Palliative and Supportive Care

cambridge.org/pax

Sedation in pediatric palliative care: The role of pediatric palliative care teams

Maria José Peláez Cantero, PH.D.[1], Jose Miguel Morales Asencio, M.D.[2], Fátima Parra Plantagenet-Whyte, PH.D.[3], Moisés Leyva Carmona, PH.D.[4], Mireille Rosique Antonelli, PH.D.[5], Teresa Gili Bigatá, PH.D.[6] and Ricardo Martino Alba M.D.[7]

[1]Department of Paediatric Palliative Medicine, Maternal–Child of Malaga, Regional University Hospital. University of Málaga, Málaga, Spain; [2]Malaga Biomedical Research Institute (IBIMA), University of Málaga, Málaga, Spain; [3]Department of Paediatric Palliative Medicine, Miguel Servet University Hospital, Zaragoza, Spain; [4]Department of Paediatric Palliative Medicine, Torrecardenas Maternal–Child Hospital, Almería, Spain; [5]Department of Paediatric Palliative Medicin, Virgen de la Arrixaca University Hospital, Murcia, Spain; [6]Department of Paediatric Palliative Medicine, Parc Taulí Hospital, Barcelona, Spain and [7]Department of Paediatric Palliative Medicine, Niño Jesus University Children's Hospital, Madrid, Spain

Original Article

Cite this article: Peláez Cantero MJ, Morales Asencio JM, Parra Plantagenet-Whyte F, Leyva Carmona M, Rosique Antonelli M, Gili Bigatá T, Martino Alba R (2023). Sedation in pediatric palliative care: The role of pediatric palliative care teams. *Palliative and Supportive Care*. https://doi.org/10.1017/S1478951523000846

Received: 04 March 2023
Revised: 26 April 2023
Accepted: 03 June 2023

Keywords:
Child; End of life; Palliative care; Palliative care team; Palliative sedation; Prospective study; Terminal care

Corresponding author:
Maria José Peláez Cantero;
Email: 0617268561@alu.uma.es

Abstract

Objectives. Palliative sedation (PS) consists of the use of drugs to alleviate the suffering of patients with refractory symptoms, through a reduction in consciousness. The aim of this study is to describe the incidence of and indications for PS in patients treated by pediatric palliative care teams (PPCT), and the relationship between PS, the place of death, and the characteristics of the care teams.

Methods. Ambispective study with the participation of 14 PPCT working in Spain.

Results. From January to December 2019, a total of 164 patients attended by these PPCT died. Of these, 83 (50.6%) received PS during their last 24 hours. The most frequent refractory symptoms were terminal suffering ($n = 40$, 48.2%), dyspnea ($n = 9$, 10.8%), pain ($n = 8$, 9.6%), and convulsive state ($n = 7$, 8.4%). Sedation in the last 24 hours of life was more likely if the patient died in hospital, rather than at home (62.9% vs. 33.3%, $p < 0.01$); if the parents had not expressed their preference regarding the place of death (69.2% vs. 45.2%, $p = 0.009$); and if the PPCT had less than 5 years' experience (66.7% vs. 45.5%, $p = 0.018$).

Significance of results. PS is a real possibility in pediatric end-of-life care and relates to care planning and team expertise.

Introduction

At the end of life, certain symptoms commonly appear as the disease progresses, and although different treatment options are available to control these symptoms, in some cases they lose effectiveness (in terms of benefit achieved or duration) or produce results that are more negative than positive (de Graeff and Dean 2007). When the symptoms are very severe, becoming intolerable for the patient, and can be considered refractory, palliative sedation (PS) may be considered as a treatment option (Arantzamendi et al. 2021).

PS in the context of palliative medicine is 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, the family, and health-care providers (Cherny and Radbruch 2009). PS may be continuous or intermittent and its depth is graduated to provide the minimum level of sedation that achieves symptomatic relief (guia_sedaccion_paliativa.pdf 2021). The intent of PS, therefore, is to relieve the burden of otherwise intolerable suffering for terminally ill patients (Cherny and Portenoy 1994).

This measure is indicated for adult and pediatric palliative care patients with advanced, incurable illness (Palliative sedation – UpToDate 2023), under the condition that its introduction does not directly provoke a detrimental effect on survival (Maeda et al. 2016; Maltoni et al. 2012).

Several studies of this question, referring to palliative care for adults, have been published, mainly focusing on the development of clinical guidelines (Cherny 2014; Cherny and Radbruch 2009; guia_sedaccion_paliativa.pdf 2021), and usually based on expert opinion and retrospective reviews. In contrast, hardly any case series have been published with respect to the pediatric population (Chen et al. 2022; de Noriega et al. 2021; Kiman et al. 2011), although this lack of data does not mean that the practice is uncommon (Korzeniewska-Eksterowicz et al. 2014). More knowledge is needed of the habitual approaches of health-care professionals regarding

CAMBRIDGE UNIVERSITY PRESS

pediatric PS, and of the clinical and contextual circumstances in which it is carried out, in order to identify areas for improvement, and to provide indications for future research, thus strengthening the evidence supporting protocols and guidelines for clinical practice.

The aim of the present study is to describe the incidence of PS in patients treated by pediatric palliative care teams (PPCT), to determine the indications considered, the drugs used and, in a more innovative way, the relationship between PS, the place of death, and the characteristics of the care teams.

Methods

This ambispective, analytical, multicenter study was conducted from 1 January to 31 December 2019. Data collection was performed by 14 PPCT at 219 public hospitals in Spain with pediatric services (Consulta Interactiva del SNS 2021). Of this total, only 26 hospitals had a PPCT when the study period began.

All patients treated by the PPCT were followed up during the study period, and data were also compiled on those who died. All data collection was performed through the analysis of medical records.

The following study variables were recorded for each patient: sex, age, underlying disease, medication, doses provided during the week prior to death, reason for death, place of death, expression of preference by the family regarding the place of death, and the performance of and reason for sedation. In addition, the year of creation of each PPCT was recorded, to determine its length of experience.

The patient's underlying disease was described according to the classification system for pediatric complex chronic diseases (v.2), developed by Feudtner et al. (2014).

Analysis

Descriptive statistics were obtained by exploratory data analysis, with measures of central tendency, dispersion, and frequency. The normality of the distributions was determined by the Kolmogorov–Smirnov test, together with an evaluation of asymmetry and kurtosis. Variables with a normal distribution are described by the mean and standard deviation; otherwise, by the median and interquartile range (IQR). Bivariate analysis was performed using the chi-square and Fisher's exact tests where necessary, as well as analysis of variance for the comparative analysis by Feudtner subgroups, with measures of central robustness in the event of non-homoscedasticity (verified with the Levene test) using the Brown–Forsythe test, and determining the difference in means for independent groups using the Mann–Whitney *U* test. Subsequently, a multivariate logistic regression model was constructed with the presence of sedation as the dependent variable and the introduction of predictors from the variables that presented a significant association in the bivariate analysis, or which had significant clinical plausibility. All analyses were performed using SSPS 26 (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp) and JAMOVI (The jamovi project (2021). jamovi (Version 1.6) [Computer Software]. Retrieved from https://www.jamovi.org 2021) statistical software.

Results

The study sample consisted of 164 patients, of whom 84 (51.2%) were female and 80 (48.8%), male. Table 1 describes the underlying diseases identified, most of which correspond to oncological, neurological, and neuromuscular processes. The median age at death was 6.9 years (IQR 11.2). The reasons for death were the progression of the underlying disease ($n = 101$ patients; 61.6%), comorbidity ($n = 51$ patients, 31.1%), or unexpected cause ($n = 12$ patients, 7.3%).

Table 1. Baseline disease

Baseline disease	*n* (%)
Malignancy	79 (48.2)
Neurological/Neuromuscular disease	39 (23.8)
Metabolic disease	15 (9.1)
Prematurity/Neonatal disease	14 (8.5)
Congenital disease or genetic defects	12 (7.3)
Other	5 (3.1)

In total, 52 patients (31.7%) received sedation in the last 7 days of life, while 83 (50.6%) received PS in the last 24 hours. Among the refractory symptoms, we found terminal suffering in 40 patients (48.2%), dyspnea ($n = 9$, 10.8%), pain ($n = 8$, 9.6%), and convulsive state ($n = 7$, 8.4%). The most frequently used drug for PS was midazolam in continuous infusion ($n = 74$ patients, 89.2%), which was supplied intravenously to 45 patients (54.2%), with a median dose of 0.1 mg/kg/h (IQR 0.2).

A total of 95 patients (57.9%) died in the hospital and 67 (40.9%), at home. Sedation was more likely to be given in the last 24 hours if the patient died in the hospital (62.9% vs. 33.3%, χ^2: 13.7, $p < 0.01$).

One of the study variables considered was whether the PPCT had previously discussed with the family their preference regarding the place of death. In this regard, 125 families (76.2%) had expressed a preference, with 70 (56%) stating the home should be the place of death. The children whose parents had stated this preference were less likely to be sedated during the last 24 hours of life (45.2% vs. 69.2%, χ^2: 6.9, $p = 0.009$, OR: 0.37 95% CI: 0.17 to 0.79). When no preference was expressed, sedation was supplied up to 3 times more frequently when the child was in a situation of terminal suffering (72.7% vs. 46.2%; OR: 3.1 95% CI: 1.05 to 9.21; χ^2: 4.4, $p = 0.036$).

Focusing on the teams' experience, those with less than 5 years' practice sedated 66.7% of their patients during the last 24 hours of life, compared to 45.5% of the units with greater experience (χ^2: 5.6, $p = 0.018$, OR: 0.21, 95% CI: 0.04 to 0.38). The indications for sedation were similar in both groups. Moreover, higher infusion doses were given by the teams with less experience, at both 1 week before and at 24 hours before death (0.31 vs. 0.16 mg/kg/h, $z = 2.60$; $p = 0.009$ and 0.27 vs. 0.15 mg/kg/h, $z = 2.13$, $p = 0.033$, respectively).

Multivariate analysis, adjusted for age and sex, showed that the likelihood of receiving sedation in the last 24 hours of life was greater in patients who were treated by a PPCT with less than 5 years' experience (OR: 2.84, 95% CI: 1.09 to 7.37) and that this value decreased when the family's preference regarding the place of death had been discussed and the child died at home (OR: 2.43, 95% CI: 1.14 to 5.18). In this respect, there was no influence by age or sex (Table 2).

Discussion

This study was conducted to determine the incidence of PS in patients treated by a PPCT, and the association between this value

https://doi.org/10.1017/S1478951523000846 Published online by Cambridge University Press

Table 2. Factors associated with the use of sedation during the 24 hours before death

Predictor	*B*	*p*	OR (95% CI)
Constant	−0.64	0.100	0.52 (0.24 to 1.13)
Gender			
Male–Female	−0.21	0.578	0.81 (0.38 to 1.71)
Age of death	−0.01	0.814	0.99 (0.93 to 1.05)
Experience of the PPCT			
<5 years to ≥5 years	104.25	0.032	2.84 (1.09 to 7.37)
Preference expressed			
Hospital–Home	0.89	0.021	2.43 (1.14 to 5.18)

McFadden's R^2: 0.07, variance inflation factor range: 1–1.03, tolerance range: 0.97–0.99.

and the clinical care and contextual circumstances in which the sedation was given. To our knowledge, this is the first multicenter investigation of its type to be performed in Spain.

During the study period, slightly more than 30% of the terminal pediatric patients treated by a PPCT received sedation in the last 7 days of life. This value rose to 50% in the last 24 hours. To our knowledge, no previous study has examined such a large sample of pediatric patients treated with PS. In a broader context, the above rates of incidence are lower (Libro-de-ponencias-y-comunicaciones-III-Congreso-PedPal.pdf 2019) or similar to those reported in some cases (Chen et al. 2022; Korzeniewska-Eksterowicz et al. 2014; Vallero et al. 2014) but higher than has been published in other, recent, publications (Cuviello et al. 2023; de Noriega et al. 2021; Maeda et al. 2020). These discrepancies might be explained, at least in part, by the existence of differences between the respective study cohorts and by the lack of a unified definition.

The question of definitions remains controversial, and most have been developed from experience with adult patients. Nevertheless, despite this variability, a common concept in many of the definitions of PS is "the use of sedative medications to alleviate the intolerable suffering of refractory symptoms through a reduction in the patient's consciousness" (Cherny 2014; Cherny and Radbruch 2009). Given this premise, the presence of refractory symptoms at the end of life is an essential requirement for prescribing PS. Refractory symptoms are usually considered to be those which are physical; in our sample, the most common of these symptoms were dyspnea, pain, and convulsive status. The first 2 of these are corroborated in the literature, where dyspnea, pain, and delirium are most frequently mentioned (Arantzamendi et al. 2021; de Noriega et al. 2021; Korzeniewska-Eksterowicz et al. 2014; Maltoni et al. 2012). Despite receiving optimal palliative care, some children still experience severe uncontrolled symptoms in their last weeks of life. In these circumstances, no measure to alleviate suffering should be spared and PS must be considered.

However, reducing refractory symptoms to those physically apparent would be too simplistic a view of human suffering (Goldman 2012; Rodrigues et al. 2018). There is a situation that precedes death and in which there is intense physical deterioration, extreme weakness, high frequency of cognitive disorders and consciousness, difficulty relating, and eating with a prognosis of life limited to hours or days that sometimes causes suffering. The Spanish Society for Palliative Care (SECPAL) coined the expression *terminal suffering palliative sedation* to refer to the sedation employed when the patient has only hours or a few days to live, and is experiencing intense suffering (guia_sedaccion_paliativa.pdf, 2021). This situation, affecting 48.2% of the patients in our sample, was the most frequent reason for initiating PS. As specific data under this description are compiled only in Spain, the latter result cannot be compared with other research findings.

In this context, there may sometimes be difficulty in treating suffering at the end of life when it is secondary to a symptom, but you do not have enough time. It will also be difficult to distinguish between a refractory symptom and one that is merely difficult to treat, the latter type being one requiring intensive therapeutic intervention: pharmacological, instrumental, and/or psychological ("salud_5af19569afca1_02_definiciones_cpali_sedacion.pdf" 2005). Our analysis shows that when the PPCT in question had sufficient expertise and experience to treat difficult symptoms and did not consider them refractory, rates of PS were lower and, when necessary, they were supplied at lower doses than those given by teams with less experience. Therefore, before classifying a symptom as refractory, professionals should be advised by experienced palliative care specialists (de Graeff and Dean 2007). Furthermore, if the physician is unable to relieve a distressing symptom, he/she may feel pressured to use PS, or even to provide disproportionate sedation. It has been suggested that physician fatigue and burnout may be associated with an increased use of PS (Coyle et al. 1990; "Practices and attitudes of Japanese oncologists and palliative care physicians concerning terminal sedation: a nationwide survey – PubMed" 2002). In this regard, the development of explicit institutional PS protocols could help reduce uncertainty and variability in this practice (Henderson et al. 2017).

In our sample, midazolam was the drug most frequently used for PS, as recommended elsewhere for use with pediatric and adult populations (Cherny 2014; Cherny and Radbruch 2009) and as reported in most previous studies of this question (de Graeff and Dean 2007; de Noriega et al. 2021; Maeda et al. 2020; Vallero et al. 2014), although recent studies have highlighted that pain medicine specialists opted for opioids as the first-line drug for the initiation of PS therapy, followed by benzodiazepines (Cuviello et al. 2022).

Although previous research has shown that families prefer the death to take place in the home (Goldman et al. 1990; Woodman et al. 2015), which is consistent with our findings, in practice more deaths occur in hospital settings. It is here where PS is more likely to be applied in the last 24 hours of life (62.9% vs. 33.3% at home), a proportion similar to that reported for the treatment of adults (Pousset et al. 2011). Our study results also show that among the families who expressed a preference in this respect, there was a lower probability of PS. Some authors suggest that PS, in pediatric care, is most appropriately supplied in the home. It is also less costly than the standard care model for hospitalized patients (Korzeniewska-Eksterowicz et al. 2014). However, we must be cautious in this regard; on the one hand, PS in the home might be considered less invasive, but on the other hand, patients with more difficult-to-control symptoms should be hospitalized to ensure optimum monitoring and treatment.

Our study results also show that children whose parents had expressed their preference regarding the place of death were less likely to receive PS in the last 24 hours of life, and that in families where no such preference had been expressed, sedation during terminal suffering was up to 3 times more frequent. We believe these results highlight the importance of advanced care planning, which if carried out by the PPCT can reduce the need for PS

https://doi.org/10.1017/S1478951523000846 Published online by Cambridge University Press

(Kiman et al. 2011). In this respect, an important consideration arises: any discussion of preferences for the place of death are focused on an impending death, a process in which the patient (when possible and appropriate) and his/her family should be actively involved. In the case of PS, a significant aspect of advanced care planning is the need to clarify the intentions underlying any intervention made (fundamentally, the treatment team should seek to maximize the patient's well-being and manage the symptoms observed, but not accelerate death), to obtain verbal consent, to provide sufficient time (if circumstances allow it) for the patient and/or family to assimilate the situation, and to provide support to all family members involved.

Among other limitations of this study, it was not possible to record the duration of the PS, nor the level of sedation provided, nor any side effects that may have been caused.

Conclusions

Some children who are terminally ill die peacefully and painlessly, without the need for PS; others, however, present refractory symptoms, for which PS can be considered as an option. In the latter case, the decision to offer sedation to alleviate intolerable suffering during the last weeks of life does not present any ethical problem. Quite the opposite: deciding upon and applying this treatment option represents a continuation of good clinical practice, based on a careful evaluation of the patient and concern for his/her ultimate well-being.

The application of PS requires the professionals involved to have sufficient experience and appropriate communication skills.

Funding. Funding for open access charge: Universidad de Málaga.

Competing interests. None.

Ethical approval. The study was approved by the Research Ethics Committee of Málaga Regional University Hospital (code 1054-N-21).

References

Arantzamendi M, Belar A, Payne S, ***et al.*** (2021) Clinical aspects of palliative sedation in prospective studies. A systematic review. *Journal of Pain and Symptom Management* **61**(4), 831–844.e10. doi:10.1016/j.jpainsymman.2020.09.022

Chen Y, Jiang J, Peng W, ***et al.*** (2022) Palliative sedation for children at end of life: A retrospective cohort study. *BMC Palliative Care* **21**(1), 57. doi:10.1186/s12904-022-00947-y

Cherny NI and ESMO Guidelines Working Group (2014) ESMO Clinical Practice Guidelines for the management of refractory symptoms at the end of life and the use of palliative sedation. *Annals of Oncology: Official Journal of the European Society for Medical Oncology* **25**(3), iii143–iii152. doi:10.1093/annonc/mdu238

Cherny NI and Portenoy RK (1994) Sedation in the management of refractory symptoms: Guidelines for evaluation and treatment. *Journal of Palliative Care* **10**(2), 31–38. doi:10.1177/082585979401000207

Cherny NI and Radbruch L and Board of the European Association for Palliative Care (2009) European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. *Palliative Medicine* **23**(7), 581–593. doi:10.1177/0269216309107024

(2021) Consulta interactiva del SNS. https://pestadistico.inteligenciadegestion.sanidad.gob.es/publicoSNS/S.

Coyle N, Adelhardt J, Foley KM, ***et al.*** (1990) Character of terminal illness in the advanced cancer patient: Pain and other symptoms during the last four weeks of life. *Journal of Pain and Symptom Management* **5**(2), 83–93. doi:10.1016/s0885-3924(05)80021-1

Cuviello A, Johnson L-M, Morgan KJ, ***et al.*** (2022) palliative sedation therapy in pediatrics: An algorithm and clinical practice update. *Children* **9**(12), 1887. doi:10.3390/children9121887

Cuviello A, Pasli M, Bhatia S, ***et al.*** (2023) Dexmedetomidine and propofol at end of life in pediatric oncology: Trends in palliative sedation therapy. *Journal of Palliative Medicine* **26**(1), 79–86. doi:10.1089/jpm.2021.0650

de Graeff A and Dean M (2007) Palliative sedation therapy in the last weeks of life: A literature review and recommendations for standards. *Journal of Palliative Medicine* **10**(1), 67–85. doi:10.1089/jpm.2006.0139

de Noriega I, Rigal Andrés M and Martino Alba R (2021) Descriptive analysis of palliative sedation in a pediatric palliative care unit. *Anales De Pediatria* **96**(5), 385–393. doi:10.1016/j.anpedi.2021.01.005

Feudtner C, Feinstein JA, Zhong W, ***et al.*** (2014) Pediatric complex chronic conditions classification system version 2: Updated for ICD-10 and complex medical technology dependence and transplantation. *BMC Pediatrics* **14**(1), 199. doi:10.1186/1471-2431-14-199

Goldman A, Beardsmore S and Hunt J (1990) Palliative care for children with cancer–home, hospital, or hospice? *Archives of Disease in Childhood* **65**(6), 641–643. doi:10.1136/adc.65.6.641

Goldman A, Hain H and Liben S (2012) *Oxford Textbook of Palliative Care for Children*, 2nd edn. Oxford University Press.

(2021) guia_sedaccion_paliativa.pdf. https://www.cgcom.es/sites/main/files/mig/guia_sedaccion_paliativa.pdf.

Henderson CM, FitzGerald M, Hoehn KS, ***et al.*** (2017) Pediatrician ambiguity in understanding palliative sedation at the end of life. *The American Journal of Hospice & Palliative Care* **34**(1), 5–19. doi:10.1177/1049909115609294

IBM Corp. Released (2019) IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.

The jamovi Project (2021) jamovi (Version 1.6) [Computer Software]. https://www.jamovi.org (accessed 9 November 2022).

Kiman R, Wuiloud AC and Requena ML (2011) End of life care sedation for children. *Current Opinion in Supportive and Palliative Care* **5**(3), 285–290. doi:10.1097/SPC.0b013e3283492aba

Korzeniewska-Eksterowicz A, Przysło Ł, Fendler W, ***et al.*** (2014) Palliative sedation at home for terminally ill children with cancer. *Journal of Pain and Symptom Management* **48**(5), 968–974. doi:10.1016/j.jpainsymman.2014.01.012

(2019) Libro-de-ponencias-y-comunicaciones-III-Congreso-PedPal.pdf. https://www.pedpal.es/site/wp-content/uploads/2019/03/Libro-de-ponencias-y-comunicaciones-III-Congreso-PedPal.pdf.

Maeda S, Kato I, Umeda K, ***et al.*** (2020) Continuous deep sedation at the end of life in children with cancer: Experience at a single center in Japan. *Pediatric Hematology and Oncology* **37**(5), 365–374. doi:10.1080/08880018.2020.1744781

Maeda I, Morita T, Yamaguchi T, ***et al.*** (2016) Effect of continuous deep sedation on survival in patients with advanced cancer (J-Proval): A propensity score-weighted analysis of a prospective cohort study. *The Lancet Oncology* **17**(1), 115–122. doi:10.1016/S1470-2045(15)00401-5

Maltoni M, Scarpi E, Rosati M, ***et al.*** (2012) Palliative sedation in end-of-life care and survival: A systematic review. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology* **30**(12), 1378–1383. doi:10.1200/JCO.2011.37.3795

(2023) Palliative sedation - UpToDate. https://www.uptodate.com/contents/palliative-sedation#H21551878.

Pousset G, Bilsen J, Cohen J, ***et al.*** (2011) Continuous deep sedation at the end of life of children in Flanders, Belgium. *Journal of Pain and Symptom Management* **41**(2), 449–455. doi:10.1016/j.jpainsymman.2010.04.025

(2002) Practices and attitudes of Japanese oncologists and palliative care physicians concerning terminal sedation: A nationwide survey – PubMed. https://pubmed.ncbi.nlm.nih.gov/11821458/ (accessed 9 November 2022).

https://doi.org/10.1017/S1478951523000846 Published online by Cambridge University Press

Rodrigues P, Crokaert J and Gastmans C (2018) Palliative sedation for existential suffering: A systematic review of argument-based ethics literature. *Journal of Pain and Symptom Management* **55**(6), 1577–1590. doi:10.1016/j.jpainsymman.2018.01.013

(2005) salud_5af19569afca1_02_definiciones_cpali_sedacion.pdf. https://www.juntadeandalucia.es/export/drupaljda/salud_5af19569afca1_02_definiciones_cpali_sedacion.pdf.

Vallero SG, Lijoi S, Bertin D, ***et al.*** (2014) End-of-life care in pediatric neuro-oncology – PubMed. *Pediatr Blood Cancer* **61**(11), 2004–2011.

Woodman AC, Mawdsley HP and Hauser-Cram P (2015) Parenting stress and child behavior problems within families of children with developmental disabilities: Transactional relations across 15 years. *Research in Developmental Disabilities* **36C**, 264–276. doi:10.1016/j.ridd.2014.10.011

https://doi.org/10.1017/S1478951523000846 Published online by Cambridge University Press