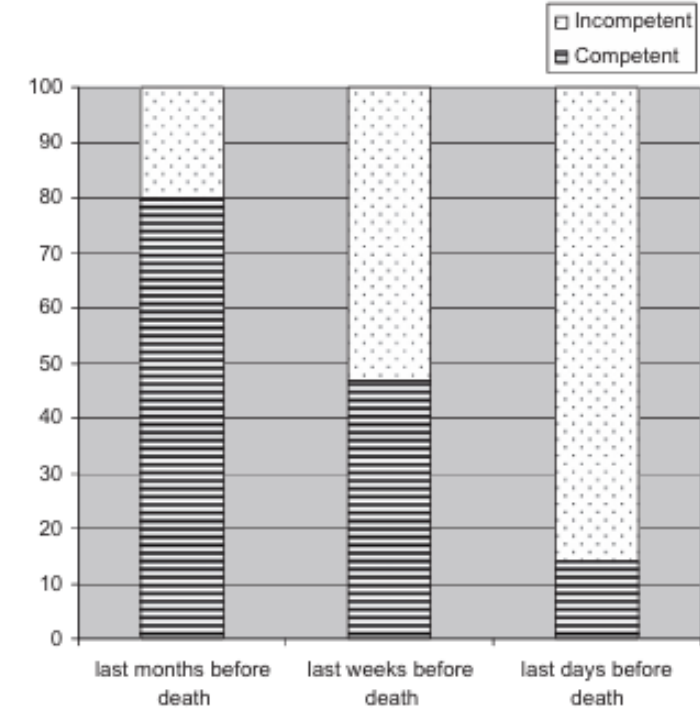
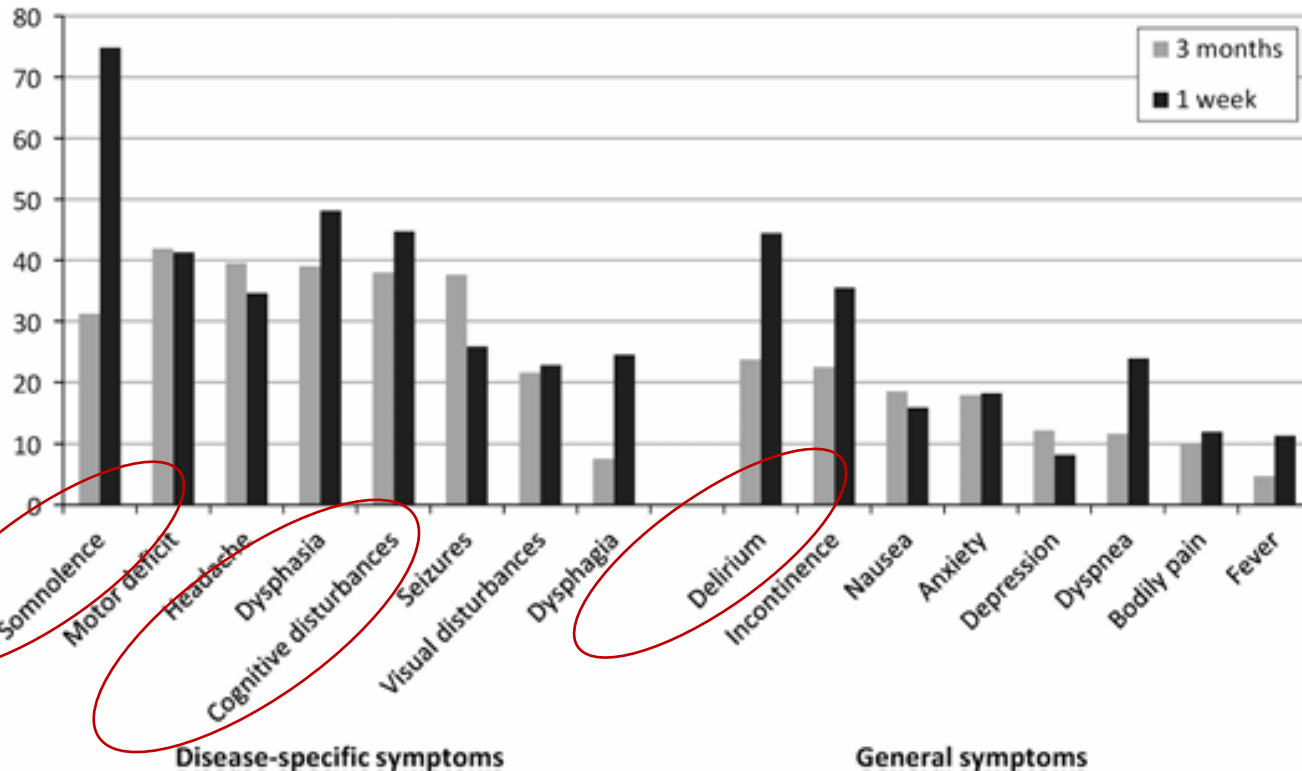
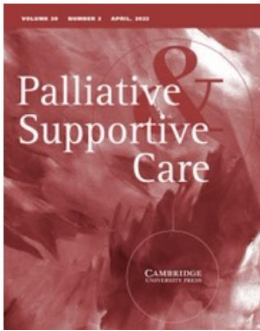


Fig. 2 – Proportion of patients competent to participate in end of life decision-making at various time points before death (n = 101; physician data).



## Predisposing and precipitating risk factors for delirium in palliative care patients

Published online by Cambridge University Press: 14 November 2019



[Annina Seiler](#) , [Maria Schubert](#), [Caroline Hertler](#), [Markus Schettle](#), [David Blum](#), [Matthias Guckenberger](#), [Michael Weller](#), [Jutta Ernst](#), [Roland von Känel](#) and [Soenke Boettger](#) 

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## Delirium is associated with an increased morbidity and in-hospital mortality in cancer patients: Results from a prospective cohort study

Published online by Cambridge University Press: 12 January 2021

[Annina Seiler](#) , [David Blum](#), [Jeremy Werner Deuel](#), [Caroline Hertler](#), [Markus Schettle](#), [Carl Moritz Zipser](#), [Jutta Ernst](#), [Maria Schubert](#), [Roland von Känel](#) and [Soenke Boettger](#) 

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- Up to 34% of patients with cancer
- **8x risk in brain tumors**
- Increases mortality risk, especially in older patients

## Advance care planning (ACP) in glioblastoma patients: Evaluation of a disease-specific ACP program and impact on outcomes

Lara Fritz<sup>†</sup>, Marthe C. M. Peeters<sup>†</sup>, Hanneke Zwinkels, Johan A. F. Koekkoek, Jaap C. Reijneveld, Maaïke J. Vos, H. Roeline W. Pasman, Linda Dirven<sup>○</sup>, and Martin J. B. Taphoorn

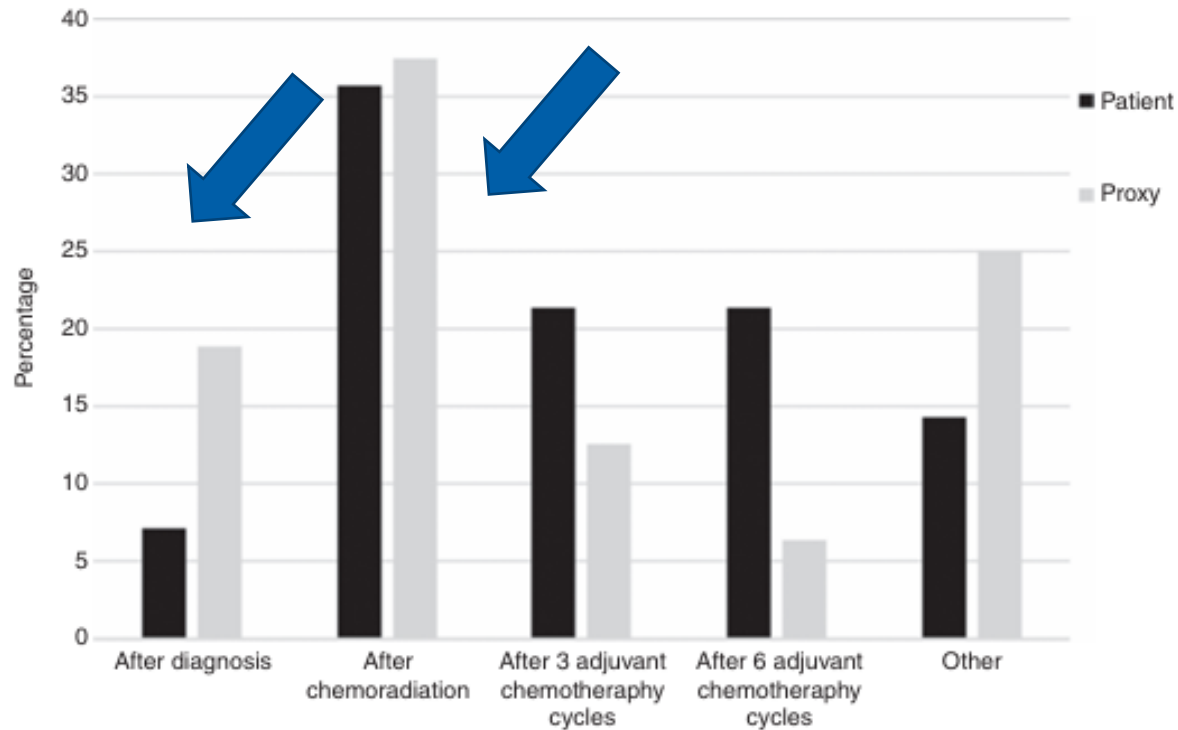
## Set up and timing of the ACP

- Invitation to participate shortly after chemoradiation
- If patient/proxy agreed → study specific folder with topics to be discussed
- 2 scheduled ACP sessions by trained facilitator
  - Session 1: introduction, main topics
  - Session 2: additional topics 4 weeks later
- Acceptability of ACP program according to patients
- No increase in levels of anxiety and depression



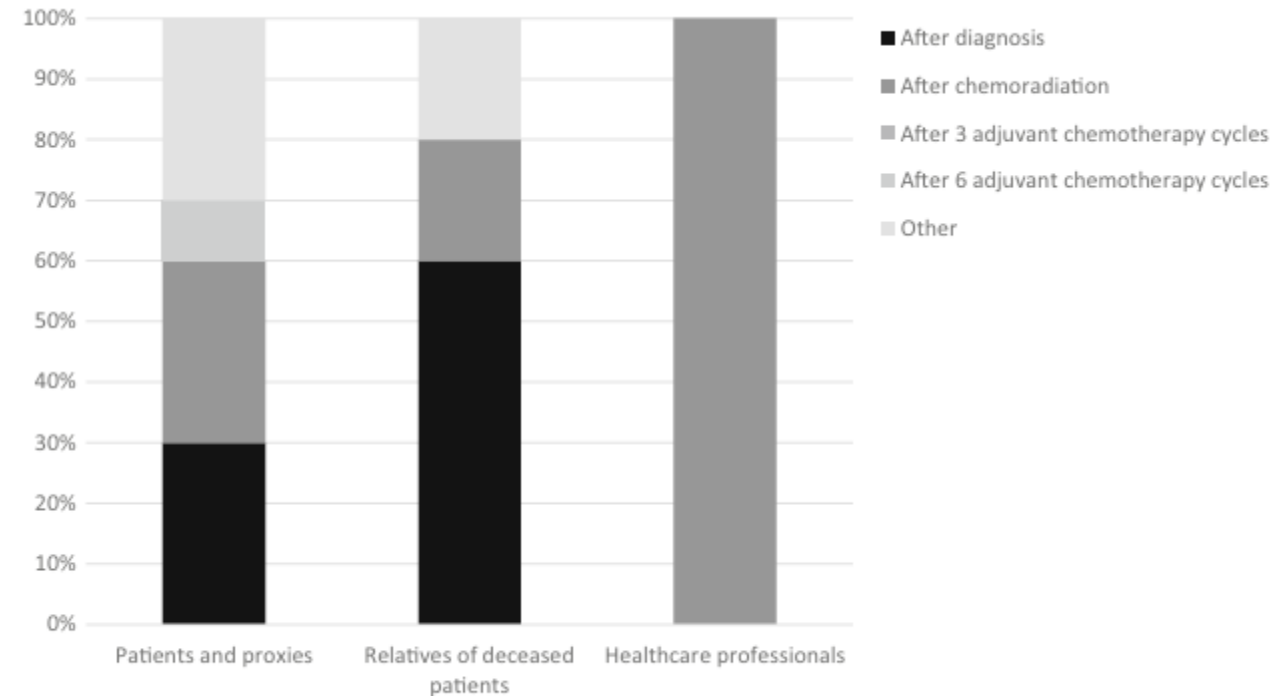
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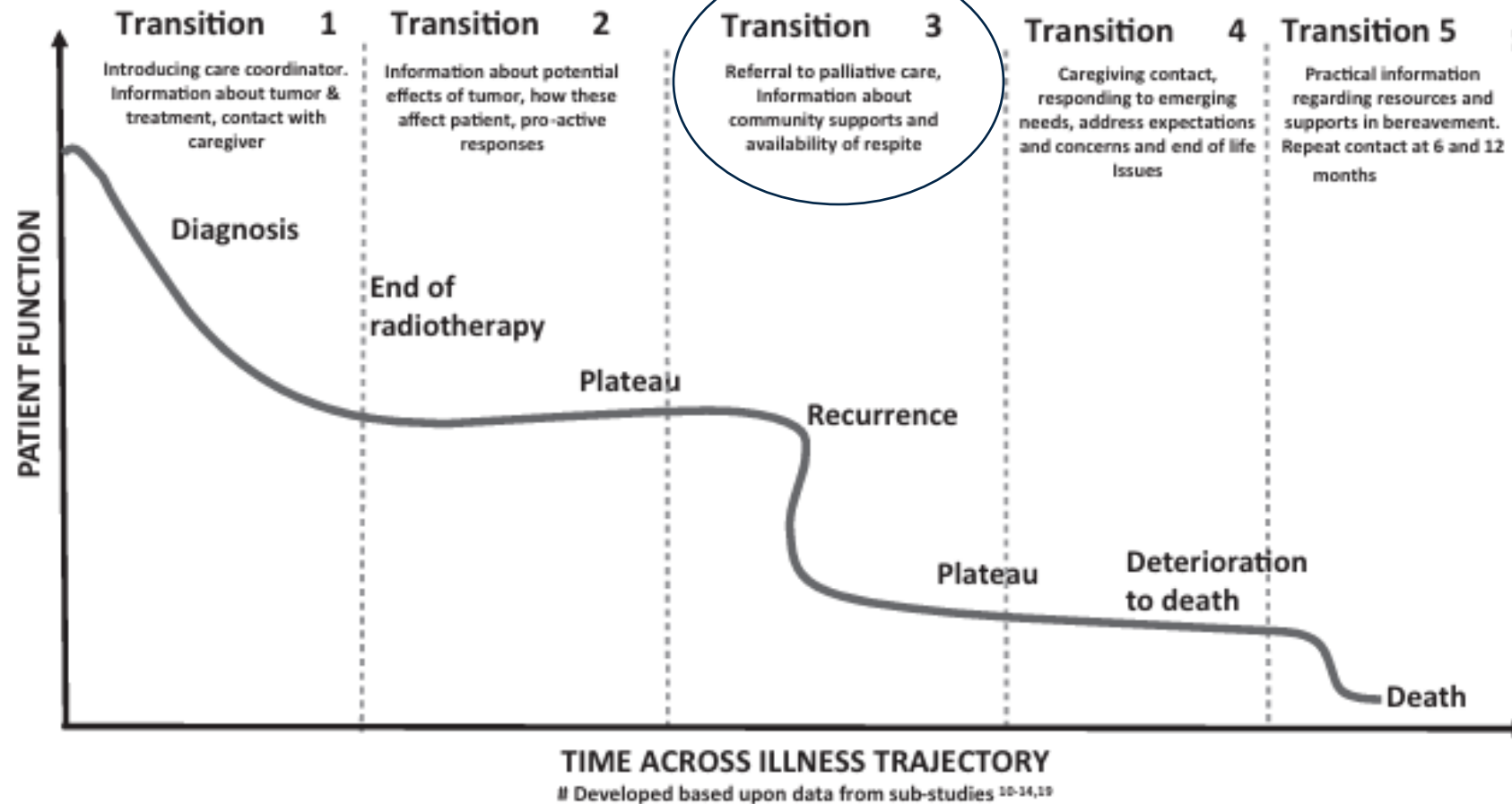
## Advance care planning in glioblastoma patients: development of a disease-specific ACP program

Lara Fritz<sup>1</sup> · Hanneke Zwinkels<sup>1</sup> · Johan A. F. Koekkoek<sup>1,2</sup> · Jaap C. Reijneveld<sup>3,4</sup> · Maaïke J. Vos<sup>1</sup> · Linda Dirven<sup>1,2</sup> · H. Roeline W. Pasman<sup>5</sup> · Martin J. B. Taphoorn<sup>1,2</sup>



## A proposed framework of supportive and palliative care for people with high-grade glioma

Jennifer Philip, Anna Collins, Caroline Brand, Vijaya Sundararajan, Carrie Lethborg, Michelle Gold, Rosalind Lau, Gaye Moore, and Michael Murphy



# The End-of-Life Phase of High-Grade Glioma Patients:

## Dying With Dignity?

EEFJE M. SIZOO,<sup>a</sup> MARTIN J.B. TAPHOORN,<sup>a,b</sup> BERNARD UITDEHAAG,<sup>a,c</sup> JAN J. HEIMANS,<sup>a</sup> LUC DELIENS,<sup>d,e</sup> JAAP C. REIJNEVELD,<sup>a,f</sup>  
H. ROELINE W. PASMAN<sup>d</sup>

### Quality of end-of-life care

Satisfied with physician last week ( $n_{\text{valid}} = 81$ )

Yes ( $n = 59$ )

No ( $n = 22$ )

Quality of Care ( $n_{\text{valid}} = 79$ )

High ( $n = 59$ )

Low ( $n = 20$ )

Deceased at preferred place of death ( $n_{\text{valid}} = 81$ )

Yes ( $n = 60$ )

No ( $n = 21$ )

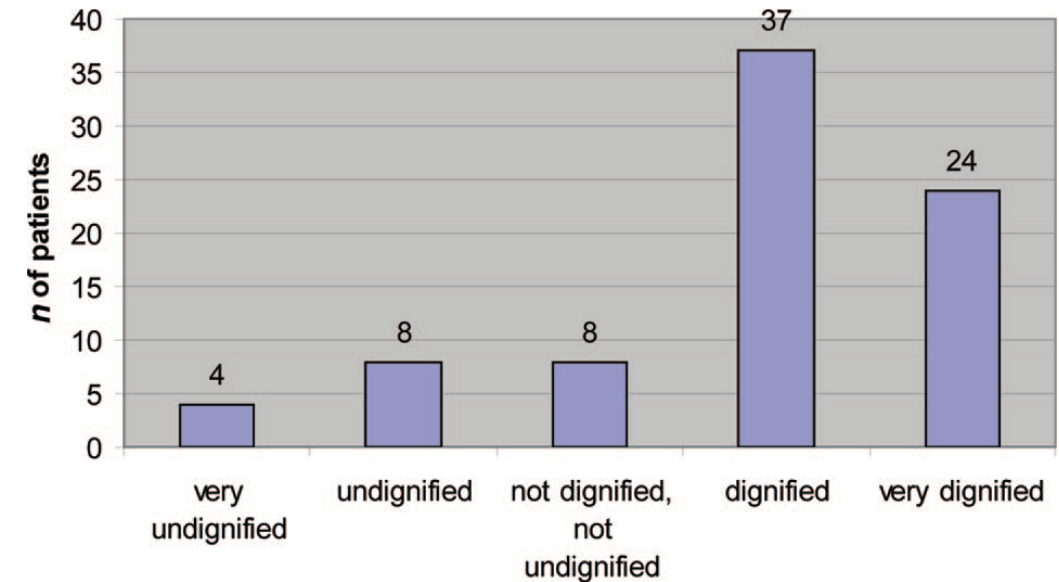
Transition in health care setting last month ( $n_{\text{valid}} = 81$ )

No ( $n = 52$ )


Yes ( $n = 29$ )

All patients ( $n = 81$ )

- Satisfaction with physician
- Ability to communicate
- Absence of transition



# Aggressiveness of care at end of life in patients with high-grade glioma

Rebecca A. Harrison<sup>1</sup>  | Alexander Ou<sup>2</sup> | Syed M. A. A. Naqvi<sup>3</sup> | Syed M. Naqvi<sup>4</sup> |  
Shiao-Pei S. Weathers<sup>1</sup> | Barbara J. O'Brien<sup>1</sup> | John F. de Groot<sup>1</sup> | Eduardo Bruera<sup>3</sup>

*Cancer Medicine.* 2021;10:8387–8394.

## Six indicators in the last 30 days of life:

- $\geq 2$  ER visits,
- $\geq 2$  hospital admissions
- $\geq 14$  days of hospitalization
- Intensive care unit (ICU) admission
- Death in a hospital
- Receipt of chemotherapy within the last 14 days of life.

EoL care score

# Acute healthcare utilization in end-of-life among Swedish brain tumor patients – a population based register study

Magnus Lindskog<sup>1\*</sup> , Torbjörn Schultz<sup>2</sup> and Peter Strang<sup>3</sup> 

Lindskog *et al. BMC Palliative Care* (2022) 21:133

**Table 3** Acute healthcare utilization during the last month of life among brain tumor patients in relation to receipt of specialized palliative care

Care utilization	Total	With SPC	Without SPC	<i>p</i> -value <sup>1</sup>
Emergency room visits	213/780 (27%)	144/604 (24%)	69/176 (39%)	< 0.0001
Hospital admissions	258/780 (33%)	181/604 (30%)	77/176 (44%)	0.0006
Hospital as place of death	60/780 (8%)	14/604 (2%)	46/176 (26%)	< 0.0001

<sup>1</sup> Chi-2; SPC = receipt of specialized palliative care in the last three months of life



# Pattern of care of brain tumor patients in the last months of life: analysis of a cohort of 3045 patients in the last 10 years

Andrea Pace<sup>1</sup> · Valeria Belleudi<sup>2</sup> · Antonio Tanzilli<sup>1</sup>  · Veronica Villani<sup>1</sup> · Francesca Romana Poggi<sup>2</sup> · Dario Benincasa<sup>1</sup> · Marina Davoli<sup>2</sup> · Luigi Pinnarelli<sup>2</sup>

Neurological Sciences 28 February 2023

	last 2 months (%)	last month (%)
H readmission	43	33
ICU admission	4,5	3,7
ER access	38	24
Chemotherapy	24,5	11,4
Radiotherapy	12,1	6



Quality of care at the end of life in BT patients is still an unmet need.

## Reasons

- Specific symptom burden complicates EoL homecare / dying at home (delirium / seizures / loss of consciousness / personality changes / hemiparesis and risk of fall)
- Caregiver burden is extremely high in brain tumors

# Case

-

## Mr. G

### Caregiver burden


6/2012 – WHO II

9/2016 – WHO II

2/2018 – WHO III

8/2018 – WHO IV

8/2019

- 
- Clinical visits alone from 2012-2018
  - Brings wife for the first time at first PC consult
  - First discussions together reveal:
    - Husband sole bread winner – now unable to work
    - 4 children age 7-15 – all react differently
    - Wife has to mediate between all family members
    - Wife has to drive to all appointments now (living in the country)
    - Motor function impaired translates into inability to life in the house with 3 floors
    - Progressing aphasia impairs dialog that had not taken place so far
    - Psychological burden and anger of the patient directed to the wife

# Caregiver in oncology



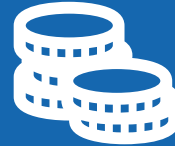
Female

Caring for  
partner or  
parents

Mean age  
50-65



Half of  
them are  
working



Cost  
equivalent:  
35,000 USD  
(excluding  
loss of  
income)



Time > 20h/  
week, up  
to 17h / d

# What do NO CG need?

- Understanding of the disease
- Involvement in informed consent discussions
- Identification of symptoms and progression
- Support systems
- Communication about the future
- Preparation ( especially transition tumor-treatment to supportive care)
- Dialogue neurologist – primary physician – care team

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## End-of-life care for glioma patients; the caregivers' perspective

Clinical Study | Published: 30 March 2020

Volume 147, pages 663–669, (2020) [Cite this article](#)

[Caroline Hertler](#) ✉, [Günter Eisele](#), [Dorothee Gramatzki](#), [Katharina Seystahl](#), [Fabian Wolpert](#), [Patrick Roth](#) & [Michael Weller](#)

JOURNAL ARTICLE

### End-of-life caregivers' perception of medical and psychological support during the final weeks of glioma patients: a questionnaire-based survey

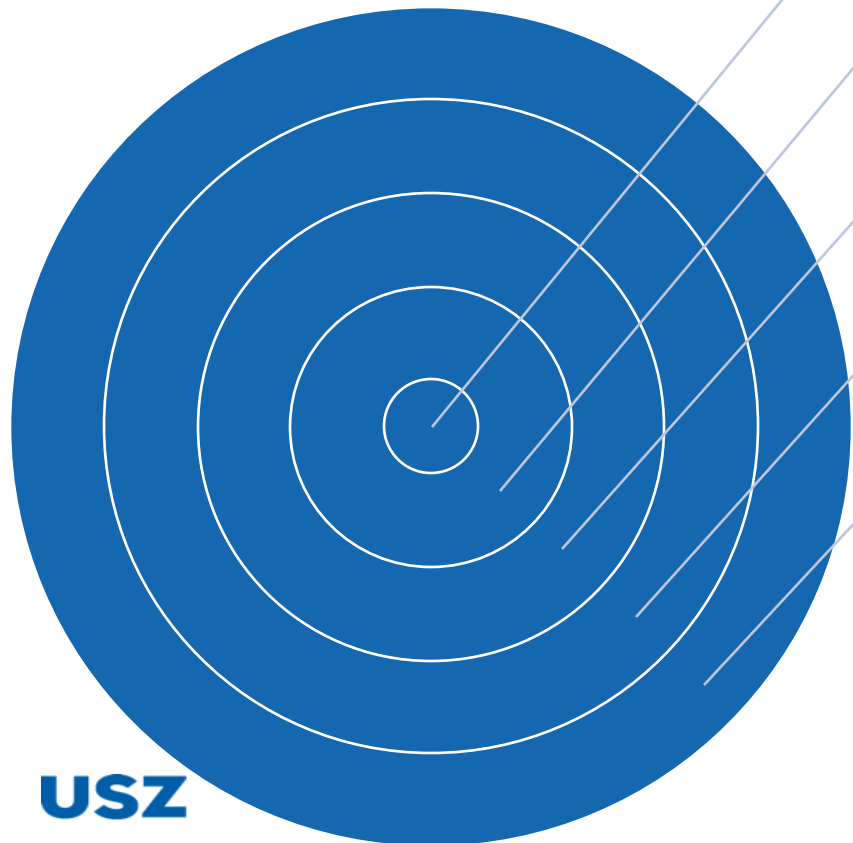
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[Oliver Heese](#) ✉, [Eva Vogeler](#), [Tobias Martens](#), [Oliver Schnell](#), [Jörg-Christian Tonn](#), [Matthias Simon](#), [Johannes Schramm](#), [Dietmar Krex](#), [Gabriele Schackert](#), [Thomas Reithmeier](#) ... [Show more](#)

*Neuro-Oncology*, Volume 15, Issue 9, September 2013, Pages 1251–1256,  
<https://doi.org/10.1093/neuonc/not089>



# CARES framework



**C**onsider Caregiver as part of the unit of care

**A**ssess needs and perceptions

**R**efers to support services

**E**ducate about practical aspects

**S**upport through bereavement

- Acknowledge the importance of the caregiving role
- Include caregivers in decision-making

- Assess capacity and willingness to provide care
- Inquire about physical and mental health
- Assess the impact of caregiving for the caregiver
- Inquire about the perception of the patient status

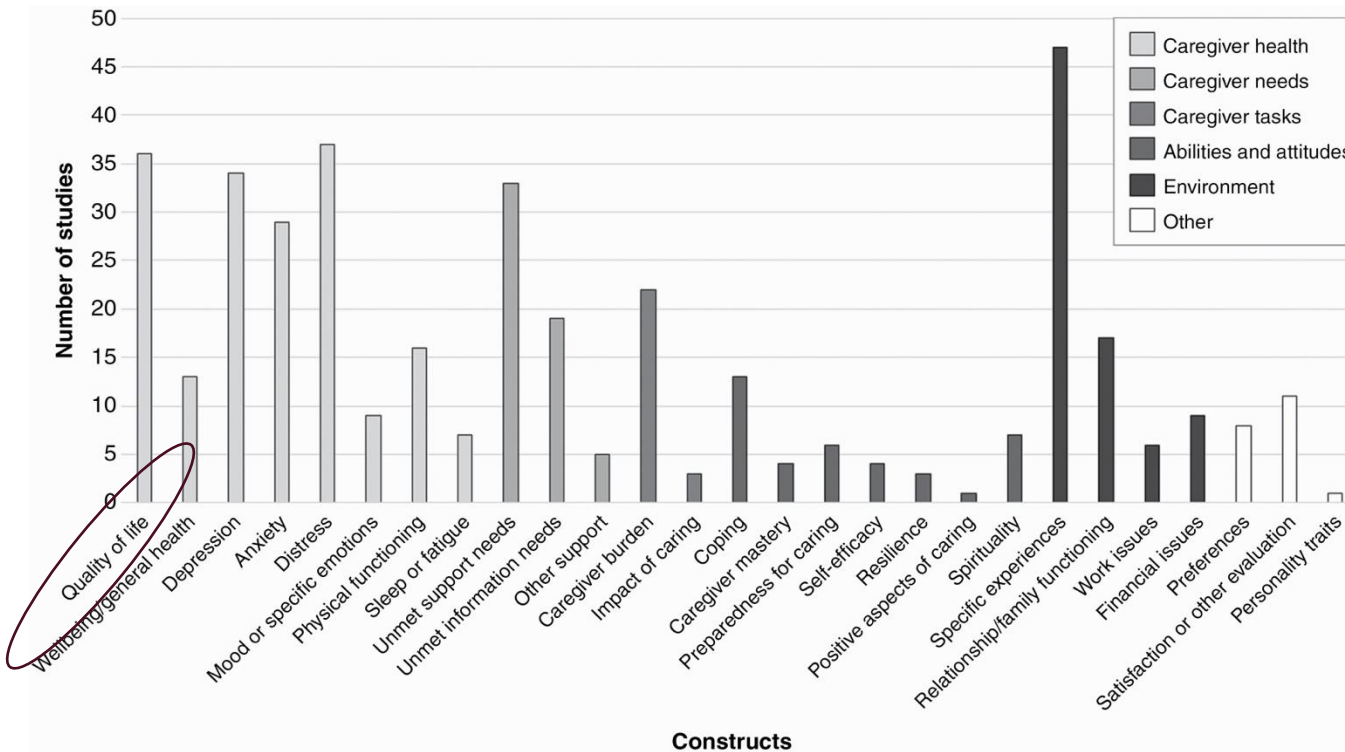
- Ensure patient and caregiver have a joint understanding of the disease, course and signs of progression
- Ensure education for practical skills
- Highlight the importance of self-care

- Offer to call to discuss concerns
- Offer referral to support systems
- Call or send a card to the caregiver

## Family caregiver constructs and outcome measures in neuro-oncology: A systematic review

Florien Boele<sup>✉</sup>, Caroline Hertler<sup>✉</sup>, Linda Dirven<sup>✉</sup>, Karin Piil<sup>✉</sup>, and Paula Sherwood<sup>✉</sup>—on behalf of the International Neuro-oncology Caregiver Consortium (INCC)

- 36 studies on QoL
- 15 different instruments
- Only 3 used > 2 times



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## Reporting standards in randomized controlled trials involving neuro-oncology caregivers: A systematic review report from the RANO-Cares working group

Florien W. Boele<sup>✉</sup>, Caroline Hertler<sup>✉</sup>, Paula Sherwood, David Cachia, Linda Dirven, Jacob S. Young<sup>✉</sup>, Tobias Walbert<sup>✉</sup>, Macy Stockdill, Eduardo Rodriguez Almaraz, and Karin Piil<sup>✉</sup>; RANO-Cares Working Group

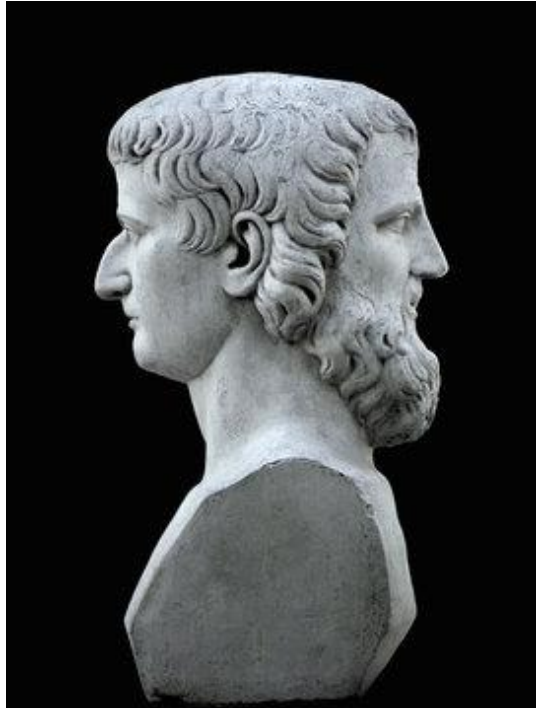
- 80% satisfied  $\geq 2/3$  of key methodological criteria

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Applebaum 2022	+	+	+	+	+	+
Boele 2013	+	-	+	-	+	+
Boele 2022	+	+	+	+	+	+
Boele 2020	+	+	+	+	+	+
Clark 2013	+	+	+	+	+	+
Halkett 2023	+	+	+	+	+	+
Locke 2008	-	+	+	+	+	-
Milbury 2019	+	-	+	+	+	-
Milbury 2023	+	+	-	+	+	-
Milbury 2020	+	-	+	+	+	-
Reblin 2018	+	+	+	+	+	+

Domains:  
 D1: Bias arising from the randomization process.  
 D2: Bias due to deviations from intended intervention.  
 D3: Bias due to missing outcome data.  
 D4: Bias in measurement of the outcome.  
 D5: Bias in selection of the reported result.

Judgement  
 - Some concerns  
 + Low

# Summary



- Early impairment of neurocognitive functioning makes early ACP and early integration of supportive care crucial
- Double-diagnosis of neuro-symptoms and cancer disease increases burden and complicates care
- Caregiver are double-burdened as well

