Radiotherapy and Oncology 168 (2022) 147–210

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Review Article

Defining the expected 30-day mortality for patients undergoing palliative radiotherapy: A meta-analysis

Justin Henry Kutzko [a], Parvati Dadwal [b], Tanya Holt [c,d,*], Muhammed Aashiq Rahman [b], Syeda Farah Zahir [e], Brigid Hickey [c,d,f]

[a] Royal Brisbane Women's Hospital, Herston; [b] Cairns Hospital; [c] Princess Alexandra Hospital – ROPART, South Brisbane; [d] University of Queensland; [e] QCIF Facility for Advanced Bioinformatics, Institute for Molecular Bioscience, The University of Queensland; and [f] Queensland University of Technology, Brisbane, Australia

ARTICLE INFO

Article history:
Received 10 September 2021
Received in revised form 16 January 2022
Accepted 18 January 2022
Available online 29 January 2022

Keywords:
Prognostic factors
Palliative radiotherapy
Clinical protocols
Radiation oncology
30 day mortality
End of life

ABSTRACT

Background: The expected 30-day mortality rate for patients treated with palliative radiation is not established. The primary objective of this study is to define the proportion of patients with advanced cancer who die within 30-days of palliative radiotherapy (PR). Additionally, we explored the short term survival of patient subgroups undergoing PR treatment.

Methods: We searched MEDLINE, CINAHL, Embase and Cochrane Database of Systematic Reviews from January 1st 1980 to June 26, 2020. We included PUBMED's related search and reference lists to further identify articles. A meta-analysis of these research studies and reviews was performed. Published and unpublished English language randomized controlled trials, observational or prospective studies, and systematic reviews that reported 30-day mortality for patients with advanced cancer who received PR were eligible. Data extraction was done by two independent authors and included study quality indicators. To improve distribution and variance, all proportions were transformed using logit transformation. A random-effects model was used to pool data, using Der Simonian and Laird method of estimation where possible and appropriate.

Results: The data from 42 studies contributing 88,516 patients with advanced cancer who received PR were evaluated. The summary proportion of mortality in patients with advanced cancer within 30 days of receiving PR was 16% (95% CI = 14% to 18%). We found substantial heterogeneity in our data (I^2 = 98.76%, $p < 0.001$), hence we applied subgroup analysis to identify potential moderating factors. We found a higher 30-day mortality rate after PR in the following groups: multiple treatment sites (QM(1) = 9.54, $p = 0.002$), hepatobiliary primary (QM(1) = 24.20, $p < 0.001$), inpatient status (QM (1) = 92.27, $p < 0.001$), Eastern Cooperative Oncology Group performance status (ECOG) 3–4 (QM (1) = 8.70, $p = 0.003$), United States (U.S.) patients (QM(1) = 28.70, $p < 0.001$) among others.

Conclusions: We found that 16% of patients with advanced cancer receiving PR die within 30 days of treatment. Our finding can be used as a benchmark to establish a global quality metric for radiation oncology practice audits.

Patients diagnosed with incurable cancer will predominantly succumb to the disease itself as the cause of their death [1]. Palliative radiotherapy (PR) is used to alleviate cancer-related symptoms and is given to 19% of patients with cancer [2]. Common indications for PR include pain and fracture prevention from bone metastases [3], neurological symptoms from spinal cord/cauda equina compression or nerve root compression [4], symptoms from brain metastases [5], and haemostasis [6,7]. Symptomatic responses to PR may take several weeks. This delay means patients treated with PR need to survive long enough to derive a benefit [8]. Oncologists can be optimistic when estimating survival for patients with advanced cancer [9,10], as a consequence patients who are treated can die before deriving any benefit from PR.

Patients with advanced disease should be selected carefully before treatment with PR, especially multi-fraction radiation treatments (RT), which may be futile close to end

Abbreviations: PR, palliative radiotherapy; ECOG, Eastern Cooperative Oncology Group performance status; U.S., United States of America; RT, radiation treatments; ROB, risk of bias; ESR, externally studentized residuals; CI, confidence interval.

* Corresponding author at: Princess Alexandra Hospital – ROPART, 31 Raymond Terrace, South Brisbane, QLS 4101, Australia.
E-mail address: Tanya.Holt@health.qld.gov.au (T. Holt).

https://doi.org/10.1016/j.radonc.2022.01.030
0167-8140/

of life and can increase patient burden and health care costs [11]. Achieving the appropriate balance between providing useful symptom relief and avoiding potentially futile interventions is challenging near end of life [12]. One evidence-based solution to this problem is using short treatment courses (i.e. fewer RT fractions) for symptomatic patients with poor prognosis [9,12]. The 30-day mortality after PR is commonly used to audit how many patients with advanced cancer are treated at end of life [136][13]. The 30-day mortality after PR has been considered as a possible quality metric [14]. The use of chemotherapy within 30 days of death is an accepted quality metric, with evidence to support what should be considered standard of care [15–18]. The recommendation from the Royal College of Radiologists that "no more than 20% of patients should die within 30 days of receiving their PR treatment", however, is not evidence-based [19]. We found no published meta-analysis reporting 30-day mortality rate for patients with advanced cancer treated with PR.

We completed a systematic review and meta-analysis to estimate the average proportion of patients who are reported to have died within 30 days of PR. Additionally, we performed subgroup analyses by computing subgroup summary proportions.

Methods

Our research was conducted in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement. The protocol is available on the PROSPERO website: protocol number CRD42020181567 [20]. Low risk ethics approval was obtained from the Metro South Human Research Ethics Committee (reference: HREC/2021/QMS/73488 on 7 April 2021) and approval from the Queensland Public Health Act for use of the Queensland government (Australia) data [2] (PHA 73488).

Search strategy

We searched MEDLINE (PubMed), Embase, CINAHL, and Cochrane Database of Systematic Reviews from January 1st, 1980 to June 26th, 2020. Specific search strategies for each database were built and reported in Appendix A. Citations from the searches were uploaded into EndNote X9, and from here uploaded into Covidence [21], a data management program software. The reference lists of all studies that met inclusion criteria were examined for further identification of relevant studies. A pre-determined study inclusion criterion was used. The study selection process involved title and abstract screening and finally a full text review using Covidence. The selection process as per PRISMA guidelines is presented in Fig. 1 [22]. Two independent reviewers decided on study inclusion after full text review.

Protocol and eligibility criteria

(i) Inclusion criteria

Published or unpublished English language studies reporting data for patients of any age, with locally advanced or metastatic cancer treated with external beam PR.

Analytical epidemiological studies including retrospective or prospective cohort and case-control studies, meta-analyses, randomized controlled trials and systematic reviews were eligible.

(ii) Exclusion criteria

Studies were excluded if they did not report the primary outcome measure. Studies that focused on palliative chemotherapy only, and radiotherapy (RT) studies that did not report the number of patients treated with PR were excluded.

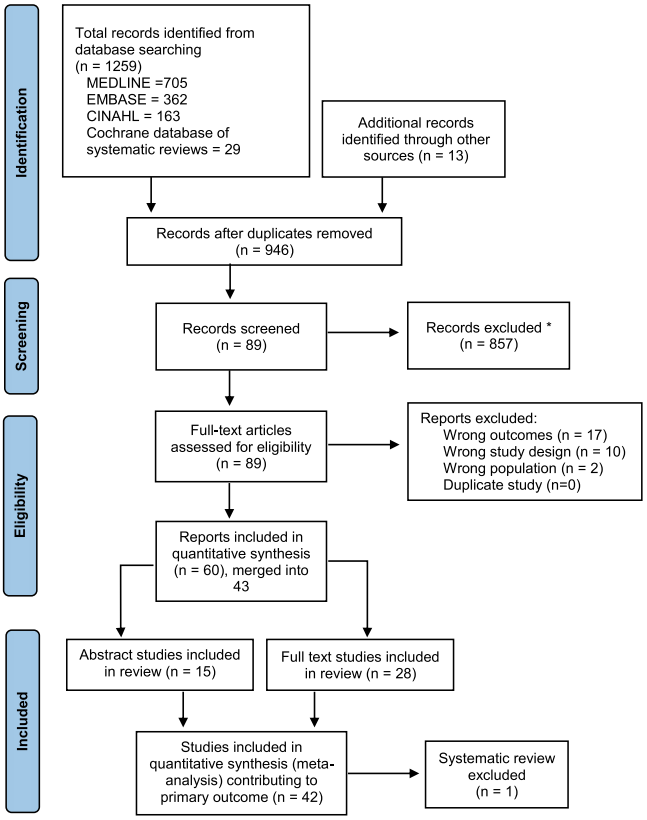

Fig. 1. PRISMA flow diagram. * = 857 records were excluded after abstract screening by two independent reviewers for not containing the terms "30-day/1-month mortality" or similar.

(iii) Outcomes

The primary outcome was the proportion of patients with locally advanced or metastatic cancer treated with PR who died within 30-days of starting treatment.

The secondary outcomes were the impact of the following on the 30-day mortality rate: planned number of fractions, the proportion of patients who died within 30-days of start of treatment who did not complete the planned PR course, radiation technique i.e., highly conformal RT including stereotactic body radiotherapy (SBRT) and volume modulated arc therapy (VMAT) or intensity modulated radiation therapy (IMRT) vs. simple field arrangements; indications for PR.

We investigated the following prespecified groups: indications for PR, primary diagnosis of cancer, inpatient vs. outpatient status at time of RT referral, patient performance status, synchronous or prior chemotherapy, steroid treatment at the time of RT referral, patients who are resident to a care-home at referral for RT, number of patients known to a hospice team at the time of referral for PR, age, patients with non-bone metastases, and those with liver metastases getting PR. For post-hoc subgroup analysis the following was collected: U. S. studies, year of publication, and studies measuring 30-days metric timeline from the start vs. end of the patient's PR course.

We systematically searched for any unpublished data by contacting authors of studies accepted for the full text-review stage of our study screening process. If unpublished data matching our outcomes/subgroups of interest was found, it was included in our meta-analysis. In total, 32 authors were contacted, 15 replied

resulting in 7 studies providing unpublished data used in this meta-analysis.

Data extraction

We used Covidence [21] to merge and extract data from studies included after full-text screening was completed. The data was then coded in a spreadsheet to collate information from each included study. Two reviewers independently extracted: name of primary author, publication year, demographic data, and the total number of PR courses of treatment given to patients in each study. Mortality rate after PR was extracted as the primary outcome of interest.

Moderators: The secondary outcomes and moderator data extracted pre- and post-hoc are listed in the outcomes section above.

Risk of bias (ROB) assessment

The quality of individual studies was assessed using a modified version of the ROBINS-I tool [23] (Appendix B.1). Each study was assessed for bias and scored at high, moderate, and low ROB. We assessed the following 6 study ROB domains: study population definition, confounding variables, selection bias, missing data, duplicate publication bias and outcome reporting bias. The Overall ROB for each domain was assigned either low, moderate or high ROB based on the percentage of studies assessed at a certain level of risk: if >/=60% of individual studies were assessed as low ROB for that domain then the overall ROB for this domain was low. If <60% of studies were low ROB for a domain, then the domain ROB was assessed as moderate (sum total number of low + moderate ROB studies for a domain > number of high ROB studies for that domain) or high (number of high ROB studies for a domain > sum total of low + moderate ROB studies for that domain) ROB (Appendix B.2). ROB across studies (publication bias) was assessed by plotting the effect by the inverse of its standard error. The symmetry of this funnel plot was assessed both visually and via regression test for funnel plot asymmetry.

Data synthesis and analysis

The included studies are single arm non-comparative studies, so meta-analysis of proportions using a "random effects model" [24] was done. One randomised-controlled trial was included that reported those patients getting PR for bone metastases who were randomised to two different doses of PR comparing single fraction treatment to multi-fraction doses for pain. We were able to obtain our primary outcome, which was reported for the total population (including both treatment arms) of this study, so it was included in our analysis [25]. Visualisation through histogram (Appendix C.1) and Shapiro-Wilk's test [26] indicated non-normality of the primary outcome, hence a logit transformation of proportions was applied [27–29]. Pooled proportion was estimated using the transformed proportions which conformed to normal distribution after transformation, ensuring accurate estimation of summary proportion. All analyses were conducted on transformed proportions with Der Simonian and Laird method of estimation using a random effects model [30]. The transformed proportions, and 95% confidence intervals (95% CI), were reverted to original proportions for ease of reporting and interpretation. The summary proportion and their 95% CI is presented in a Forest plot. We assessed heterogeneity using Cochran's Q [30] and I^2 statistic [31]. Visual inspection of Forest plots, externally studentized residuals (ESRs) and leave-one-out analysis were used to screen for influential studies, and more specifically, to discover whether the one paediatric study [32] or two U.S. studies [33,34] (consisting of restricted adult populations) included in our review was statistically influential on the summary proportion of 30-day mortality rate after PR [35]. Because of the high number of studies extracted in this review, the studies with ESR z-values greater than 3 were considered outliers. Leave one out analysis was conducted to examine the influence of outliers. We used subgroup analysis to investigate the potential modifier effect (calculating summary coefficients and 95% CIs) each subgroup has on the overall summary 30-day mortality proportion after PR using a random-effects model as specified in our protocol [36,31]. Each subgroup of interest only included extracted studies that reported the 30-day mortality after PR for that subgroup, and they (as a group) were statistically compared with the 30-day mortality rates of the other of the 42 extracted studies (the studies not reporting the 30-day mortality rate for the subgroup of interest) to be used as a comparator group (called "Other Studies"). Finally, we used funnel and scatter plots to assess for publication/small-study bias [37]. All statistical analyses were performed in the package 'metaphor package in R' [24] (version 1.3.1093, http://www.R-project.org/).

Secondary outcomes and subgroups are reported unmodified (Appendix D.1 to D.6). We evaluated evidence quality according to GRADE principles, describing the primary outcome in terms of bias, precision, indirectness, heterogeneity and publication bias.

Results

We found 1259 unique publications through various database searches. 13 additional studies were found by mining references by hand and by using PubMed search for "related articles". After duplicates were removed (313 studies), titles and abstracts of 946 studies were reviewed and 857 studies were excluded at this stage. We retrieved and reviewed the full text of 89 studies for eligibility. After full text review and cross checking, 42 studies (43 studies including one systematic review [13] that was not used for extraction in order to avoid duplication of results) met the inclusion criteria and were selected for data extraction in our meta-analysis (see Fig. 1 and Table 1) while the remaining were excluded (appendix E.1) or merged (appendix E.2).

42 included studies contributed pooled data from a total of 88,516 patients treated with PR in 14 different countries. One of the 42 studies was confined to a paediatric population [32] with a median age of 10 years. The median reported age of all 41 other studies ranged from 61 to 80 years with 41% (16,575/40,742) of patients being female (gender was reported in 16/42 studies). Most studies (76%) included multiple primary sites. Lung cancer was the most common primary studied (8/42 studies), while 6/42 studies focused on patients treated with PR for bone metastases (Table 1).

No studies were excluded based on ROB assessment. We report the ROB for each study by 6 ROB domains assessed (Table 2, Appendix B.2). ROB for domains assessed were all low risk, except for the missing data domain, which was moderate ROB.

21.4% (18,958/88,516) patients in 42 studies died within 30 days of PR. The summary percentage of death within 30 days of PR - for these populations was 16% (95% CI = 14% to 18%). We detected substantial heterogeneity amongst studies (Q statistic 3302.32 ($p < 0.001$), $\tau^2 = 0.286$, $I^2 = 98.76$ % [2,25,32–34,39–55,57–76]) (Fig. 2).

Two formal tests were used to confirm potential outliers and influential studies based on initial inspection of the forest plot in Fig. 2. ESRs were performed to find studies with Z values greater than 3. No studies met the criteria based on this cut-off (Appendix F.1), which is confirmed by a leave one out forest plot (Appendix F.2).

Importantly, of the 42 studies analysed, we identified two U.S. Surveillance, Epidemiology, and End Results Program (SEER)-

Table 1
Characteristics of 42 included studies of 30-day mortality after palliative radiotherapy.

Author	Year	Type of publication	Period of study	Country	Median age (years)	Mean age (years)	Site of primary or indication for treatment of study population	Definition of 30-day mortality	n	N
Meeuse et al [25]	2010	Full text	1996–1998	Netherlands	-	-	Bone metastases	Unknown	63	1,157
Dennis et al [41] *	2011	Full text	1999–2007	Canada	-	-	Bone metastases	Start	70	918
Gupta et al [69]	2012	Abstract	2010	United Kingdom	71	-	Lung cancer	Start	18	75
Kapadia et al [39]	2012	Full text	2007–2010	USA	-	-	Non-small cell lung cancer	Both	209	730
Tursunovic et al [72]	2013	Abstract	2010	Denmark	-	-	Lung cancer	Unknown	65	293
Jung et al [58]	2013	Full text	2011–2012	Canada	65	-	Brain metastases	Start	7	75
Sherman et al [61]	2013	Abstract	Unknown	USA	63	-	Mixed including haematological cancers	Unknown	10	39
Murphy et al [33]	2013	Full text	2000–2007	USA	-	-	Mixed	End	7,093	21,279
Ellsworth et al [43]	2014	Full text	2012	USA	65	-	Bone metastases	End	89	339
Boardman et al [54]	2014	Letter	2012–2013	United Kingdom	-	-	Mixed	Start	46	396
Chan et al [73]	2015	Abstract	2013	United Kingdom	-	-	Non-small cell lung cancer	Start	11	60
Petrushevski et al [44] *	2015	Full text	1997–2009	Australia	67	-	Bone metastases	End	873	5,683
Spencer et al [46]	2015	Full text	2004–2011	United Kingdom	70	-	Mixed	Start	1,846	11,096
Nieder et al [47]	2015	Full text	2007–2011	Norway	68	-	Mixed	Start	105	873
Lerner et al [63]	2015	Abstract	2014	United Kingdom	-	-	Mixed	Unknown	30	202
Chawla et al [55]	2015	Abstract	2013	USA	70	-	Mixed inpatients	Unknown	29	68
Aladili et al [65]	2016	Abstract	2013–2014	United Kingdom	-	-	Thoracic RT for chest primaries	End	4	72
Buergy et al [68]	2016	Full text	2006–2013	Germany	67	-	Re-irradiation of spinal metastases	End	5	44
Bingham et al [64]	2016	Abstract	2012	USA	-	-	Mixed	End	33	262
Ryoo et al [71]	2017	Full text	2007–2011	USA	-	65.1	Non-small cell lung cancer	End	149	639
Maung Maung Myint et al [74]	2017	Abstract	2015	United Kingdom	-	-	Lung cancer getting high dose palliative RT	End	3	39
Morris et al [45]	2017	Abstract	2014	Ireland	-	69.1	Mixed	Unknown	17	122
Lefresne et al [66] *	2017	Full text	2013	Canada	-	-	Mixed	Start	12	79
Wallace et al [34]	2018	Full text	2012–2015	USA	73	-	Bone metastases	End	92	569
Nieder et al [49]	2018	Full text	2012–2015	Norway	-	71	Mixed	Start	11	101
Shukor et al [51]	2018	Full text	2012–2014	Malaysia	61	-	Mixed	Start	133	585
Tseng et al [60]	2018	Full text	2014–2015	USA	-	-	Mixed	Start	39	203
Fraser et al [40]	2019	Full text	2014–2015	Canada	-	-	Lung cancer	Start	448	2,569
Ali et al [57]	2019	Full text	2014–2017	United Kingdom	80	-	Bladder cancer	End	44	241
Cho et al [42]	2019	Full text	2003–2015	Canada	69	-	Metastatic prostate cancer getting palliative RT to bone metastases	Unknown	334	2,203
Wu et al [48]	2019	Full text	2012–2016	USA	63	-	Secondary metastatic sites	Start	125	518
Denholm et al [50] *	2019	Abstract	2018	United Kingdom	-	-	Mixed	Unknown	28	214
Shaw et al [52]	2019	Abstract	2017	United Kingdom	-	-	Mixed	Start	108	1,112
Clement-Zhao et al [53]	2019	Full text	2015–2016	France	65	-	Mixed	End	7	59
Moreno-Santiago et al [62]	2019	Abstract	2018	Spain	64	-	Mixed	Start	27	284
Wong et al [32] *	2019	Abstract	2008–2018	USA	10	-	Mixed	Unknown	18	113
Lewis et al [75]	2020	Full text	2013–2018	United Kingdom	-	69	Thoracic lung cancer tumours	Start	85	925
Lee et al [59]	2020	Full text	2007–2017	Hong Kong	64	-	Mixed	Start	995	5,795
Kain et al [67]	2020	Full text	2012–2013,2016–2017	New Zealand	71	-	Mixed	Start	178	1,744

Table 1 (*continued*)

Author	Year	Type of publication	Period of study	Country	Median age (years)	Mean age (years)	Site of primary or indication for treatment of study	Definition of 30-day mortality	n	N
Pitson et al [70]	2020	Full text	2009–2015	Australia	-	-	Mixed	Unknown	309	3,811
Mojica-Marquez et al [76]	2020	Full text	2017–2019	USA	67	-	Mixed	Start	193	429
Qld Government [2]	2021	Full text	2012–2017	Australia	69	-	Mixed	End Total	4,997 18,958	22,501 88,516

*unpublished data obtained by correspondence with authors of study, - unknown data.
n = number of patients receiving palliative radiotherapy that died within 30 days of treatment, N = total number of patients getting palliative radiotherapy, full text = study published as full text manuscript, abstract = published abstract only, letter = published letter, Mixed = population of patients getting palliative radiotherapy for various indications and containing patients with different primary cancers, start = 30 days were counted from the start of palliative radiotherapy treatment, end = 30 days were started from the end of the palliative radiotherapy treatment, USA = United States of America, RT = radiotherapy, Qld = Queensland, Australia.

Table 2
Risk of bias (ROB) assessment for extracted studies.

Study Domain	Low ROB	Moderate ROB	High ROB	Overall
Definition of population	26/42	15/42	1/42	Low
Confounds defined	24/42	12/42	6/42	Low
Selection bias	36/42	4/42	2/42	Low
Missing data	24/42	2/42	16/42	Moderate
Duplicate publication bias	35/42	1/42	6/42	Low
Outcomes reporting bias	42/42	0/42	0/42	Low
All extracted studies combined (based on domains)	5/6	1/6	0/5	Low

Medicare linked studies containing only patients > 65 years of age, that did not significantly influence the overall 30-day mortality after PR: One was the second largest study in our review having a raw 30-day mortality of 33% (7093/21,279), ESR Z score = 2.39 [33] (study 10 in Fig. F.1), while the second U.S. SEER-Medicare linked study had a 30-day mortality of 16% (92/569) after PR, ESR Z score = 0.02 [34] (study 3 in Fig. F.1). The lone published paediatric study, with a raw 30-day mortality after PR of 16% (18/113), was also non-influential on our summary effect 30-day mortality after PR (ESR Z score = 1.56) [32] (study 2 in Fig. F.1). The study closest to being influential on our summary effect 30-day mortality after PR was by Mojica-Marquez et al (2020) [76] reporting a relatively high 30-day mortality rate of 45% (193/429), ESR analysis of this study revealing a Z score = 2.75 (study 12 in Fig. F.1). The largest study included in our meta-analysis was a Queensland, Australia state-wide study reporting a 30-day mortality after PR of 22% (4,997/22,501) [2]. The ESR for this study resulted in a Z score = 0.65, and therefore was also not influential on the summary effect (study 40 in Fig. F.1).

Subgroup analysis for moderators of 30-day mortality rate after PR are detailed in Table 3 (for subgroup analysis raw data see Appendix D, for subgroup Forest plots see Appendix G). Potential effect modifiers increasing the overall 30-day mortality summary effect included: patients treated with PR treatment at multiple body sites, those with hepatobiliary, melanoma and mesothelioma primaries, those treated with PR as inpatients, those with ECOG performance status 3–4, those with liver metastases, patients who did not complete their planned PR course, and those treated in the United States. Potential effect modifiers decreasing the overall 30-day mortality summary effect included: patients with ECOG performance status 0–1, those treated with synchronous chemotherapy, those treated with SBRT for brain metastases.

Appendix H.1 demonstrates a funnel plot of all 42 extracted studies in the above meta-analysis showing standard error as a measure of precision for each study. Upon visual inspection of this plot clear publication (small study) bias is difficult to ascertain, but the existence of a high degree of study heterogeneity is clear. Fig. 3 contains a scatter plot illustrating study sample size as a measure of precision in order to investigate if funnel plot asymmetry is being induced by the method of funnel plot construction in Fig. H.1. It is unclear, based on visual inspection, if Fig. 3 shows asymmetry and therefore publication bias. In order to further investigate this, an unweighted regression test for funnel plot asymmetry (mixed-effects meta-regression model) was calculated, resulting in a non-significant funnel plot asymmetry with a 95% degree of confidence ($Z = -1.74$, $p = 0.081$).

Discussion

An evidence-based quality metric defining the expected 30-day mortality rate after PR for RT regulators worldwide to use in audit of radiation oncology departments is currently lacking in the liter-

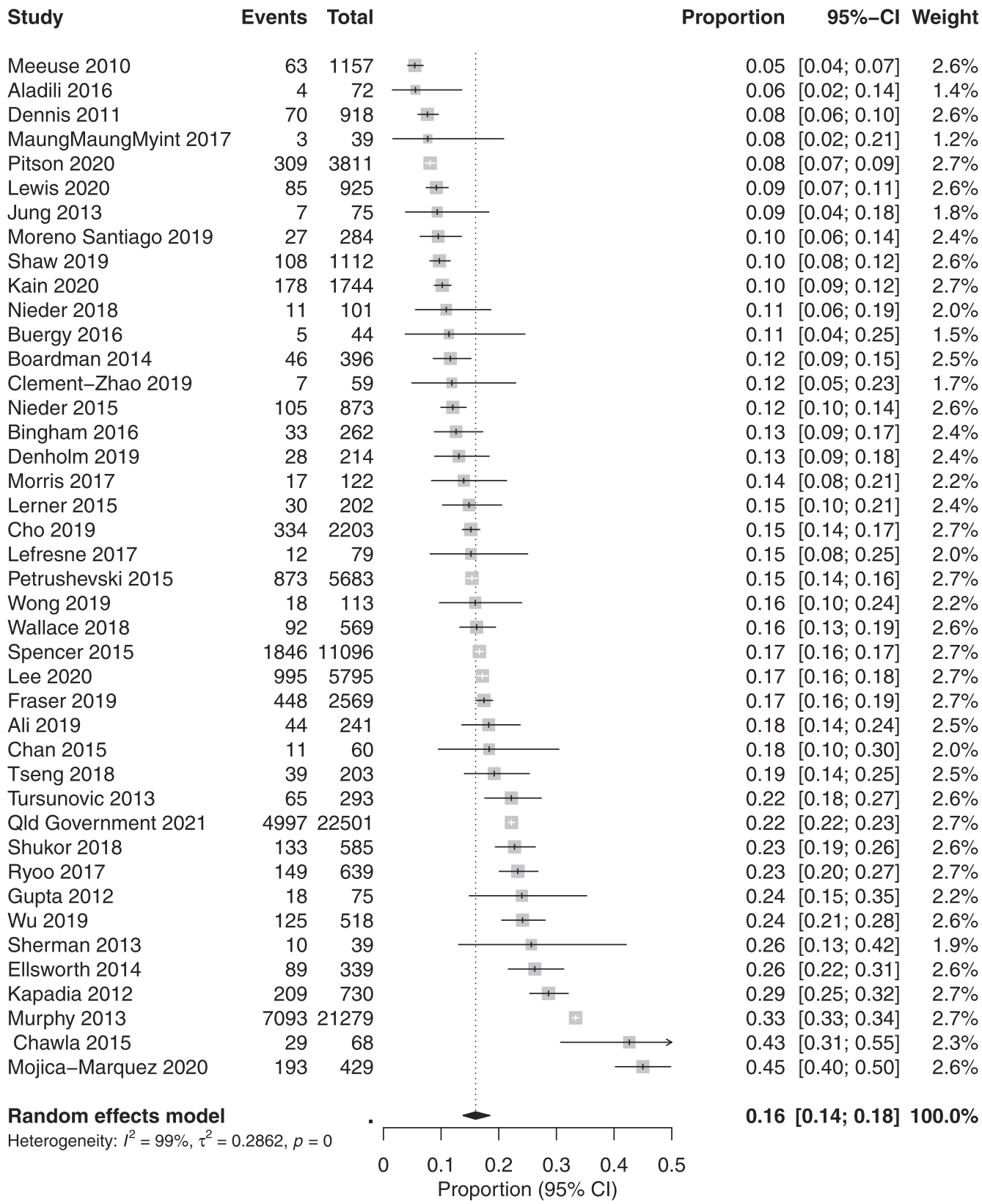

Fig. 2. Forest plot displaying the summary proportion of 30-day mortality rate after palliative radiotherapy: 16% (95% CI = 14% to 18%). Events indicates the number of patients that died within 30 days of palliative radiotherapy), Total indicates the total number of patients getting palliative radiotherapy and Proportion indicates the proportion of patients dying within 30 days of palliative radiotherapy (events/total) with their 95% confidence interval, Weight (study weighting), Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

Table 3
Subgroup moderator analysis for 30-day mortality after palliative radiotherapy.

Subgroup of participants getting PR vs. other studies	# of pts. in subgroup of total pts. in all studies † (as a %)	Test for subgroup effect (coefficient 2 = QM (df = 1), p value)
Indication for treatment		
Bone metastases	*11836/88516 (13.4%)*	*0.37, 0.544*
Brain Metastases	*1010/88516 (1.1%)*	*1.13, 0.287*
Multiple treatment sites	*64/88516 (<0.1%)*	***9.54, 0.002***‡
Primary cancer		
Bladder cancer	*285/88516 (0.3%)*	*0.34, 0.559*
Breast cancer	*3779/88516 (6.5%)*	*2.50, 0.113*
Colorectal cancer	*2087/88516 (2.4%)*	*0.67, 0.413*
Lung cancer	*13341/88516 (15.1%)*	*3.10, 0.078*
Oesophageal cancer	*68/88516 (<0.1%)*	*3.50, 0.061*
Prostate cancer	*4990/88516 (5.6%)*	*1.02, 0.313*
GI cancer	*28/88516 (<0.01%)*	*0.05, 0.819*
Gynaecological cancers	*749/88516 (0.8%)*	*2.91, 0.088*
Hepatobiliary cancer	*514/88516 (0.5%)*	***24.20, <0.001***‡
Head and neck cancer	*633/88516 (0.7%)*	*1.34, 0.246*
Genitourinary cancer	*2005/88516 (2.3%)*	*0.16, 0.689*
Melanoma cancer	*1432/88516 (1.6%)*	***16.19, <0.001***‡
Renal cell carcinoma	*11/88516 (<0.01%)*	*2.99, 0.084*
CNS cancers	*318/88516 (0.4%)*	*0.70, 0.404*
Sarcoma	*16/88516 (<0.01%)*	*1.01, 0.315*
Mesothelioma	*292/88516 (0.3%)*	***8.89, 0.003***‡
Inpatient status		
Inpatients	*549/88516 (0.6%)*	***92.27, <0.001***‡
Outpatients	*369/88516 (0.6%)*	*0.16, 0.690*
Performance status		
ECOG 0–1	*886/88,516 (1.0%)*	***56.68, <0.001***‡
ECOG 2	*505/88,516 (0.6%)*	*2.05, 0.153*
ECOG 3–4	*727/88,516 (0.3%)*	***8.70, 0.003***‡
Other subgroups		
Synchronous chemotherapy	*239/88,516 (0.3%)*	***20.66, <0.001***‡
Known to hospice	*1,137/88,516 (1.3%)*	*0.28, 0.599*
Age > 60 years	*24,177/88,516 (27.3%)*	*0.60, 0.439*
Age <= 60 years	*676/58005 (1.2%)*	*0.00, 0.96*
Patients with liver metastases	*106/88516 (0.1%)*	***14.96, <0.001***‡
Fractionation		
Patients getting 1 fraction	*5,713/88,516 (6.5%)*	*3.11, 0.078*
Patients getting 2–5 fractions	*10,881/88,516 (12.3%)*	*0.10, 0.749*
Patients getting 6–10 fractions	*6,553/88,516 (7.4%)*	*1.34, 0.246*
Patients > 10 fractions	*3,425/88,516 (3.9%)*	*1.06, 0.304*
Incomplete PR treatment		
Patients not completing tx	*120/88,516 (0.1%)*	***26.51, <0.001***‡
Type of PR technology		
Patients getting SBRT for brain metastases	*126/88,516 (0.1%)*	***10.54, 0.001***‡
U.S. studies (post-hoc analysis)		
Studies from the U.S.	*25,189/88,516 (28.5%)*	***28.70, <0.001***‡
Year of study publication (post-hoc analysis)		
Studies published prior to year 2016	*43,283/88,516 (49.0 %)*	*0.85, 0.358*
Timing 30-day mortality (post-hoc analysis)		
Measured from end vs. from start of treatment	*51,727/79,564 (65.0%)*	*0.73, 0.392*

† total number of patients included in study = 88,516.
pts = patients, PR = palliative radiotherapy, df = degrees of freedom, SBRT = stereotactic body radiotherapy, U.S. = United States of America, CNS = central nervous system, GI = gastrointestinal, tx = treatment, ECOG = Eastern Cooperative Oncology Group performance status.
‡ = significant p value ≤ 0.05.

ature. Our meta-analysis demonstrates an overall 30-day mortality rate of 16% following PR across all included studies, however, significant heterogeneity was observed. Due to considerable heterogeneity in our data, we applied various subgroup analyses which revealed that a higher 30-day mortality rate after PR was associated with: a) multiple sites treated with PR, b) patients with the following primaries: hepatobiliary, melanoma, mesothelioma cancers, c) inpatients, d) ECOG score 3–4, e) patients with liver metastases, f) patients not completing their PR treatment, and g) patients receiving PR in the United States. Conversely, a lower 30-day mortality rate after PR was associated with: a) ECOG 0–1, b) patients treated with synchronous chemotherapy, and c) patients who had brain metastases treated using SBRT.

To assess the statistical conclusions drawn from this meta-analysis, an assessment of certainty is required. Our systematic literature search meant that our findings are unlikely to be at risk of publication bias and unpublished data was included. Indeed, funnel plot examination and unweighted regression test for funnel plot asymmetry support this finding with no detectable small-study effect. To ensure we met our primary outcome we employed a very stringent inclusion/exclusion criterion. Our rationale was to avoid including studies that did not differentiate curative radiotherapy treated patients from PR ones. Studies were excluded from our review if authors were unable to distinguish between patients receiving PR versus patients receiving curative radiotherapy [77,78,12]. For example, Guadagnolo et al (2013) [77] reported 7.6% of the 15,287 patients included in their study getting radiotherapy died within 30 days of treatment. It is possible that by excluding these types of studies we have lost data that would change both our primary outcome and some of our primary cancer

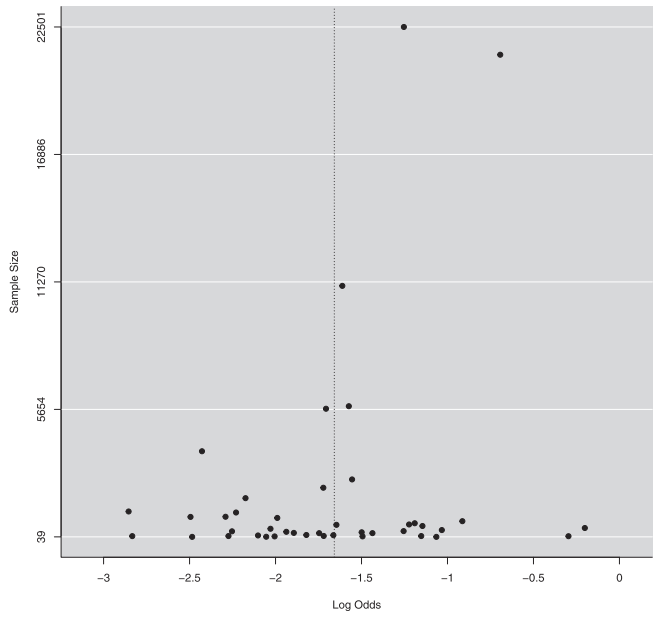

Fig. 3. Scatter plot displaying study sample size as a measure of precision to investigate funnel plot asymmetry. The existence of asymmetry is unclear.

subgroup analyses. Nonetheless, the bias created by including these studies into our analyses would be too great given our primary outcome and objectives of assessing all patients getting PR, not curative radiotherapy.

Furthermore, except for the missing data domain, overall, ROB for the included studies was low. Retrospective palliative studies involving patients nearing the end of their lives are at a high risk of missing data, given the nature of the included patients [79]. However, since our study had an objectively measurable endpoint (patient's death) and the remaining subgroup analysis was not dependent on patient recall, missing data may have been less of an issue for our study.

A limitation of our study was that we did not include non-English studies. Consequently, some studies from non-English speaking countries may have been missed and our results may not be applicable to radiation oncology centers from those countries. Given the large number of patients from various countries included in our review, the risk of biased results based on our inclusion criteria would likely be minimal. Another potential source of bias was the different ways that the 30-day mortality timeline was measured by the included studies: some studies measured the 30 days starting from the beginning of the patient's last course of treatment, while others measured this from the end of the last PR course. This may have introduced bias for the overall 30-day mortality rate reported by our meta-analysis, particularly for those patients who had longer PR courses. We attempted to measure this by performing subgroup analysis comparing studies reporting counting 30-day mortality from the beginning of patient treatment vs. those counting from the end of their treatment, which revealed that this did not significantly change the summary effect. Finally, subgroup analysis was used to explain the high heterogeneity found amongst the 42 studies extracted. Bias, however, may exist in the way subgroup analysis was performed: Most of the studies we extracted data from included a general mix of populations of patients ie. Not differentiating between primary diagnoses and the other confounding variables/secondary outcomes we measured. In many cases these studies failed to report the 30-day mortality rate for the subgroup of interest, which was key to all our secondary outcomes/subgroup analysis. These studies found to not be reporting a subgroup 30-day mortality rate after PR were added to the "Other studies" comparator subgroup and their 30-day mortality rate after PR as a group were statistically compared to the subgroup of interests' 30-day mortality rate after PR. This bias was impossible to avoid given the heterogenous nature of populations in the PR studies included in our meta-analysis, and their lack of reporting of 30-day mortality for subgroups of interest.

The diverse international patient populations and forms of PR treatments included in this meta-analysis reflect that seen in radiation oncology departments world-wide. The studies we extracted from included patients with various primaries in both inpatients and outpatients getting PR for different indications for treatment with several PR external beam technologies used. Some of these patients did not complete their planned PR treatment and patient's ages ranged from advanced age to paediatric patients. This may explain the significant heterogeneity found of the studies in our review: Q statistic 3302.32 ($p < 0.0001$), $I^2 = 98.76\%$. We were able to explore the potential effect of heterogeneity via subgroup analysis. Our findings illustrate the importance of considering the number of sites of treatment, primary cancer type, inpatient status, ECOG score, the use of synchronous chemotherapy, the presence of liver metastases and the country of treatment when determining the expected 30-day mortality rate for a specific patient population.

Finally, the summary statistic 16% (95% CI 14% to 18%) is precise, with tight confidence intervals, which exclude effect sizes that are not clinically meaningful. This outcome, along with the above assessment of heterogeneity, bias, and well-defined inclusion/exclusion criteria, and no detectable small study bias for our review lead us to conclude that our primary outcome and subgroup analysis was truly a representative measure of the 30-day mortality after PR.

Our post-hoc U.S. study vs. non-U.S. study subgroup analysis showed that there may be a higher expected 30-day mortality rate for those treated with PR in the U.S. compared to elsewhere. The U.S. has a unique and complex collection of private and publicly based health insurance funds used to pay for health care utilization, including for cancer treatment. U.S. based studies have identified a disparity in use of cancer treatments, including radiotherapy, at the end of life depending on a patient's health insurance coverage [80,16,77]. It may be that U.S.-specific demographic, socio-economic and insurance coverage-related factors influence the possible difference found in the expected 30-day mortality rate for those receiving PR in the U.S. vs. elsewhere in the world.

To date, only one systematic review has been completed analyzing patients receiving radiotherapy who died within 30 days of their treatment. This review by Park and colleagues [13] included 20 English studies for analysis (search dates Jan. 1960 to Dec. 2016). Of these only seven of the studies met our rigorous inclusion criteria whilst the remaining 13 studies were excluded due to meeting our exclusion criteria mentioned above: studies did not report both the total number of patients receiving PR and the total number of patients dying within 30 days of PR. Since Park and colleagues' original publication five years ago, there has been renewed interest in this field as evidenced by the plethora of publications [2,32,52,53,57,59,60,62,66,67,70,71,34,74–76,40,42,45,48–51]. In addition, our review found 14 other studies published pre-2017 reporting 30-day mortality after PR not reported by Park and colleagues [41,44,46,54,55,58,61,63–65,68,72,73,81].

As noted by the Park and colleagues review, 53–82% of patients did not complete their RT [12,13,39,56,78,82], with poor performance status and patient's death being the primary causes [12,13,39,82]. Our subgroup analysis indicates that patients who did not complete their PR treatment had a higher expected 30-

day mortality rate after PR. This may reflect an inappropriately longer planned treatment course of PR for those patients with a poor prognosis. Further research is needed into this population of patients.

Park and colleagues [13] reported an overall 30-day mortality after PR of between 9–15.3% ($\mu \pm \sigma = 12.1 \pm 3.2$), which is close to the finding of our meta-analysis: 16% (95% CI 14% to 18%). This fits with our finding that study publication date ($\geq$2016 vs. $<$2016) did not modify our summary 30-day mortality rate after PR. We report a consistent finding to the literature that a higher 30-day mortality rate after PR occurs in the following subgroups: a) patients being treated for multiple metastatic sites, b) patients with ECOG scores 3–4 [13,33,39,43,77,78,82–87]. In addition, we found subgroups of patients with hepatobiliary, melanoma, and mesothelioma primaries, inpatients receiving PR, and patients with liver metastases at PR referral also had higher expected 30-day mortality rates after PR, which are novel findings and based on data from studies published after Park and colleagues [13] was published. Notably lung primary and patient age did not modify the overall summary effect of 30-day mortality rate after PR of all studies, which was in contrast to what Park et al. (2017) reported: both lung [13,43,77,78,82–86] and greater age [33,39,87] were found to be predictors of PR at the end-of-life. The difference in some of the above findings may be related to our subgroup analysis being heavily reliant on studies published after the Park et al (2017) review, which makes our findings novel and a publication first using a meta-analysis. Another reason for the differences may be that we excluded studies that did not differentiate those patients getting PR from those getting curative intent radiotherapy, whereas Park et al. (2017) included such studies in their review. In contrast to our meta-analysis, Park et al (2017) also did not report to have included unpublished results in their review.

In order to minimize 30-day mortality after PR, accurate estimation of disease related survival is imperative to know. Overestimation of prognosis by radiation oncologists (reportedly up to 34% of the time) [88] results in high intensity cancer care towards the end of life [89]. Identification of which health care workers (if any) are better at prognostication for palliative care patients has been studied. Variably, more experienced clinicians are reportedly better at prognosticating, multidisciplinary teams may be better at prognostication than individual clinicians, while others report the combination of clinicians estimation with formalized calculation of a prognostic score can result in more accurate prognostication [90].

Multiple prognostic scores specific to patients treated with PR have been developed and evaluated [91–93]. There are some prognostication factors specific to certain subsets of patients treated with PR, such as patients receiving PR for brain metastases [94], and for patients with spinal cord compression [95]. These models include a diverse set of validated prognostic factors. Performance status, site of primary cancer, and site or burden of metastases are commonly included factors in current prognostic models. This justifies the collection of 30-day mortality rate data based on these patient factors and is evidenced in our findings that primary cancer types (hepatobiliary, melanoma, and mesothelioma), patient ECOG 3–4 scores, and patients with liver metastases getting PR, all have a higher 30-day mortality rate after PR compared to that of our overall summary effect.

Minimizing burden of interventions at end of life is imperative. The use of a validated prognostic scoring tool prior to the decision to offer PR should be encouraged as a way of reducing the 30-day mortality after PR. Given the efficacy of single fraction PR for bone metastases for short term palliation is indisputable and recommended as best practice, estimation of 30-day and 90-day mortality using prognostic tools can avoid burdensome longer treatment schedules near the end of life [3,8]. Our subgroup analysis did not find PR fractionation subgroups had a significant effect on the overall 30-day mortality rate summary effect. This finding is in conflict with multiple studies showing differences in fractionation: most studies report lower 30-day mortality rates with higher fractionation of PR treatments [46,52,75,96,97], suggesting this may reflect a positive change in RT practice in reaction to evidence showing single fraction PR treatment of uncomplicated painful bone metastases should be gold standard [3]. A few studies (one including all cancer primaries [51], and another study of those with prostate cancer getting treatment for bone metastases [42]) have shown no difference in survival between PR fractionation groups. Our findings could be explained by the fact that many studies did not report the 30-day mortality rate for different fractionation groups, and in some cases, the fractionation groupings were defined differently from ours. For example, only four studies we extracted from reported the 30-day mortality rate for patients getting >= 10 fractions of PR treatment. Several studies also reported 30-day mortality rate based on total numbers of treatments given (one patient could have multiple treatments) [40,46,53,59] as opposed to reporting only the last treatment each patient received, the latter method being the outcome we used to assess fractionation and 30-day mortality rate. We did find that patients getting SBRT for brain metastases as a subgroup appeared to have a lower 30-day mortality rate after PR, which likely reflects the appropriate selection of patients with relatively good prognostic outlook for SBRT treatment. Only one study [71] reported the 30-day mortality rate for any patients getting SBRT for brain metastases, which was 4% (5/126). This low rate would be expected in patients with advanced cancer, but likely oligo-metastatic or oligo-progressive disease burden, who were given SBRT. Therefore, the data obtained for our overall summary 30-day mortality rate after PR would not apply to this select population of patients with comparably better prognoses. Our subgroup analysis for those patients getting SBRT for brain metastases confirmed that, as a subgroup, SBRT for brain metastases significantly modifies the 30-day mortality after PR summary effect by lowering it.

Unexpected deaths and rapid deterioration at end of life are inevitable and so there will always be patients who die within 30 days of their PR, however it is crucial to minimize unnecessary burden and potential toxicity for patients receiving end of life care. This review presents the strongest evidence to date to establish an evidence-based quality metric for 30-day mortality for those patients having PR. Radiation oncology sites around the world are encouraged to use the 16% 30-day mortality after PR found in this review as a benchmark for auditing of their own local 30-day mortality rates after PR. This will help improve the quality of treatment by triggering a review of radiotherapy policies in centers that have a significantly higher rate of mortality. Departments that have a 30-day mortality rate after PR that exceeds 16% must look at the distribution of factors that might influence this higher rate: i.e., histology/indications for PR/proportion of inpatients vs. outpatients etc. and seek to explain the reason their department's 30-day mortality rate is higher, and if this is justifiably so.

Future studies evaluating 30-day mortality rates after PR should report details of radiotherapy dose, fractionation and technique, given the growth in SBRT use in the palliative population. More dedicated studies examining the 30-day mortality after PR in paediatric populations are also needed in order to minimize risk of treatment at the end of life in this important group. With ongoing audit and publication of post audit results, it may be that the 30-day mortality after PR will improve further. This reduction in 30-day mortality rate should be an aim for radiation oncology practice worldwide.

Conclusion

We found 16% of patients treated with PR die within 30-days of their treatment worldwide. This is the highest quality evidence to determine a quality metric for radiation oncology centers providing PR. This quality metric can be used by peak radiation oncology regulatory bodies to evaluate individual radiation oncology centers providing patients with PR treatment. This metric can also be used to formulate guidelines for PR. The 30-day mortality rate post PR may be higher in U.S. centers (compared to non-U.S. centers), inpatients, hepatobiliary, melanoma, mesothelioma primary cancers, patients with multiple metastatic sites being treated, those with liver metastases, with higher ECOG scores and those not completing treatment. Meanwhile those with lower ECOG scores, those treated with stereotactic PR for brain metastases and those getting synchronous chemotherapy may have a lower 30-day mortality rate.

Acknowledgements

The authors would like to acknowledge the following for their contributions and advice: Dr. Chris Williams, Associate Professor Phillip Good, Marcos Riba, Tracey Guan, Julie Moore, Shoni Philpot, Danica Cossio, Dr. Cathy Hargrave, Professor Bryan Burmeister, Dr. Dominic Lunn, Queensland Cancer Control Safety and Quality Partnership Radiation Oncology Sub-Committee, Cancer Alliance Queensland, University of Queensland for assistance with database searches, and Metro South Health Biostatistics Service for statistical support.

Conflicts of interest

None.

Data availability

the data extracted for this study is available via Mendeley Data: Kutzko, Justin (2022), "30-day mortality after palliative radiotherapy", Mendeley Data, V1, doi: 10.17632/6fybjbpcxg.1

Appendices

Appendix A Database search terms used for study

Databases Searched: MEDLINE (PubMed), CENTRAL, Embase, CINAHL, Cochrane review Database

PubMed search

((((“palliative radiotherapy”) OR (“palliative radiation”)) OR (“palliative RT”)) AND ((((((“end of life”) OR (“30 day mortality”)) OR (mortality)) OR (“quality indicator”)) OR (hospice)) OR (“terminally ill”))) OR (((RT[Title/Abstract]) OR (“radiation therapy”[Title/Abstract])) AND ((“End of Life”[Title/Abstract] OR eol[Title/Abstract]) OR (“hospice care”[Title/Abstract])))

Filters: Publication date from 1980/01/01 to 2020/03/31

Embase search

('palliative radiation':ti,ab,kw OR 'palliative radiotherapy':ti,ab,kw) AND

('end of life':ti,ab,kw OR '30 day mortality':ti,ab,kw OR 'quality indicator':ti,ab,kw OR hospice:ti,ab,kw OR 'terminally ill':ti,ab,kw OR mortality:ti,ab,kw OR 'last month of life':ti,ab,kw) OR

('radiotherapy during eol':ab,ti)

Appendix B

Table B1
Risk of bias scoring template.

Category of bias					
Definition of population	No inclusion criteria describedNo details provided for: 1) Recruitment process 2) Demographic age, sex Intervention: palliative RT dose and fractionation not defined	No inclusion criteria describedSome demographic detail provided: 1) Recruitment process 2) Demographics age sex, described. Intervention: palliative radiotherapy defined 30-day mortality defined Co-interventions not described (chemotherapy, targeted therapy) RT dose and fractionation not described	Patients included in study only defined by all deaths from palliative radiotherapy (not defined clearly i.e., external beam radiotherapy) over a time period, not necessarily all patients who had palliative radiotherapy. Recruitment process description vague or incomplete. Co-interventions not described RT treatment episodes described (not in detail)	Inclusion criteria described: 1) Includes recruitment dates 2) "all sequential patients treated with palliative radiotherapy 3) Setting described 4) Demographics described Age Sex 5) Performance status reported 6) Co-morbidity reported 7) Metastatic disease/ not detailedIntervention: palliative radiotherapy defined 30-day mortality clearly defined (start & end date) Co-interventions described (chemotherapy, targeted therapy) RT treatment dose and fractionation described in detail	Inclusion criteria described: 1) Includes recruitment dates 2) "all sequential patients treated with palliative radiotherapy 3) Setting described 4) Demographics described Age sex. 5) Performance status reported 6) Co-morbidity reported 7) Metastatic disease/ not detailedCo-interventions described in detail (chemotherapy, targeted therapy) for all participants. Intervention: palliative radiotherapy defined in detail (EBRT, SBRT, 3D CRT) 30-day mortality clearly defined as "death 30 days after either end of the palliative radiotherapy or from start of treatment". Co-interventions described in detail (chemotherapy, targeted therapy) RT treatment dose /dose range and fractionation/range described in detail
	Score = 0	Score = 1	Score = 2	Score = 3	Score = 4
Confounds defined	No mention of confounding factors Confounding factors include, but not limited to: 1) Performance status 2) Patient known to Palliative care service 3) Inpatient 4) Hospice inpatient 5) Co-interventions (e.g., chemotherapy or targeted therapy) 6) Outpatient	One confounding factor describedConfounding factors include, but not limited to: 1) Performance status 2) Patient known to Palliative care service 3) Inpatient 4) Hospice inpatient 5) Co-interventions (e.g., chemotherapy or targeted therapy) 6) Outpatient	Two confounding factors describedConfounding factors include, but not limited to: 1) Performance status 2) Patient known to Palliative care service 3) Inpatient 4) Hospice inpatient 5) Co-interventions (e.g., chemotherapy or targeted therapy) 6) Outpatient	Three confounding factors describedConfounding factors include, but not limited to: 1) Performance status 2) Patient known to Palliative care service 3) Inpatient 4) Hospice inpatient 5) Co-interventions (e.g., chemotherapy or targeted therapy) 6) Outpatient	>Three confounding factors describedConfounding factors include, but not limited to: 1) Performance status 2) Patient known to Palliative care service 3) Inpatient 4) Hospice inpatient 5) Co-interventions (e.g., chemotherapy or targeted therapy) 6) Outpatient
	Score = 0	Score = 1	Score = 2	Score = 3	Score = 4

(*continued on next page*)

Duplicate publication bias	There are multiple publications involving the same (or some of the same, or different) authors, and there is uncertainty about whether the studies are true duplicates or not. Score = 0		It is clear that the study is a stand-alone study or is an exact duplicate publication of another study Score = 4	
Outcomes reporting bias	The primary outcome was not reported (but secondary ones were) based on the primary outcome listed in the methods Score = 0		The primary outcome is given for the study whether or not it is statistically significant. Score = 4	
Reporting bias	Yes, bias exists Score = 0		No reporting biases Score = 4	
Selection bias	No inclusion criteria described Score = 0	Population defined retrospectively (E.g. from a database of all deaths or all hospice patients) going from death backwards, those treated with RT identified in this population Score = 2	Patient cohort identified (patients receiving palliative RT), then outcome measured. Palliative RT not clearly defined Score = 6	Patient cohort identified (those consecutive patients receiving palliative RT), then outcome measured. Palliative RT clearly defined
Missing Data	Patient population given without numbers of patients excluded from study or lost to follow up or missing information Score = 0		Starting population defined and number of patients excluded from study, but no totals given for exclusions for missing data or patients lost to follow up. Score = 6	Clearly state starting population of patients and how/why patients were excluded to get to final population reported in study. Numbers provided for exclusions due to incomplete data and /or loss to follow up.

RT = radiotherapy, EBRT = external beam radiotherapy, SBRT = stereotactic body radiotherapy, 3D CRT = three dimensional conformal radiation therapy.
Scoring for each risk of bias category:

1. for categories out of 4 points: 0–1 = high ROB, 3–4 points = low ROB, 2 points = consensus between two reviewers for high vs. low ROB
2. for categories out of 6 points: 0–2 points = high ROB, 4–6 points = low ROB

Table B2
Individual study risk of bias assessment.

Study	Year	Definition of population	Confounds defined	Selection bias	Missing data	Duplicate publication bias	Outcomes reporting bias
Meeuse et al [25] *	2010	Low	Low	Low	Low	Low	Low
Dennis et al [41]*	2011	Moderate	Low	Low	Low	Low	Low
Gupta et al [69] ^	2012	Moderate	Moderate	Low	Low	Low	Low
Kapadia et al [39] *	2012	Low	Low	Low	Low	Low	Low
Murphy et al [33] *	2013	Low	High	High	Low	Low	Low
Tursunovic et al [72]	2013	Moderate	Moderate	Low	High	Low	Low
Jung et al [58] *	2013	Low	Low	Low	Low	Low	Low
Sherman et al [61]	2013	Moderate	Moderate	Low	High	Low	Low
Ellsworth et al [43] ^*	2014	Low	Low	Low	Low	High	Low
Boardman et al [54]	2014	Moderate	High	Moderate	High	Low	Low
Petrushevski et al [44]	2015	Moderate	High	Low	High	Low	Low
Chan et al [73]	2015	Moderate	Moderate	Low	High	Low	Low
Spencer et al [46] *^	2015	Low	Low	Low	Low	Low	Low
Nieder et al [47] *^	2015	Low	Low	Low	Low	Low	Low
Chawla et al [55]	2015	Moderate	Low	Moderate	High	Low	Low
Lerner et al [63]	2015	Moderate	High	Low	High	Low	Low
Aladili et al [65]	2016	Low	Moderate	Low	High	Low	Low
Bingham et al [64] ^	2016	Moderate	Moderate	Low	Low	High	Low
Buergy et al [68] *	2016	Low	Low	Low	Low	Low	Low
Ryoo et al [71] *	2017	Low	Low	Low	Low	Low	Low
Maung Maung Myint et al [74]	2017	High	Moderate	Low	High	Low	Low
Morris et al [45] ^	2017	Low	Moderate	Low	Low	Moderate	Low
Lefresne et al [66] *	2017	Low	Low	Low	Low	High	Low
Nieder et al [49] *	2018	Low	Low	Low	High	Low	Low
Shukor et al [51] *	2018	Low	Low	Low	High	Low	Low
Tseng et al [60]	2018	Low	Low	Low	Low	Low	Low
Wallace et al [34] *^	2018	Low	High	High	Low	High	Low
Fraser et al [40] *^	2019	Low	Low	Low	High	High	Low
Cho et al [42] *	2019	Low	Low	Low	Low	Low	Low
Wu et al [48] *^	2019	Low	Low	Low	High	High	Low
Denholm et al [50]	2019	Moderate	Moderate	Low	Moderate	Low	Low
Shaw et al [52]	2019	Moderate	High	Low	Low	Low	Low
Clement-Zhao et al [53] *	2019	Low	Low	Low	Low	Low	Low
Ali et al [57] *	2019	Low	Low	Low	High	Low	Low
Moreno-Santiago et al [62]	2019	Low	Moderate	Low	Low	Low	Low
Wong et al [32] ^	2019	Moderate	Moderate	Low	Low	Low	Low
Lewis et al [75] *	2020	Low	Low	Low	Low	Low	Low
Lee et al [59] *^	2020	Low	Low	Low	High	Low	Low
Kain et al [67] *	2020	Low	Low	Low	Low	Low	Low
Pitson et al [70] *^	2020	Moderate	Low	Moderate	High	Low	Low
Mojica-Marquez et al [81] *	2020	Low	Low	Low	Moderate	Low	Low
Queensland Government [2] *	2021	Moderate	Moderate	Moderate	Low	Low	Low

^ indicates multiple studies covering the same population were merged as one in the data extraction phase.
*indicates included studies that were published as full text manuscripts.
Definitions: High = study assessed as high risk of bias for this category, Moderate = study assessed as being between high and low risk of bias for this category, low = study assessed as being low risk of bias for this category.

Appendix C

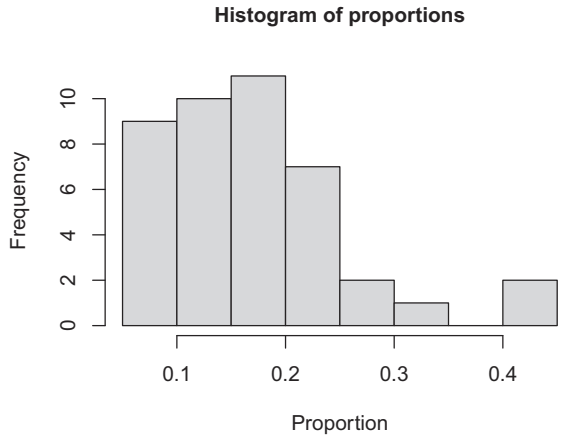

Fig. C1. A non-normal distribution of proportions was found of studies reporting 30-day mortality after palliative radiotherapy.

Appendix D

Table D1
Indications for radiotherapy subgroup analysis and raw data.

Indication for palliative RT	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
Bone metastases	Wu et al. (2019) [48]	66	293	
	Shukor et al. (2018) [51]	38	201	
	Shaw et al. (2019) [52] *	78	473	
	Dennis et al. (2011) [41]	70	918	
	Cho et al. (2019) [42]	334	2203	
	Ellsworth et al. (2014) [43]	89	339	
	Petrushevski et al. (2014) [44]	873	5683	
	Meeuse et al. (2010) [25]	63	1157	
	Wallace et al. (2018) [34]	92	569	
	Total	*1703*	*11,836*	*14%*
	Summary effect size (bone metastases)			*0.15 (0.12, 0.18)*
	Summary effect size (Other studies)			*0.17 (0.14, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*0.37, 0.544*
Brain metastases	Ryoo et al. (2017) [71]	149	639	
	Wu et al. (2019) [48]	43	146	
	Shukor et al. (2018) [51]	26	150	
	Jung et al. (2013) [58]	7	75	
	Total	*225*	*1010*	*22%*
	Summary effect size (brain metastases)			*0.20 (0.15, 0.28)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.18)*
	Test of moderators: coefficient 2 (QM, p value)			*1.13, 0.287*
Multiple treatment sites	Shukor et al. (2018) [51]	20	64	
	Total	*20*	*64*	*31%*
	Summary effect size (multiple sites)			*0.31 (0.21, 0.44)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.18)*
	Test of moderators: coefficient 2 (QM, p value)			***9.54, 0.002***‡

*unpublished data gained from correspondence with authors of study, RT = radiotherapy. QM = test for moderators (coefficient 2), (df =1). ‡ = significant p value $\leq$ 0.05.

Table D2
Primary cancer subgroup analysis and raw data.

Primary cancer diagnosis	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
Bladder cancer	Ali et al. (2019) [57]	44	241	
	Kain et al. (2020) [67]	6	44	
	Total	*50*	*285*	*17.5%*
	Summary effect size (Bladder cancer)			*0.18 (0.14, 0.22)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*0.34, 0.559*
Breast cancer	Shukor et al. (2018) [51]	20	154	
	Tseng et al. (2018) [60] *	3	16	
	Kain et al. (2020) [67]	8	245	
	Pitson et al. (2020) [70]	10	1192	
	Qld Government (2020) [2]	336	2172	
	Total	*377*	*3779*	*10%*
	Summary effect size (breast cancer)			*0.7 (0.02, 0.18)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*2.50, 0.113*
Colorectal cancer	Shukor et al. (2018) [51]	10	43	
	Kain et al. (2020) [67]	14	167	
	Pitson et al. (2020) [70]	12	302	
	Qld Government (2020) [2]	316	1575	
	Total	*352*	*2087*	*17%*
	Summary effect size (colorectal cancer)			*0.12 (0.05, 0.24)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*0.67, 0.413*
Lung cancer	Gupta et al. (2012) [69]	18	75	
	Ryoo et al. (2017) [71]	149	639	
	Shukor et al. (2018) [51]	41	168	
	Tursunovic et al. (2013) [72]	65	293	
	Chan et al. (2015) [73]	11	60	
	Tseng et al. (2018) [60] *	9	48	
	Maung Maung Myint et al. (2017) [74]	3	39	
	Kain et al. (2020) [67]	75	439	
	Pitson et al. (2020) [70]	121	616	
	Qld Government (2020) [2]	1860	6661	
	Fraser et al. (2019) [40]	448	2569	
	Lefresne et al. (2017) [66]	12	79	
	Lewis et al. (2020) [75]	85	925	
	Kapadia et al. (2012) [39]	209	730	
	Total	*3106*	*13,341*	*23%*
	Summary effect size (lung cancer)			*0.20 (0.16, 0.24)*
	Summary effect size (Other studies)			*0.15 (0.12, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*3.10, 0.0783*
Oesophageal cancer	Kain et al. (2020) [67]	5	68	
	Total	*5*	*68*	*7%*
	Summary effect size (Oesophageal cancer)			*0.07 (0.03, 0.16)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*3.50, 0.061*
Prostate cancer	Cho et al. (2019) [42]	334	2203	

(*continued on next page*)

Table D2 (*continued*)

Primary cancer diagnosis	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
	Kain et al. (2020) [67]	14	272	
	Qld Government (2020) [2]	401	2515	
	Total	*749*	*4990*	*15%*
	Summary effect size (prostate cancer)			*0.13 (0.10, 0.17)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*1.02, 0.313*
GI cancer	Tseng et al. (2018) [60] *	4	28	
	Total	*4*	*28*	*14%*
	Summary effect size (GI cancer)			*0.14 (0.05, 0.32)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.18)*
	Test of moderators: coefficient 2 (QM, p value)			*0.05, 0.819*
Gynaecological cancers	Shukor et al. (2018) [51]	10	27	
	Tseng et al. (2018) [60] *	2	5	
	Qld Government (2020) [2]	134	717	
	Total	*146*	*749*	*19%*
	Summary effect size (gynaecological cancer)			*0.27 (0.14, 0.45)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*2.91, 0.088*
Hepatobiliary cancer	Shukor et al. (2018) [51]	4	10	
	Qld Government (2020) [2]	134	504	
	Total	*138*	*514*	*27%*
	Summary effect size (hepatobiliary cancer)			*0.27 (0.23, 0.31)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			***24.20, <0.001*** ‡
Head and neck cancer	Shukor et al. (2018) [51]	8	18	
	Tseng et al. (2018) [60] *	1	14	
	Qld Government (2020) [2]	134	601	
	Total	*143*	*633*	*23%*
	Summary effect size (head and neck cancer)			*0.25 (0.12, 0.45)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*1.34, 0.246*
Genitourinary cancer	Shukor et al. (2018) [51]	15	67	
	Tseng et al. (2018) [60] *	6	19	
	Pitson et al. (2020) [70]	38	545	
	Qld Government (2020) [2]	317	1374	
	Total	*376*	*2005*	*19%*
	Summary effect size (Genitourinary cancer)			*0.18 (0.09, 0.34)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*0.16, 0.689*
Melanoma cancer	Qld Government (2020) [2]	328	1432	
	Total	*328*	*1432*	*23%*
	Summary effect size (melanoma cancer)			*0.23 (0.21, 0.25)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			***16.19, <0.001*** ‡
Renal cell carcinoma	Tseng et al. (2018) [60] *	4	11	
	Total	*4*	*11*	*36%*
	Summary effect size (Renal cell cancers)			*0.36 (0.14, 0.66)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.18)*
	Test of moderators: coefficient 2 (QM, p value)			*2.99, 0.084*
CNS cancers	Qld Government (2020) [2]	44	318	

Table D2 (*continued*)

Primary cancer diagnosis	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
	Total	*44*	*318*	*14%*
	Summary effect size (CNS cancers)			*0.14 (0.10, 0.18)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*0.70, 0.404*
Sarcoma	Tseng et al. (2018) [60] *	1	16	
	Total	*1*	*16*	*6%*
	Summary effect size (sarcoma cancers)			*0.06 (0.01, 0.34)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.18)*
	Test of moderators: coefficient 2 (QM, p value)			*1.01, 0.315*
Mesothelioma	Qld Government (2020) [2]	69	292	
	Total	*69*	*292*	*24%*
	Summary effect size (mesothelioma cancers)			*0.24 (0.19, 0.29)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value))			***8.89, 0.003*** ‡

*indicates unpublished data gained by correspondence with authors of study, RT = radiotherapy. Qld = Queensland, GI = gastrointestinal, CNS = central nervous system, QM = test for moderators (coefficient 2), (df =1), ‡ = significant p value $\leq$ 0.05.

Table D3
Inpatient and outpatient status subgroup analysis and raw data.

Patient location status	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
Inpatient	Ryoo et al. (2017) [71]	65	166	
	Shukor et al. (2018) [51]	78	216	
	Ellsworth et al. (2014) [43]	47	99	
	Chawla et al. (2015) [55]	29	68	
	Total	*219*	*549*	*40%*
	Summary effect size (inpatient)			*0.40 (0.36, 0.45)*
	Summary effect size (Other studies)			*0.15 (0.13, 0.17)*
	Test of moderators: coefficient 2 (QM, p value)			***92.27, <0.001*** ‡
Outpatient	Shukor et al. (2018) [51]	55	369	*15%*
	Total	*55*	*369*	*0.15 (0.12, 0.19)*
	Summary effect size (outpatient)			*0.16 (0.14, 0.18)*
	Summary effect size (Other studies)			*0.16, 0.690*
	Test of moderators: coefficient 2 (QM, p value)			

RT = radiotherapy. QM = test for moderators (coefficient 2), (df =1). ‡ = significant *p* value $\leq$ 0.05.

Table D4
ECOG score subgroup analysis and raw data.

Performance status	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
ECOG 0–1	Kain et al. (2020) [67]	39	886	
	Total	*39*	*886*	*4%*
	Summary effect size (ECOG 0–1)			*0.04 (0.03,0.06)*
	Summary effect size (Other studies)			*0.16 (0.14,0.19)*
	Test of moderators: coefficient 2 (QM, p value)			***56.68, <0.001***‡
ECOG 2	Kain et al. (2020) [67]	67	505	
	Total	*67*	*505*	*13%*
	Summary effect size (ECOG 2)			*0.13 (0.11, 0.17)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*2.05, 0.153*
ECOG 3–4	Nieder et al. (2015) [47]	79	219	
	Shukor et al. (2018) [51]	78	180	
	Kain et al. (2020) [67]	71	328	
	Total	*228*	*727*	*31%*
	Summary effect size (ECOG 3–4)			*0.33 (0.21, 0.47)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			***8.70, 0.003***‡

ECOG = Eastern Cooperative Oncology Group performance status. RT = radiotherapy. QM = test for moderators (coefficient 2), (df =1). ‡ = significant p value $\leq$ 0.05.

Table D5
Other subgroups analysis and raw data.

Other subgroups	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
Synchronous chemotherapy	Shukor et al. (2018) [51]	8	239	
	Total	*8*	*239*	*3%*
	Summary effect size (synchronous chemo)			*0.03 (0.02, 0.07)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.18)*
	Test of moderators: coefficient 2 (QM, p value)			***20.66, <0.001***‡
Known to hospice	Jung et al. (2013) [58]	*7*	*75*	
	Pitson et al. (2020) [70]	184	1062	
	Total	191	1137	*17%*
	Summary effect size (hospice)			*0.14 (0.08, 0.24)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			*0.28, 0.599*
Age > 60yrs	Shukor et al. (2018) [51]	63	288	
	Kain et al. (2020) [67]	145	1365	
	Murphy et al. (2013) [33]	7093	21,279	
	Wallace et al. (2018) [34]	92	569	
	Total	7393	23,501	*31%*
	Summary effect size (age > 60yrs)			*0.19 (0.10, 0.35)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.18)*
	Test of moderators: coefficient 2 (QM, p value)			*0.63, 0.429*
Age $\leq$ 60yrs	Shukor et al. (2018) [51]	70	297	
	Kain et al. (2020) [67]	33	379	
	Murphy et al. (2013) [33]	0	0	
	Wallace et al. (2018) [34]	0	0	
	Total	103	676	*15%*
	Summary effect size (age <=60yrs)			*0.15 (0.05, 0.35)*
	Summary effect size (Other studies)			*0.15 (0.14, 0.17)*
	Test of moderators: coefficient 2 (QM, p value)			*0.00, 0.96*

Table D5 (*continued*)

Other subgroups	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
Patients with liver metastases	Ryoo et al. (2017) [71]	34	106	
	Total	34	106	*32%*
	Summary effect size (liver metastases)			*0.32 (0.24, 0.42)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.19)*
	Test of moderators: coefficient 2 (QM, p value)			***14.96, <0.001***‡

RT = radiotherapy. QM = test for moderators (coefficient 2), (df =1). ‡ = significant p value $\leq$ 0.05.

Table D6
Fractionation and other subgroup analysis and raw data.

Subgroup	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
Patients getting 1 fraction	Shukor et al. (2018) [51]	36	142	
	Shaw et al. (2019) [52] *	81	427	
	Tursunovic et al. (2013) [72]	26	64	
	Cho et al. (2019) [42]	129	875	
	Ellsworth et al. (2014) [43]	7	27	
	Kain et al. (2020) [67]	45	394	
	Qld Government (2020) [2]	1171	3591	
	Wallace et al. (2018) [34]	32	193	
	Total	*1527*	*5713*	*27%*
	Summary effect size (1 fraction)			*0.22 (0.15, 0.30)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value))			*3.11, 0.078*
Patients getting 2–5 fractions	Shaw et al. (2019) [52]	22	236	
	Tursunovic et al. (2013) [72]	20	60	
	Kain et al. (2020) [67]	111	994	
	Qld Government (2020) [2]	2503	9591	
	Total	*2656*	*10,881*	*24%*
	Summary effect size (2–5 fractions)			*0.18 (0.10, 0.31)*
	Summary effect size (Other studies)			*0.16 (0.13, 0.19)*
	Test of moderators: coefficient 2 (QM, p value))			*0.10, 0.749*
Patients getting 6–10 fractions	Shaw et al. (2019) [52] *	5	223	
	Tursunovic et al. (2013) [72]	19	169	
	Qld Government (2020) [2]	1040	6161	
	Total	*1064*	*6553*	*16%*
	Summary effect size (6–10 fractions)			*0.09 (0.04, 0.19)*
	Summary effect size (Other studies)			*0.16 (0.13 , 0.19)*
	Test of moderators: coefficient 2 (QM, p value))			*1.34, 0.246*
Patients getting > 10 fractions	Shaw et al. (2019) [52] *	0	118	
	Lewis et al. (2020) [75]	0	0	
	Qld Government (2020) [2]	283	3157	
	Wallace et al. (2018) [34]	27	150	
	Total	*310*	*3425*	*9%*
	Summary effect size (>10 fractions)			*0.10 (0.04, 0.20)*
	Summary effect size (Other studies)			*0.15 (0.13, 0.18)*
	Test of moderators: coefficient 2 (QM, p value))			*1.06, 0.304*
Patients not completing treatment	Shukor et al. (2018) [51]	28	39	
	Ali et al. (2019) [57]	17	33	
	Lerner et al. (2015) [63]	5	17	
	Meeuse et al. (2010) [25]	18	31	
	Total	*68*	*120*	*57%*
	Summary effect size (pts not completing treatment)			*0.55 (0.39, 0.70)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.19)*
	Test of moderators: coefficient 2 (QM, p value))			***26.51, <0.001***‡
Patients getting SBRT for brain metastases	Ryoo et al. (2017) [71]	*5*	*126*	
		5	*126*	*4%*
	Summary effect size (patients getting SBRT)			*0.04 (0.02, 0.09)*
	Summary effect size (Other studies)			*0.16 (0.14, 0.18)*
	Test of moderators: coefficient 2 (QM, p value))			***10.54, 0.001***‡

(*continued on next page*)

Table D6 (*continued*)

Subgroup	Study	Number of patients dying within 30 days of palliative RT	Total number of patients receiving palliative RT	30-day mortality rate and subgroup moderator analysis
USA studies (post-hoc)	Ryoo et al. (2017) [71]	*149*	*639*	
	Ellsworth et al. (2014) [43]	*89*	*339*	
	Kapadia et al. (2012) [39]	*209*	*730*	
	Wu et al. (2019) [48]	*125*	*518*	
	Chawla et al. (2015) [55]	*29*	*68*	
	Tseng et al. (2018) [60]	*39*	*203*	
	Sherman et al. (2013) [61]	*10*	*40*	
	Bingham et al. (2016) [64]	*33*	*262*	
	Wong et al. (2019) [32]	18	113	
		8079	*25189*	*32%*
	Summary effect size (U.S. studies)			*0.25 (0.21, 0.30)*
	Summary effect size (other studies)			*0.13 (0.12, 0.15)*
	Test of moderators: coefficient 2 (QM, p value)			***28.70, <0.001*** ‡
Study year (≥2016) (post- hoc		*6241*	*35,998*	*17%*
	Summary effect size (studies from 2016 on)			*0.15 (0.13, 0.18)*
	Summary effect size (studies older than 2016)			*0.18 (0.13, 0.23)*
	Test of moderators: coefficient 2 (QM, p value)			*0.85, 0.358*
Timing of 30-day mortality (post-hoc)	*(from end of treatment)*	*13,389*	*51,727*	*26%*
	Summary effect size (studies 30-day mortality from end of treatment course)			*0.18 (0.14, 0.22)*
	Summary effect size (studies 30-day mortality from start of treatment course)			*0.15 (0.13, 0.18)*
	Test of moderators: coefficient 2 (QM, p value)			*0.73, 0.392*

*unpublished data gained from correspondence with authors of study, RT = radiotherapy, USA = United States of America. QM = test for moderators (coefficient 2), (df =1). ‡ = significant p value ≤ 0.05, SBRT = stereotactic Body Radiotherapy.

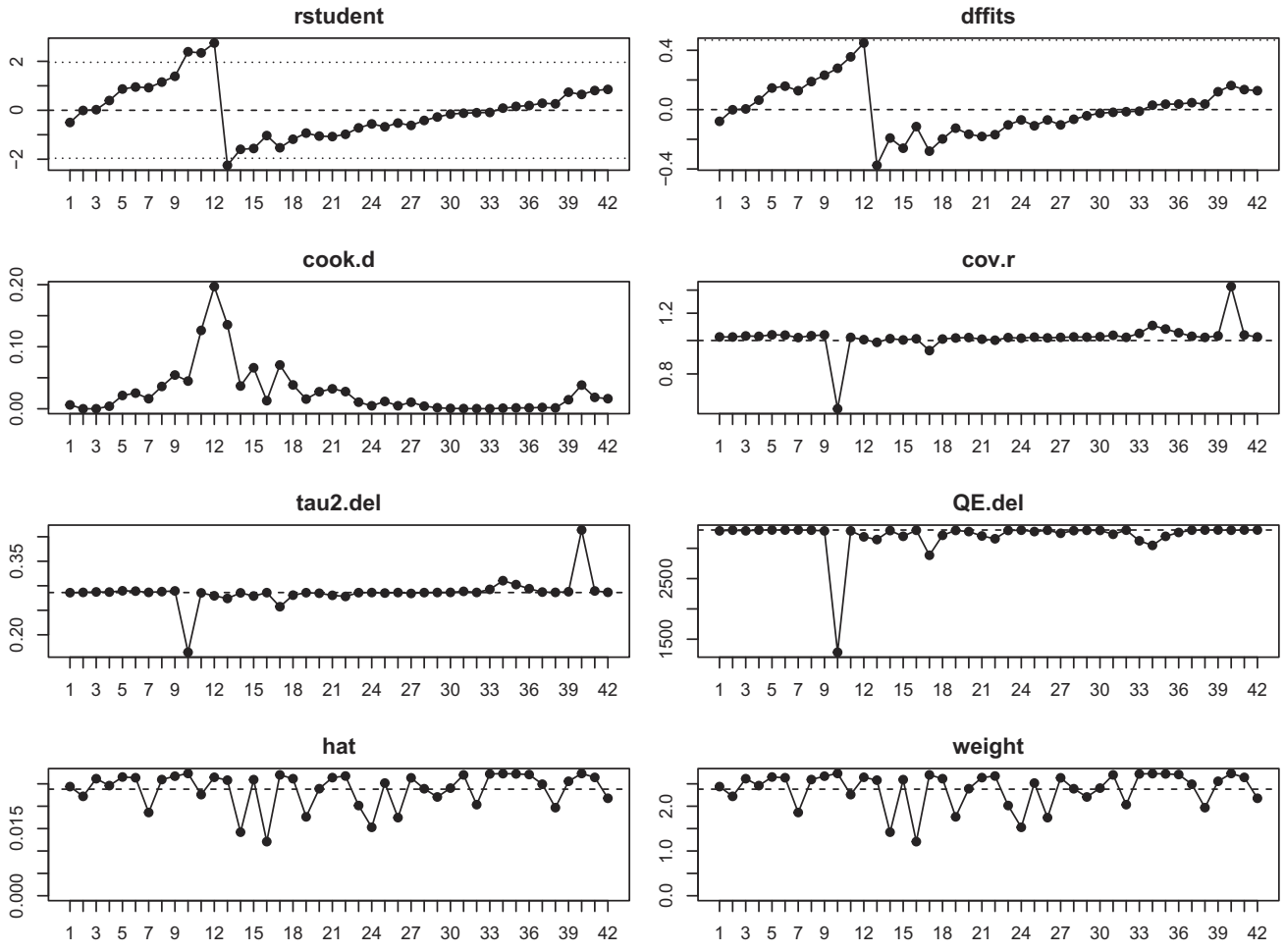

Fig. F1. Externally studentized residual screening analysis to investigate for infuential studies. None of the studies extracted were influential in this meta-analysis (based on externally studentized residuals cutoff ≥ 3 in absolute value). Study numbers correspond to ordering of studies in Fig. F.2 (1 to 42 from top to bottom of Fig. F.2).

Appendix E

Table E1
Studies excluded based on full manuscript review.

Excluded study	Reason for exclusion	Details
Yu et al. (2014) [38]	Wrong study design	Review: the studies from this article meeting inclusion/exclusion criteria have all been included in our search and in Park et al. (2017) [13] review
Anshushaug et al. (2015) [82]	Wrong study design	No total number of participants getting PR reported
Guadagnolo et al. (2013) [77]	Wrong study design	SEER Medicare-linked database excluding those under 65 years of age. Not reporting the total number of patients getting PR
Morin et al. (2016) [98]	Wrong outcomes	not reporting total that received PR
Zhang et al. (2014) [99]	Wrong outcomes	Study not reporting only those getting PR
Zhang et al. (2017) [85]	Wrong study design	Total number participants getting PR not reported. Attempted to contact author but no response
Li et al. (2017) [100]	Wrong outcomes	Not reporting 30-day mortality of all those getting PR
Nieder et al. (2017) [101]	Wrong outcomes	Not reporting those who died within 30 days of PR
Futagami et al. (2016) [102]	Wrong outcomes	30-day mortality of those getting chemotherapy for gynaecological cancers
Clement-Zhao et al. (2018) [103]	Wrong outcomes	This study did not obtain a 30-day mortality rate after PR
Huang J et al. (2014) [104]	Wrong population	Participants included had "invasive cancer", clarification requested from authors if this population had advanced or metastatic cancer, but no reply
Gallais Serezal et al. (2016) [105]	Wrong study design	Participants were all those who died in nation-wide register, but would have excluded patients dying at home or resident to a care-home
Dennis et al. (2011) [106]	Wrong outcomes	Efficacy of PR studies
Becerra et al. (2018) [107]	Wrong outcomes	Not able to confirm total that had palliative radiotherapy with the authors
Toole et al. (2012) [56]	Wrong population	Mix of palliative and curative RT population included, authors not able to confirm palliative RT numbers
Patel et al. (2014) [108]	Merged with Toole et al. (2012) [56]	
Grendarova et al. (2015) [78]	Wrong study design	Mix of palliative and curative RT population included, and authors not able to give totals of PR participants only.
Caussa et al. (2011) [109]	Wrong outcomes	Patients who died within 30 days of their PR not provided, unable to contact authors
Spencer et al. (2019) [110]	Wrong outcomes	Attempted to get unpublished data for 30-day mortality after PR but authors not able to provide
Gripp et al. (2010) [12]	Wrong outcomes	Study not differentiating those getting PR vs. curative intent radiotherapy
Varma et al. (2017) [111]	Wrong outcomes	30 day mortality after PR not reported, attempted to contact author but unable to
Sun et al. (2021) [112]	Wrong outcomes	30 day mortality after PR not reported, attempted to contact author but unable to
Berger et al. (2014) [114]	Wrong outcomes	Total that had PR not reported
Cassidy et al. (2018) [115]	Wrong outcomes	Not reporting 30-day mortality after PR. Attempted to contact author but unsuccessful
Panoff et al. (2015) [116]	Wrong population	Mix of curative and palliative patients reported
Tiwana et al. (2016) [83]	Wrong outcome	Authors can't provide number of patients who died within 30 days of PR
Tiwana et al. (2014) [117]	Merged with Tiwana et al. (2016) [83]	
Olson et al. (2014) [118]	Merged with Tiwana et al. (2016) [83]	

PR = palliative radiotherapy, SEER = Surveillance, Epidemiology, and End Results program, RT = radiotherapy.

Table E2
Studies merged into extracted studies used in this review.

Main parent extracted study	Studies merged into parent extracted study
Lee et al. (2020) [59]	Lee & Wong (2020) [119]
Pitson et al. (2020) [70]	Pitson et al. (2019) [120]
Ellsworth et al. (2014) [43]	Alcorn et al. (2013) [121]
	Alcorn et al. (2013) [122]
Gupta et al. (2012) [69]	Gupta et al. (2012) [81]
Wong et al. (2019) [32]	Hwang et al. (2018) [123]
Fraser et al. (2019) [40]	Fraser et al. (2018) [124]
Morris et al. (2017) [45]	Morris et al. (2017) [125]
Bingham et al. (2016) [64]	Dvorak et al. (2016) [64]
	Lopez et al. (2017) [126]
Wu et al. (2019) [48]	Wu et al. (2017) [127]
	Witztum et al. (2019) [128]
Spencer et al. (2015) [46]	Nieder 2015 [129]
	Hall et al. (2011) [130]
	Spencer et al. (2015) [131]
Wallace et al. (2018) [34]	Wallace et al. (2017) [132]
Nieder et al. (2015) [47]	Nieder et al. (2014) [133]
	Nieder et al. (2015) [134]
	Nieder et al. (2014) [135]
	Angelo et al. (2014) [86]
	Nieder et al. (2015) [113]

Appendix F

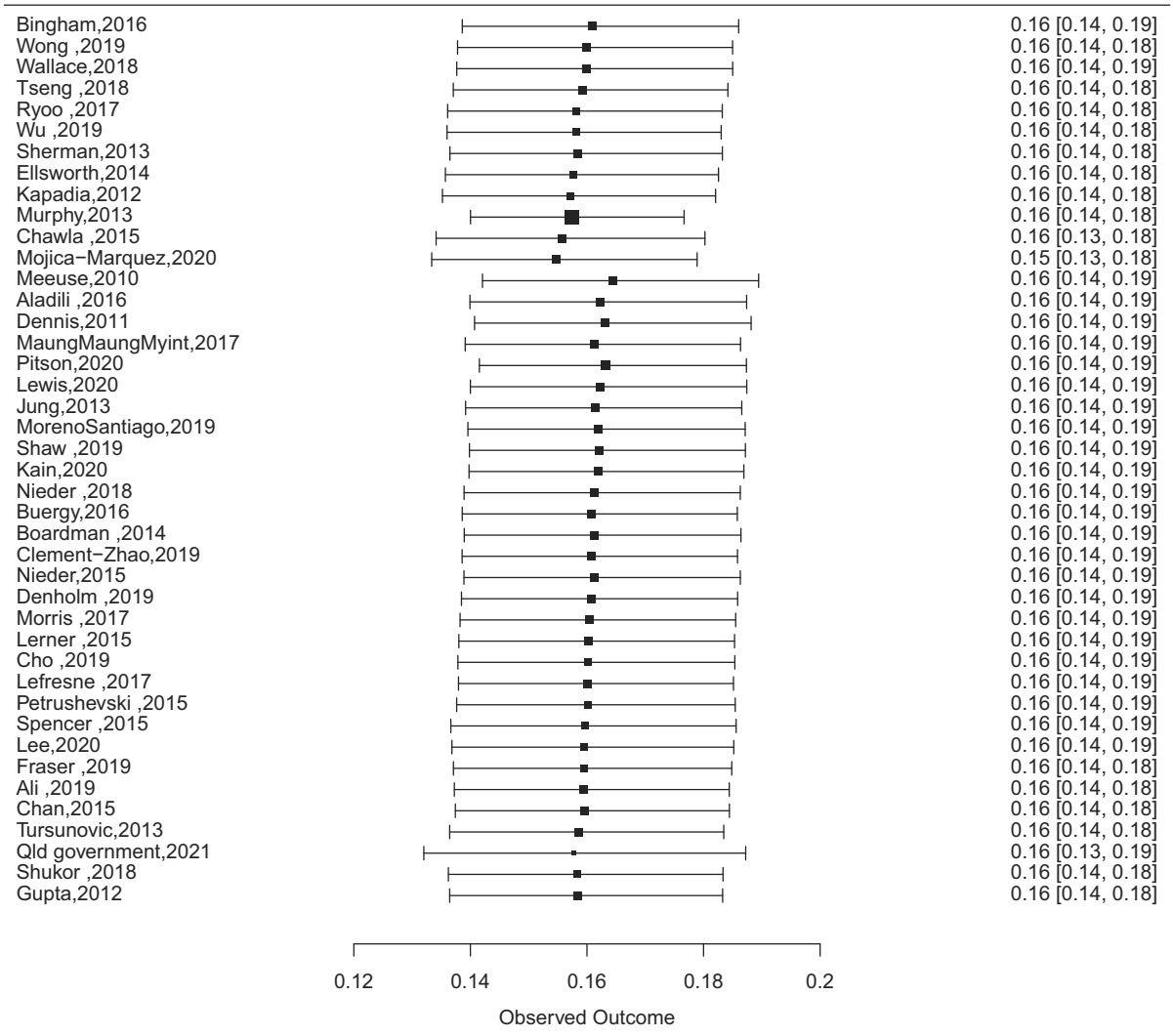

Fig. F2. Forest plot of the summary proportion with each study individually "left out" of analysis. None of the 42 studies were influential on the summary proportion 30-day mortality rate after palliative radiotherapy. Observed outcome is the proportion of patients dying within 30 days of palliative radiotherapy. Qld = Queensland, Australia.

Appendix G

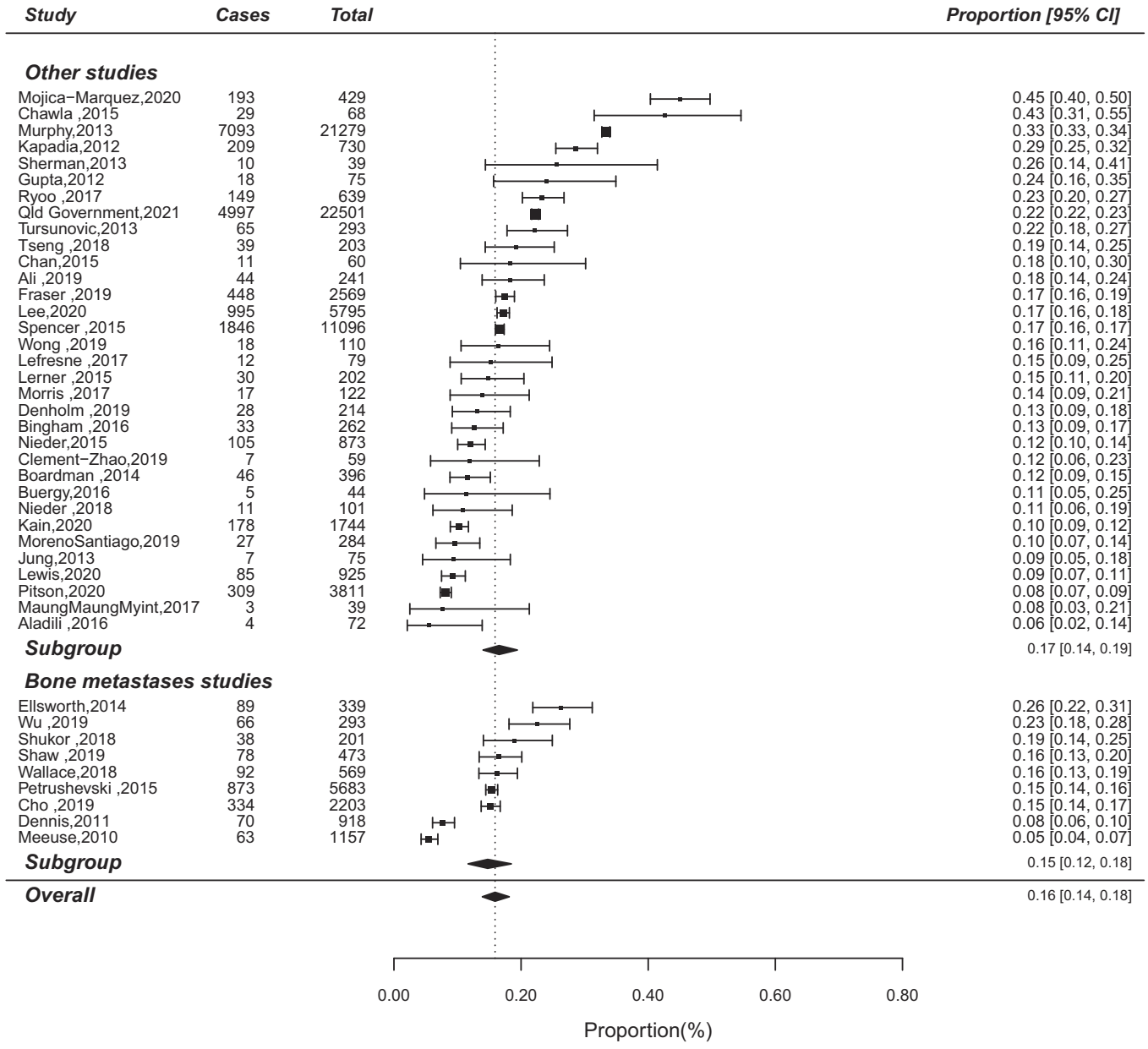

Fig. G1. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in bone metastases treatment studies vs. other studies. The bone metastases treatment subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.37, p = 0.544). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

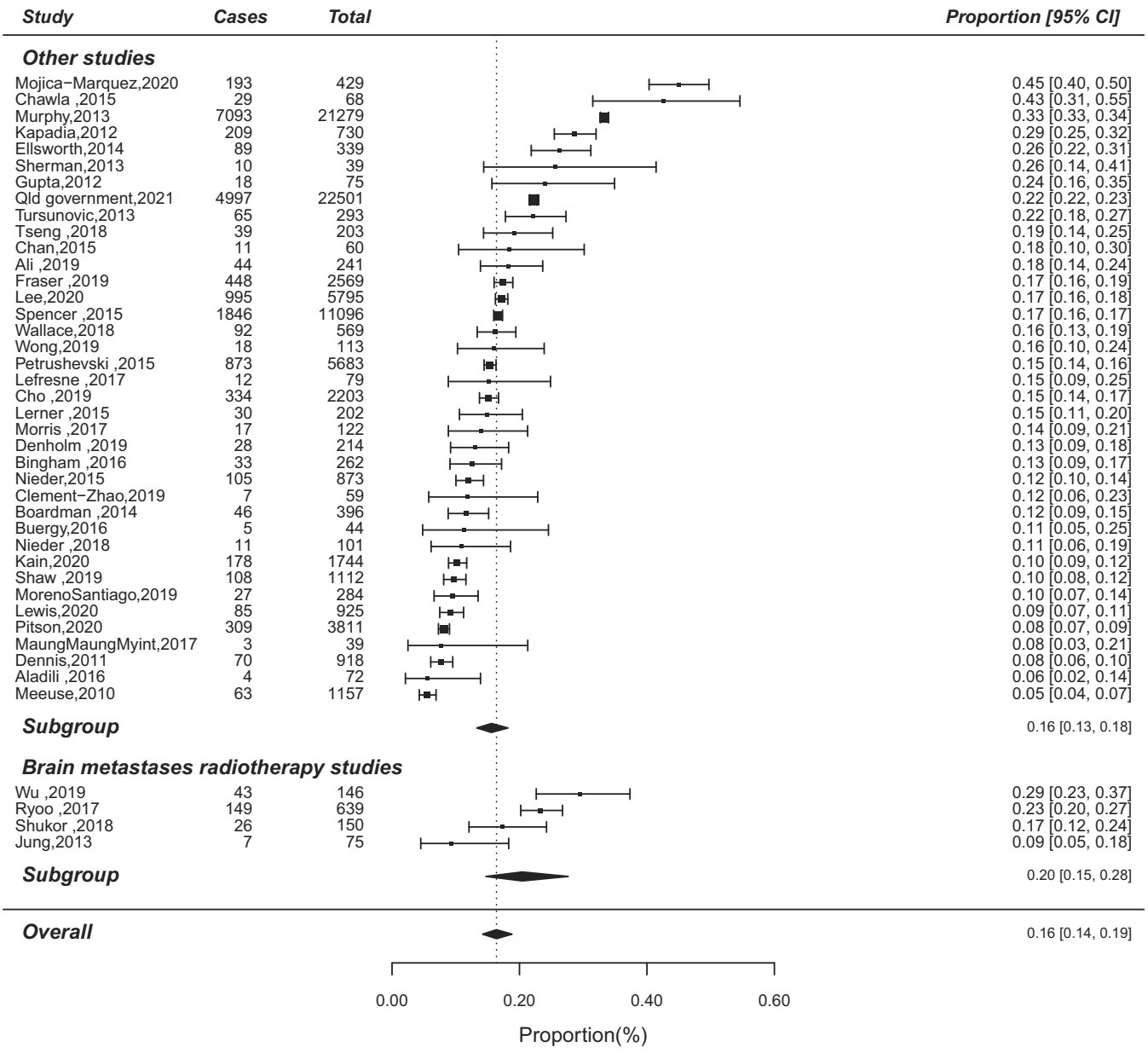

Fig. G2. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in brain metastases treatment studies vs. other studies. The brain metastases treatment subgroup did not significantly modify the overall summary effect proportion (QM(1) = 1.13, $p = 0.287$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

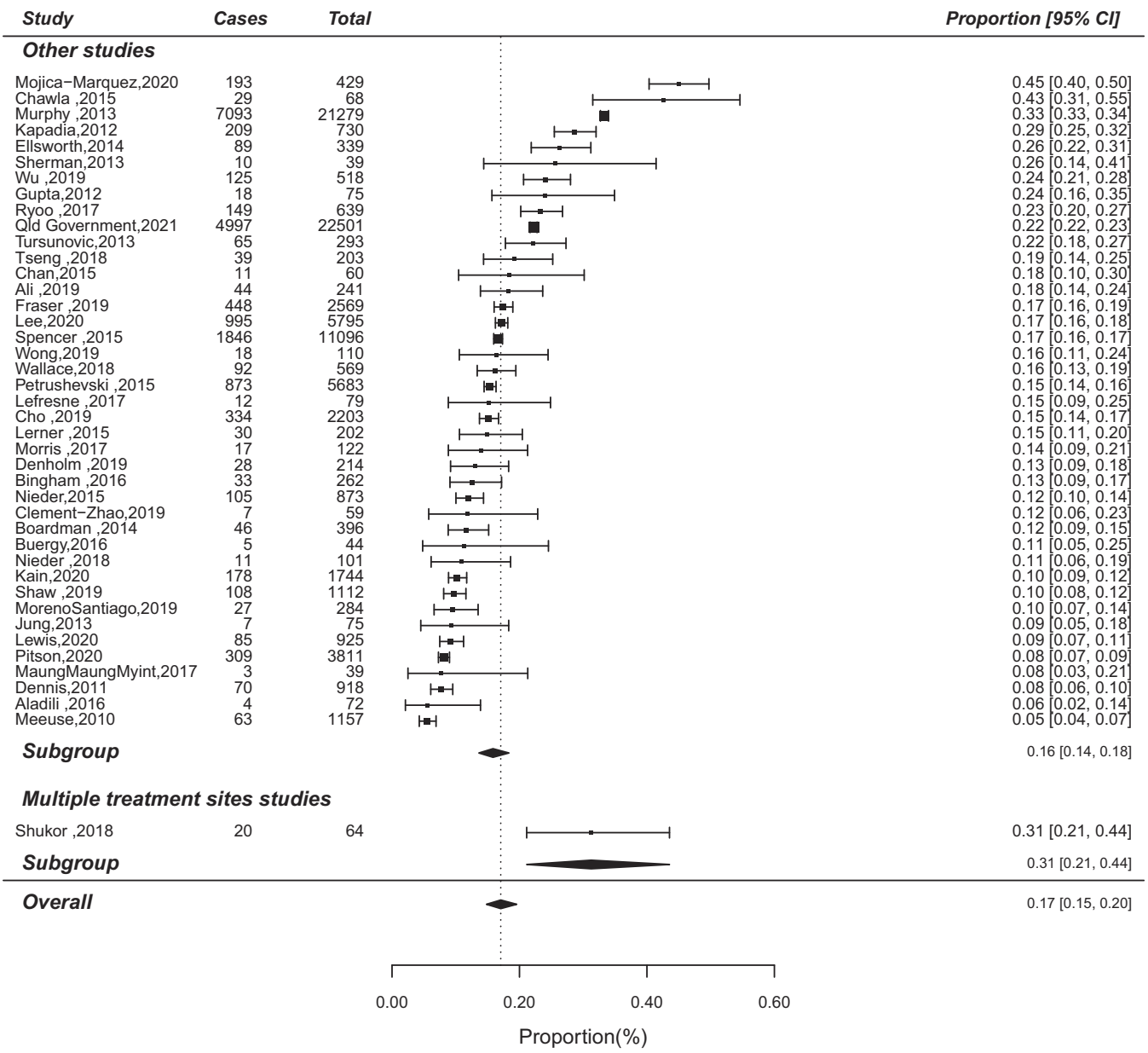

Fig. G3. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients getting treated at multiple body sites vs. other studies. The multiple treatment sites subgroup did significantly raise the overall summary effect proportion (QM(1) = 9.54, p = 0.002). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

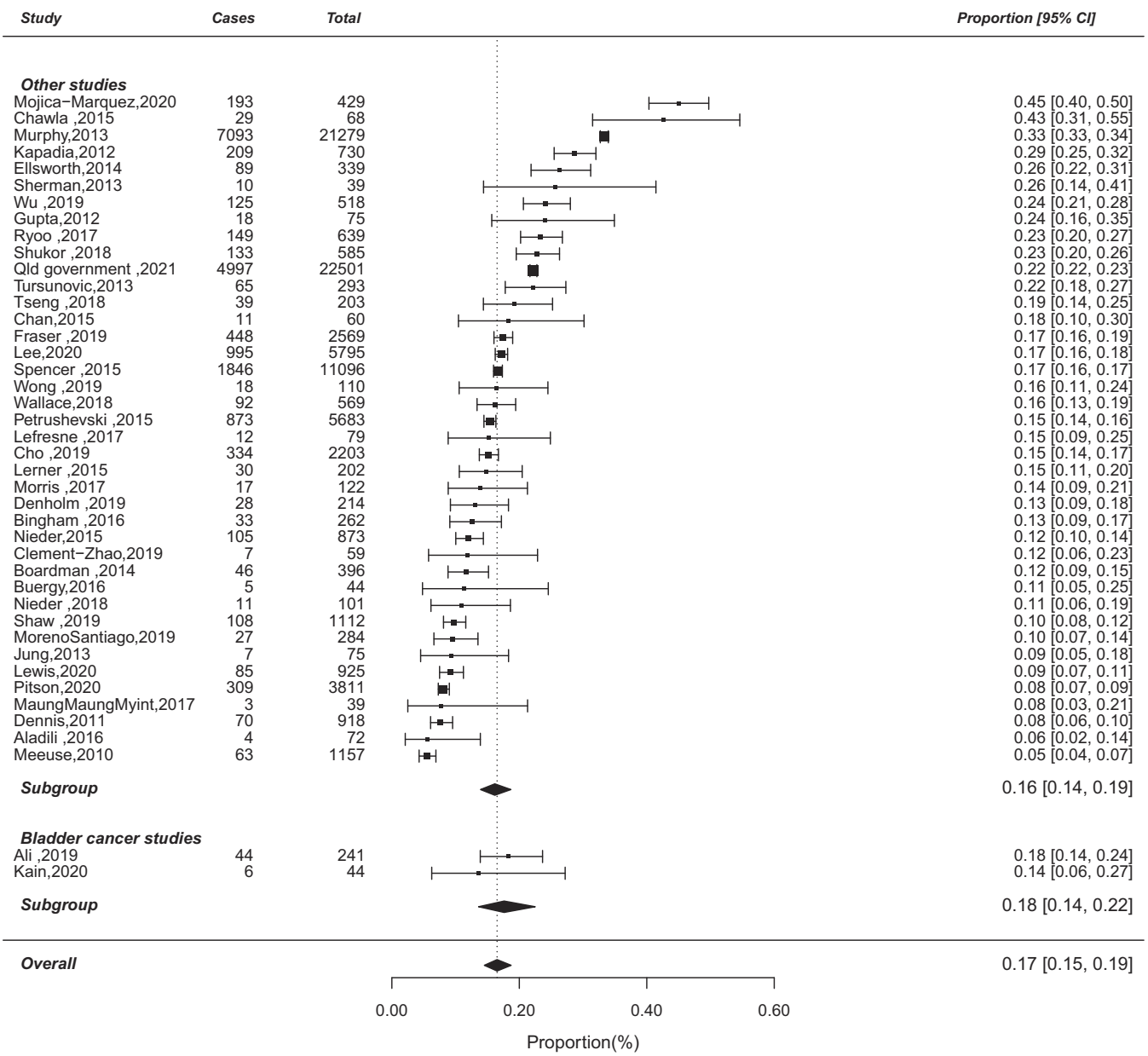

Fig. G4. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in bladder cancer studies vs. other studies. The bladder cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.34, p = 0.559). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

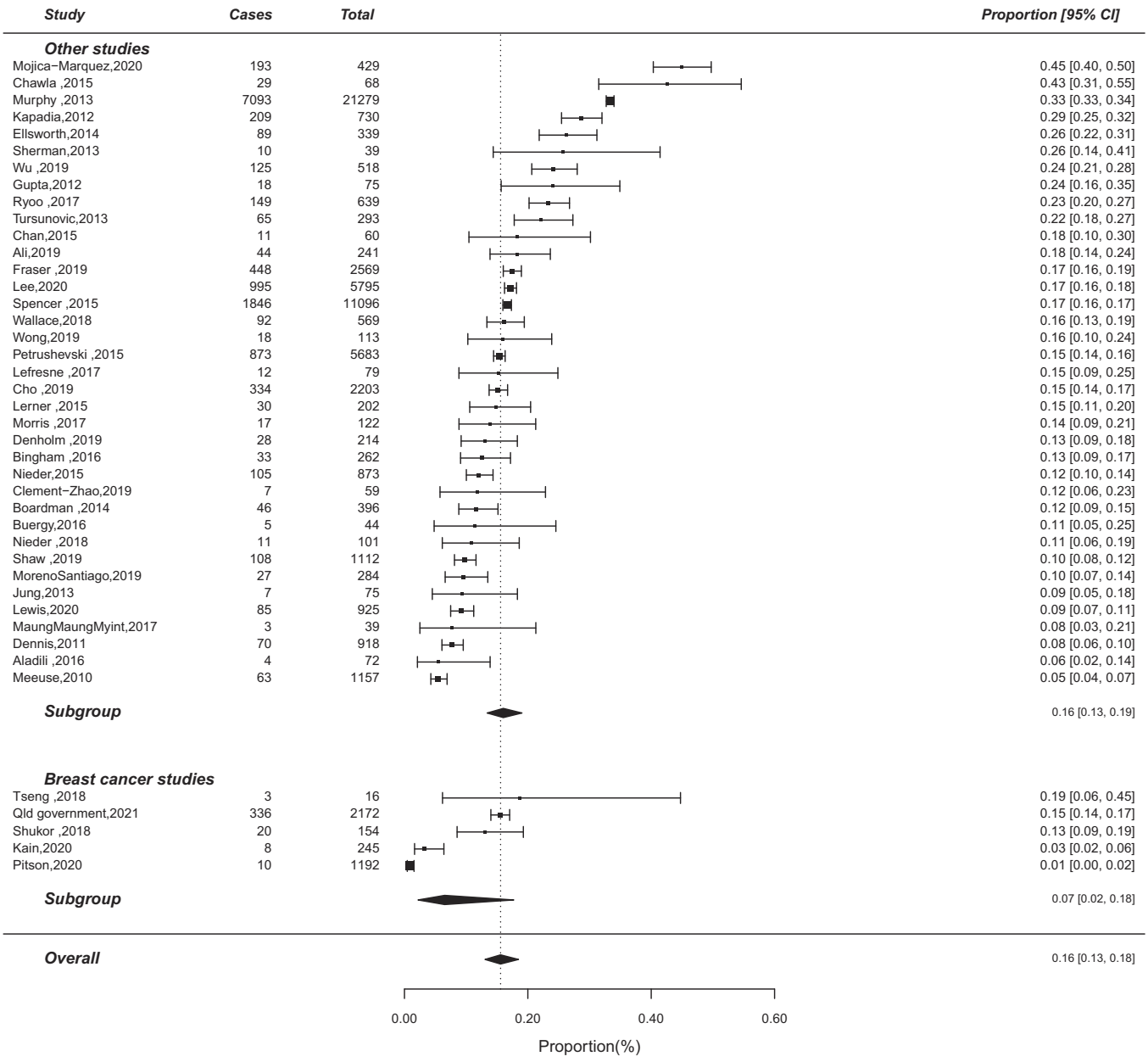

Fig. G5. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in breast cancer studies vs. other studies. The breast cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 2.50, p = 0.113). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

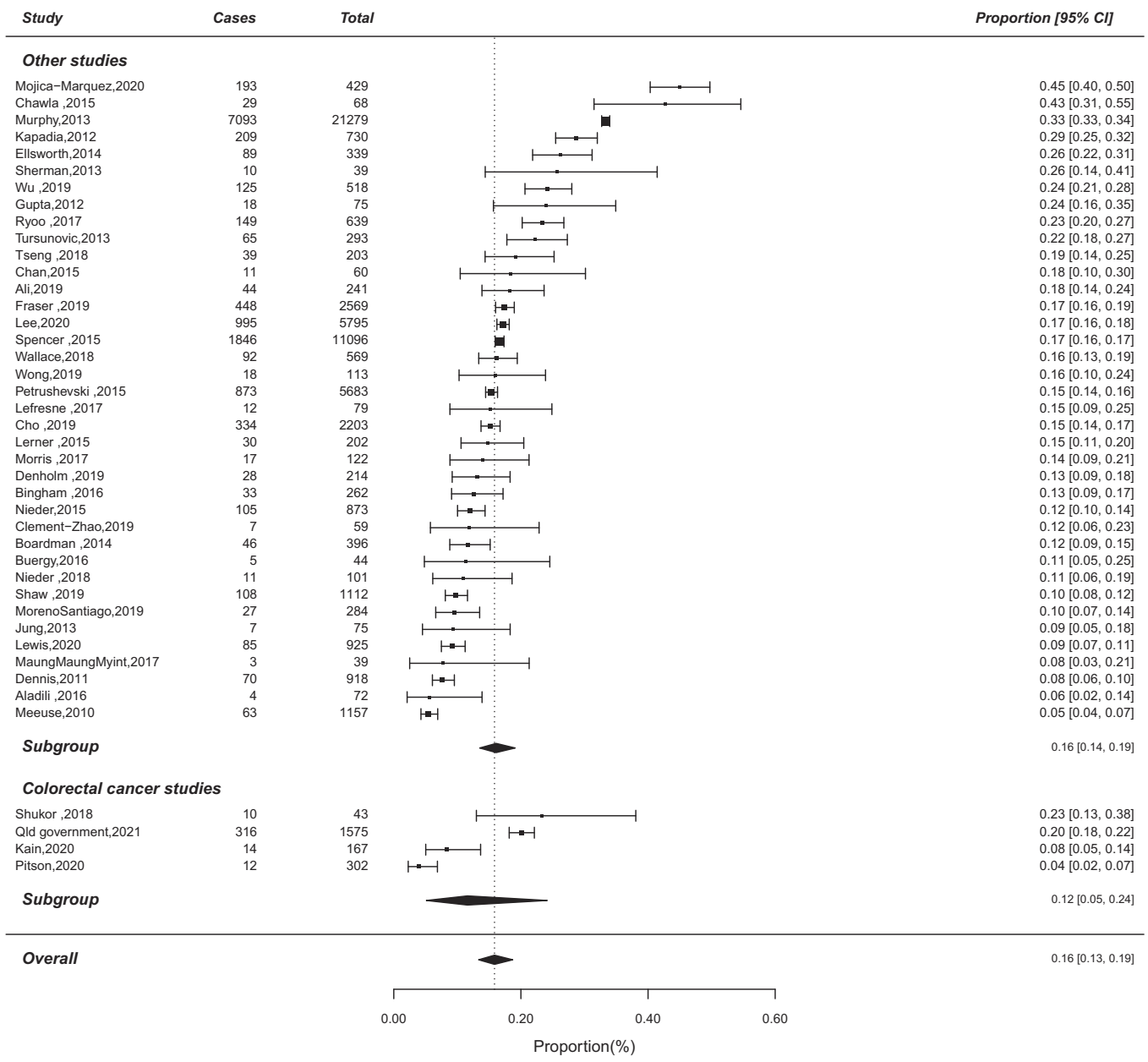

Fig. G6. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in colorectal cancer studies vs. other studies. The colorectal cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.67, p = 0.413). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

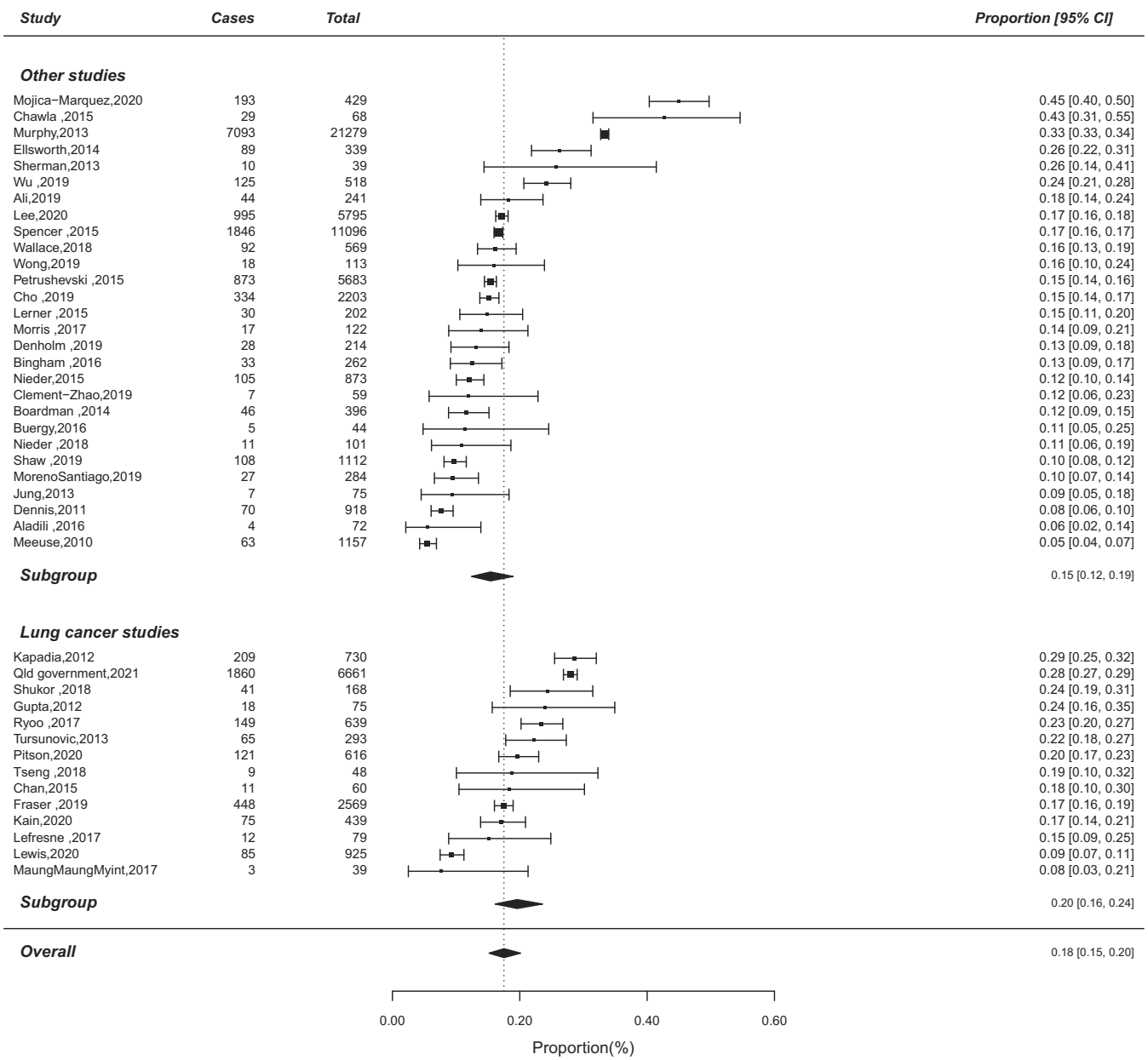

Fig. G7. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in lung cancer studies vs. other studies. The lung cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 3.10, p = 0.078). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

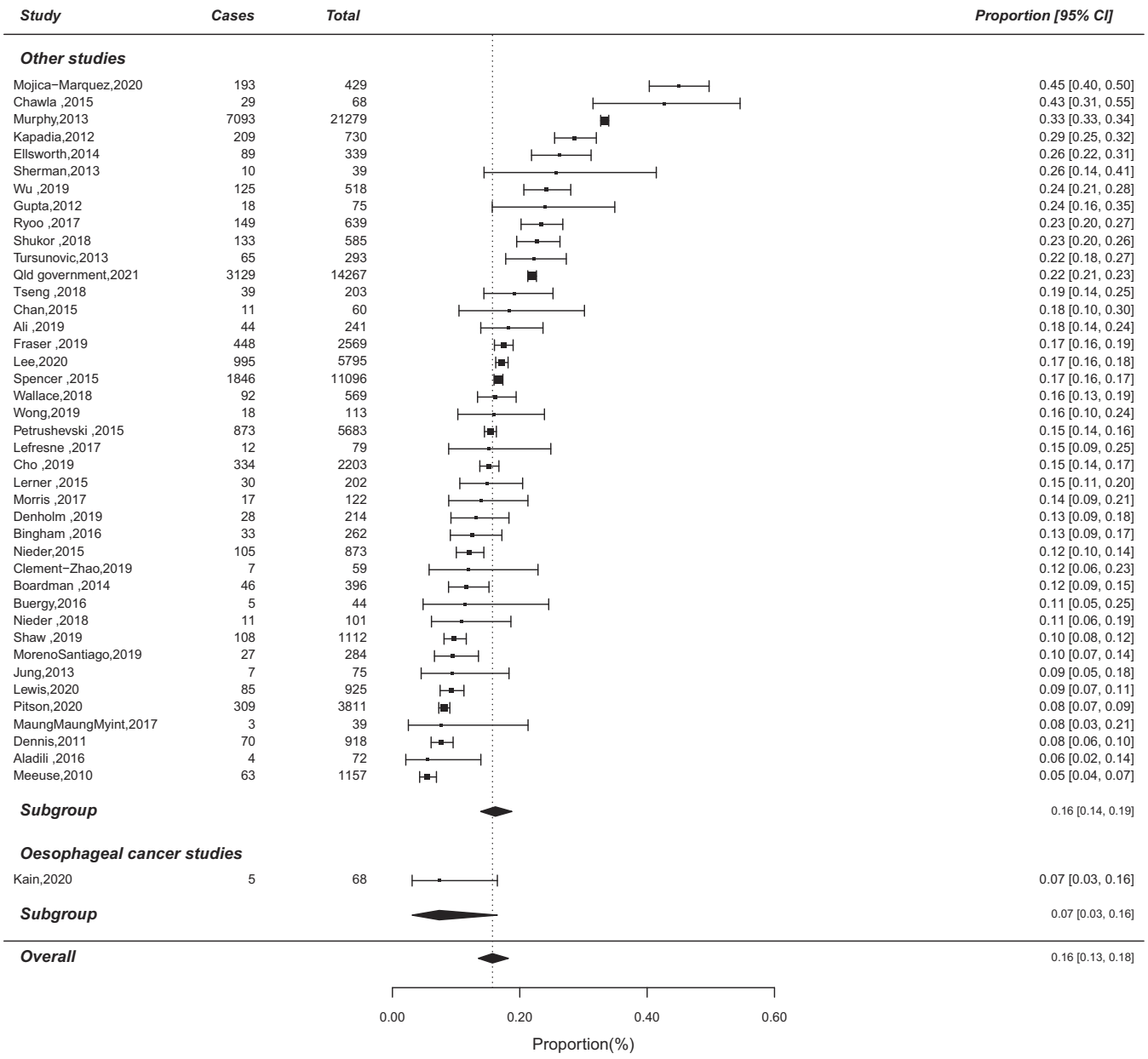

Fig. G8. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in oesophageal cancer studies vs. other studies. The oesophageal cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 3.50, $p = 0.061$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

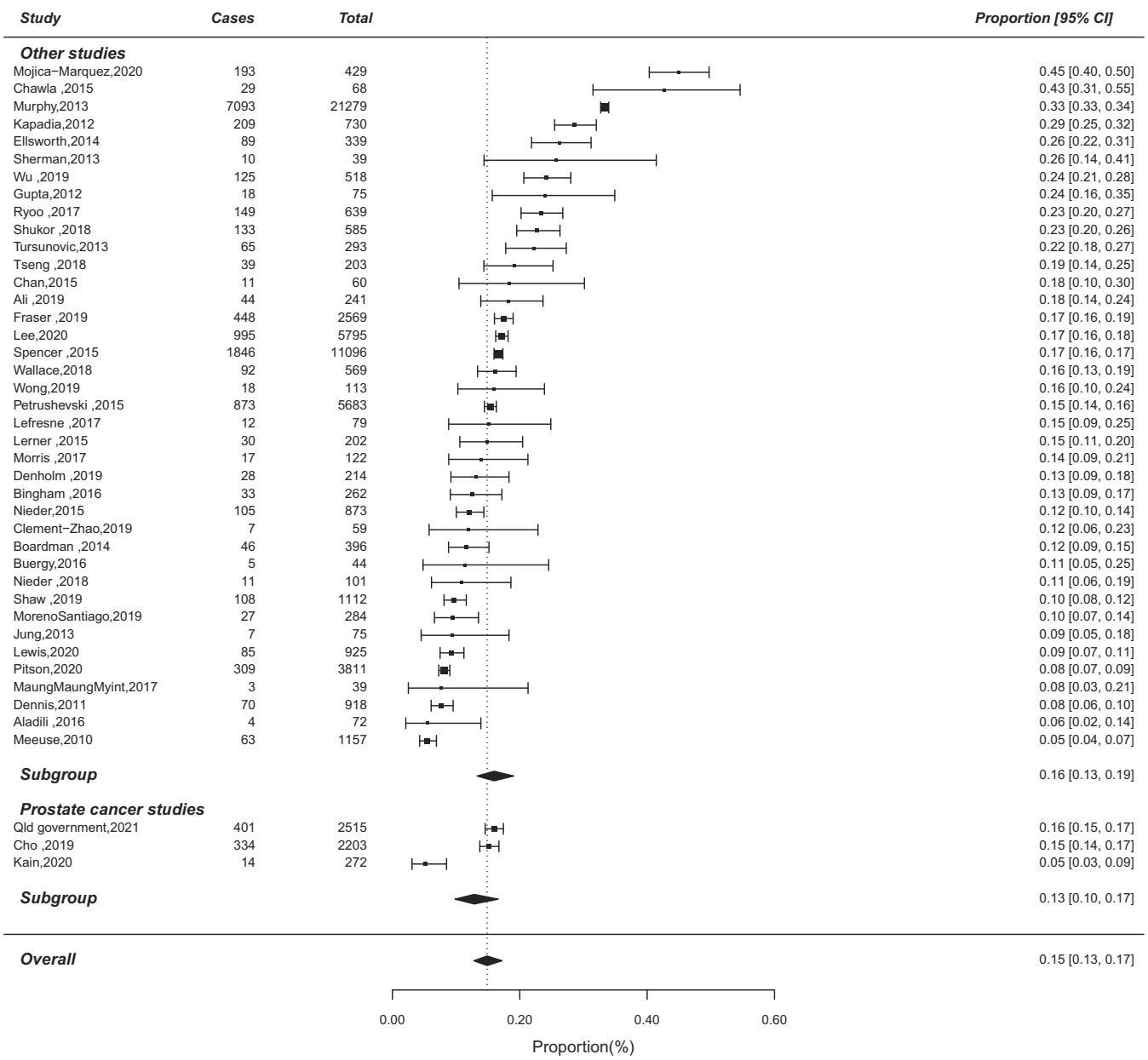

Fig. G9. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in prostate cancer studies vs. other studies. The prostate cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 1.02, p = 0.313). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

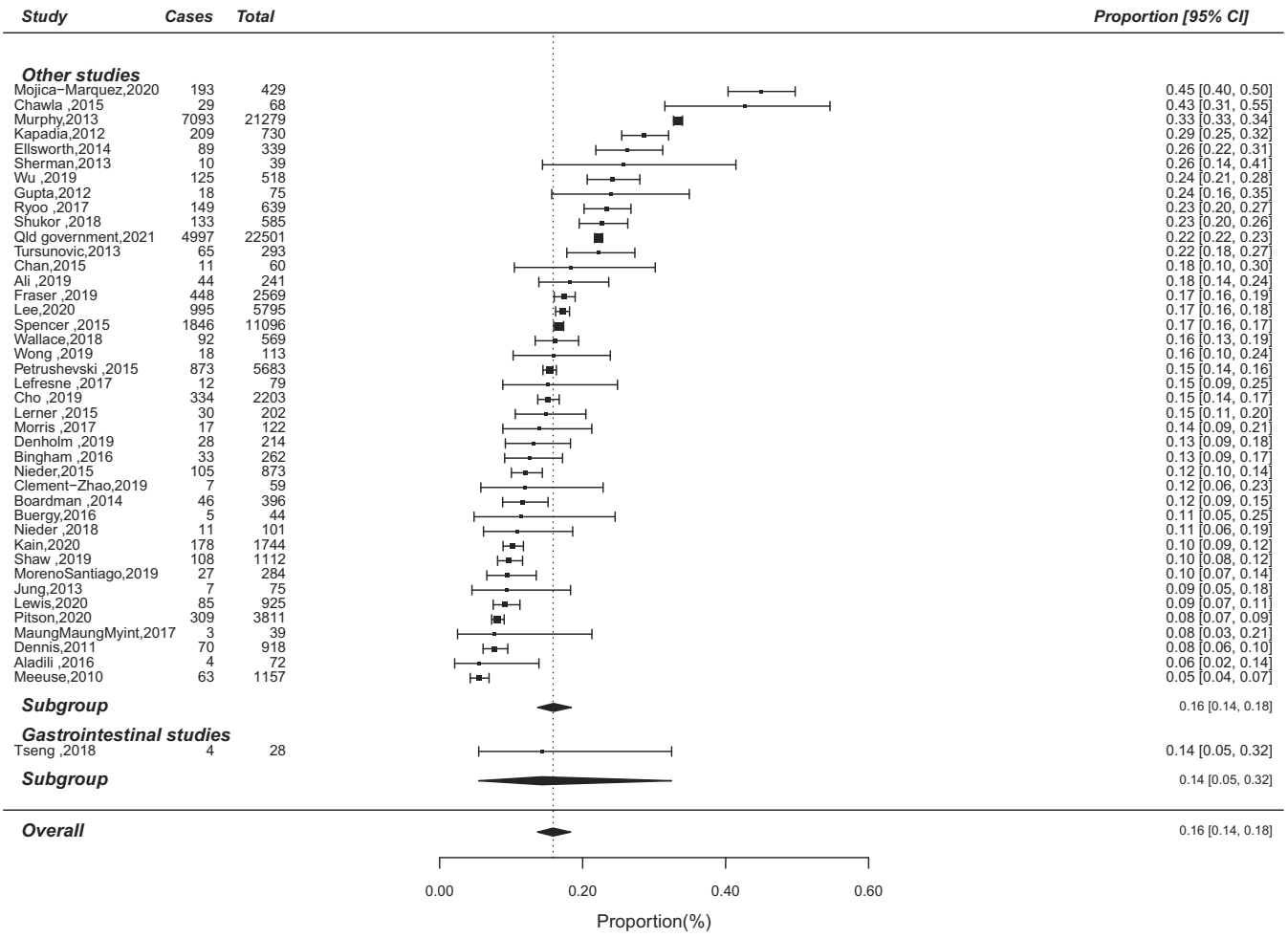

Fig. G10. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in gastrointestinal cancer studies vs. other studies. The gastrointestinal cancer subgroup did not significantly modify the overall summary effect proportion ($QM(1) = 0.05$, $p = 0.819$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

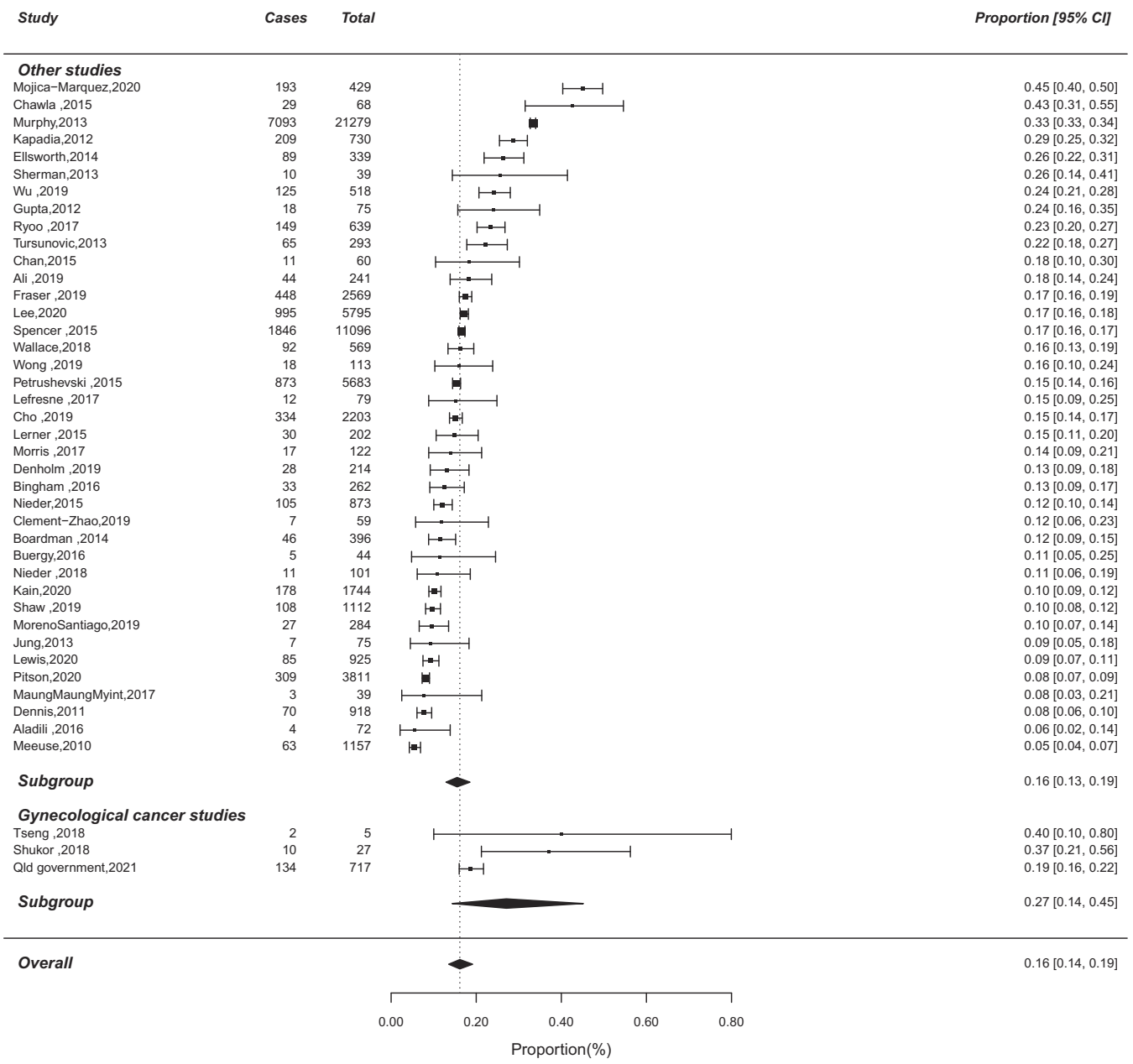

Fig. G11. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in gynaecological cancer studies vs. other studies. The gynaecological cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 2.91, $p = 0.088$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

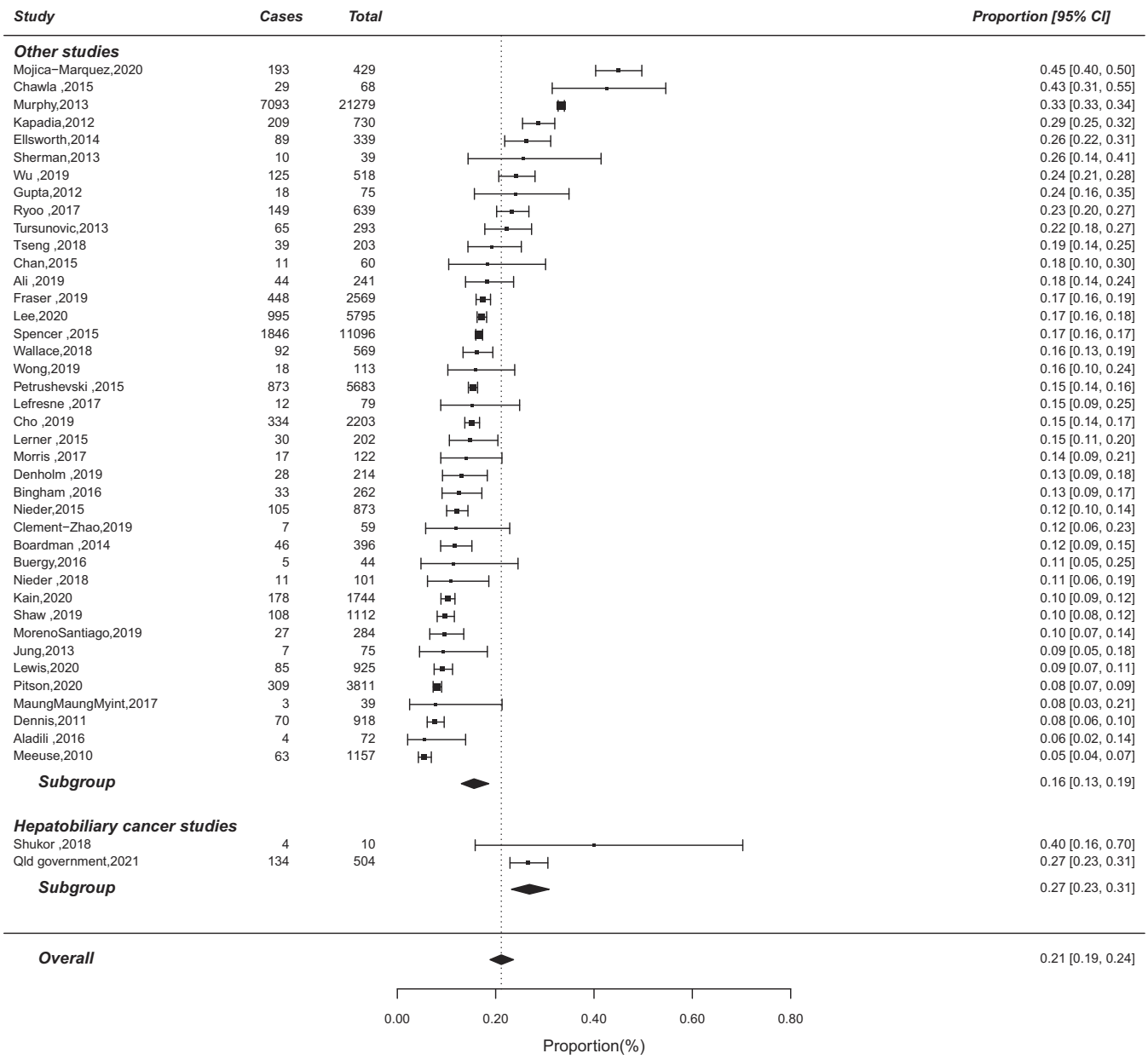

Fig. G12. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in hepatobiliary cancer studies vs. other studies. The hepatobiliary cancer subgroup did significantly raise the overall summary effect proportion (QM(1) = 24.20, $p < 0.001$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

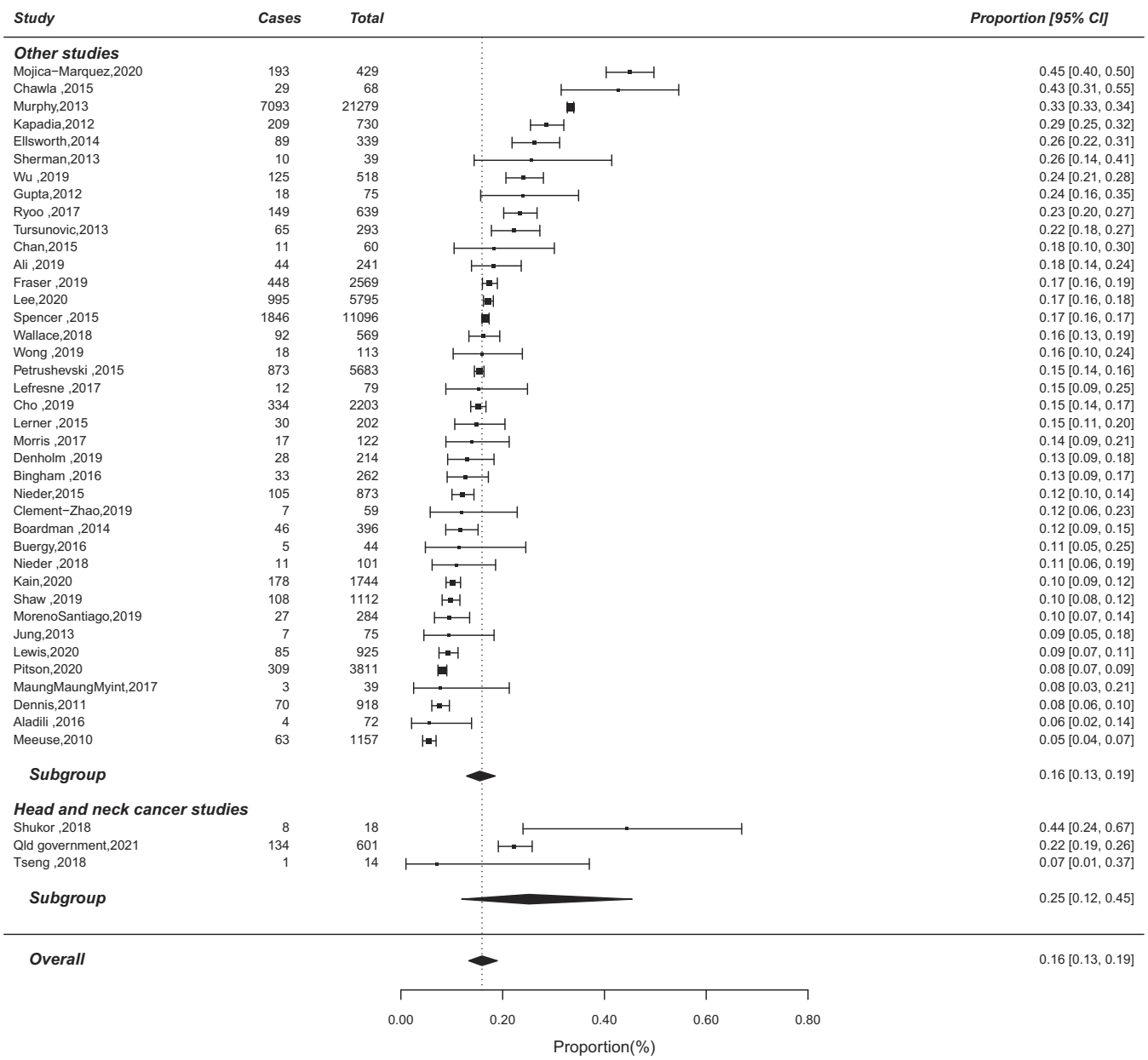

Fig. G13. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in head and neck cancer studies vs. other studies. The head and neck cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 1.34, $p = 0.246$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

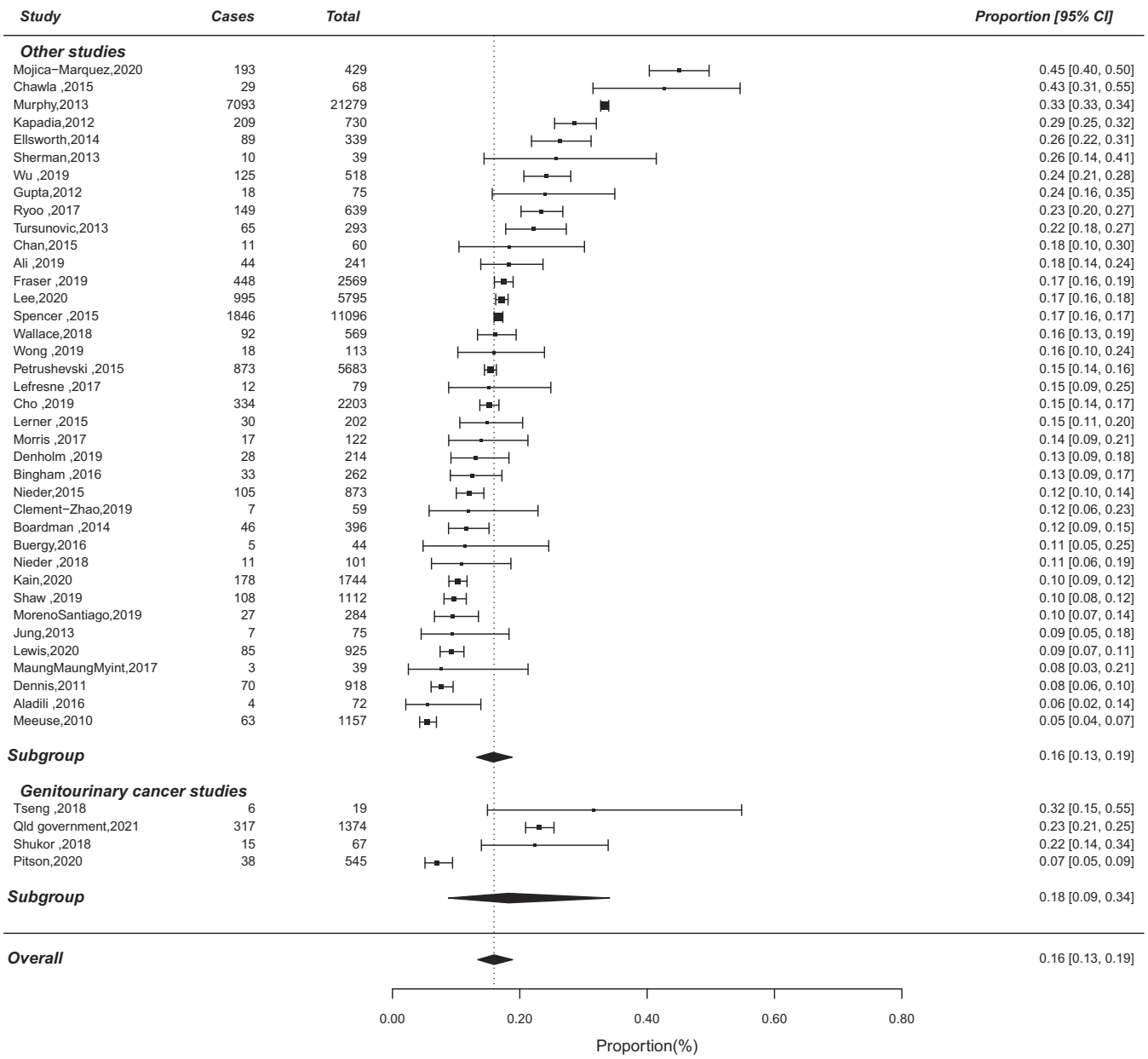

Fig. G14. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in genitourinary cancer studies vs. other studies. The genitourinary cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.16, p = 0.689). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

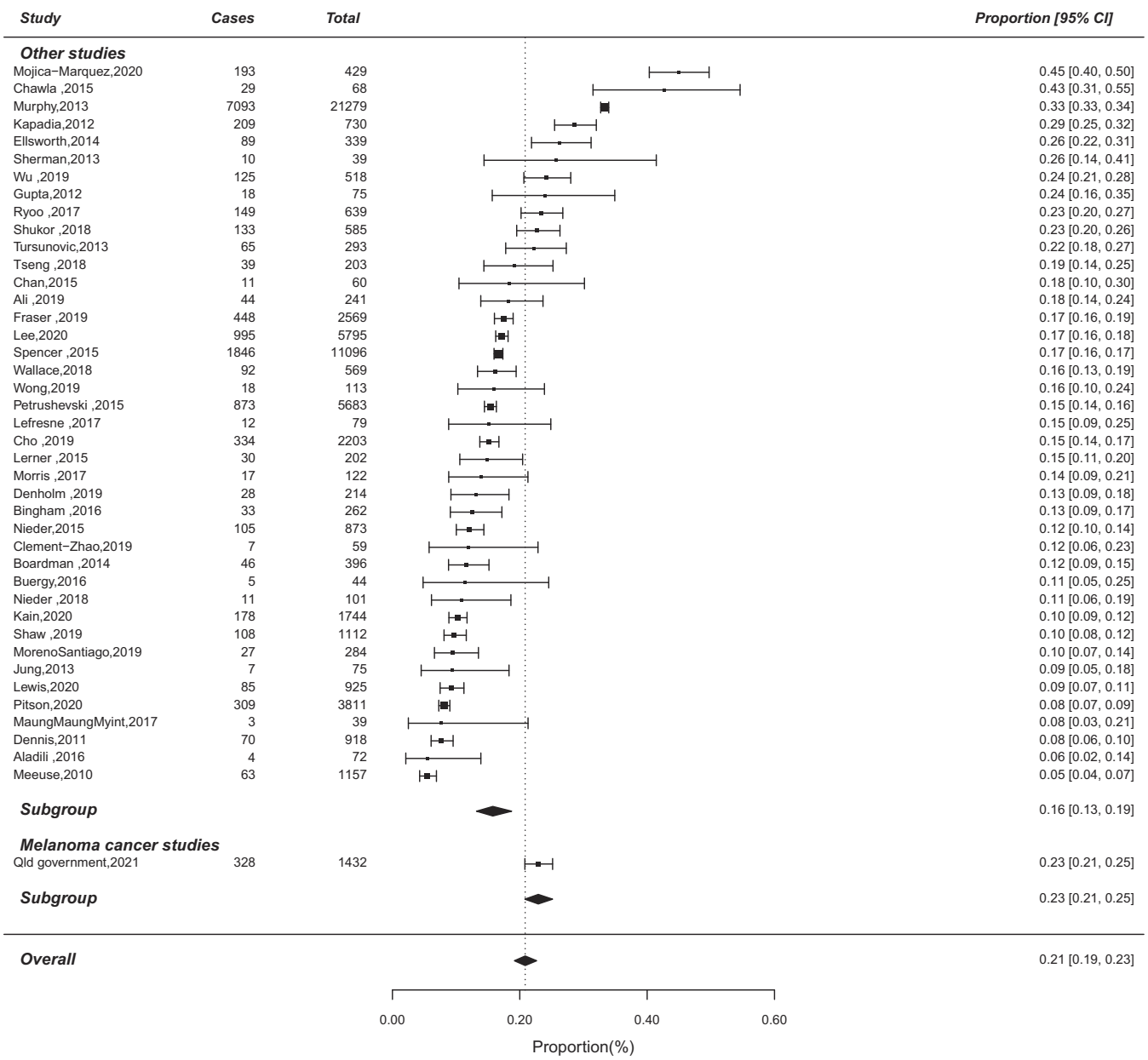

Fig. G15. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in melanoma cancer studies vs. other studies. The melanoma cancer subgroup did significantly raise the overall summary effect proportion (QM(1) = 16.19, $p < 0.001$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

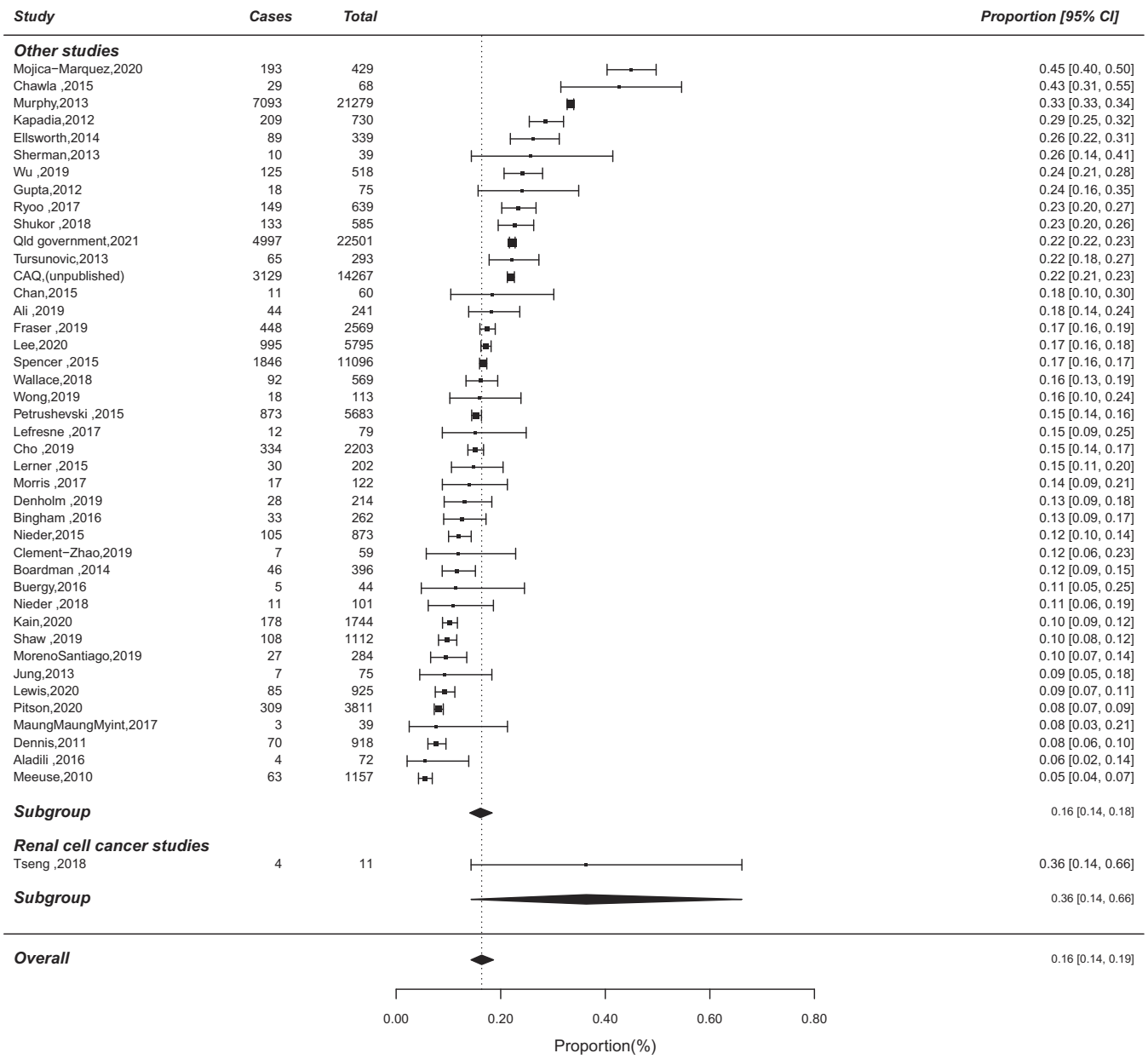

Fig. G16. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in renal cell cancer studies vs. other studies. The renal cell cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 2.99, p = 0.084). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

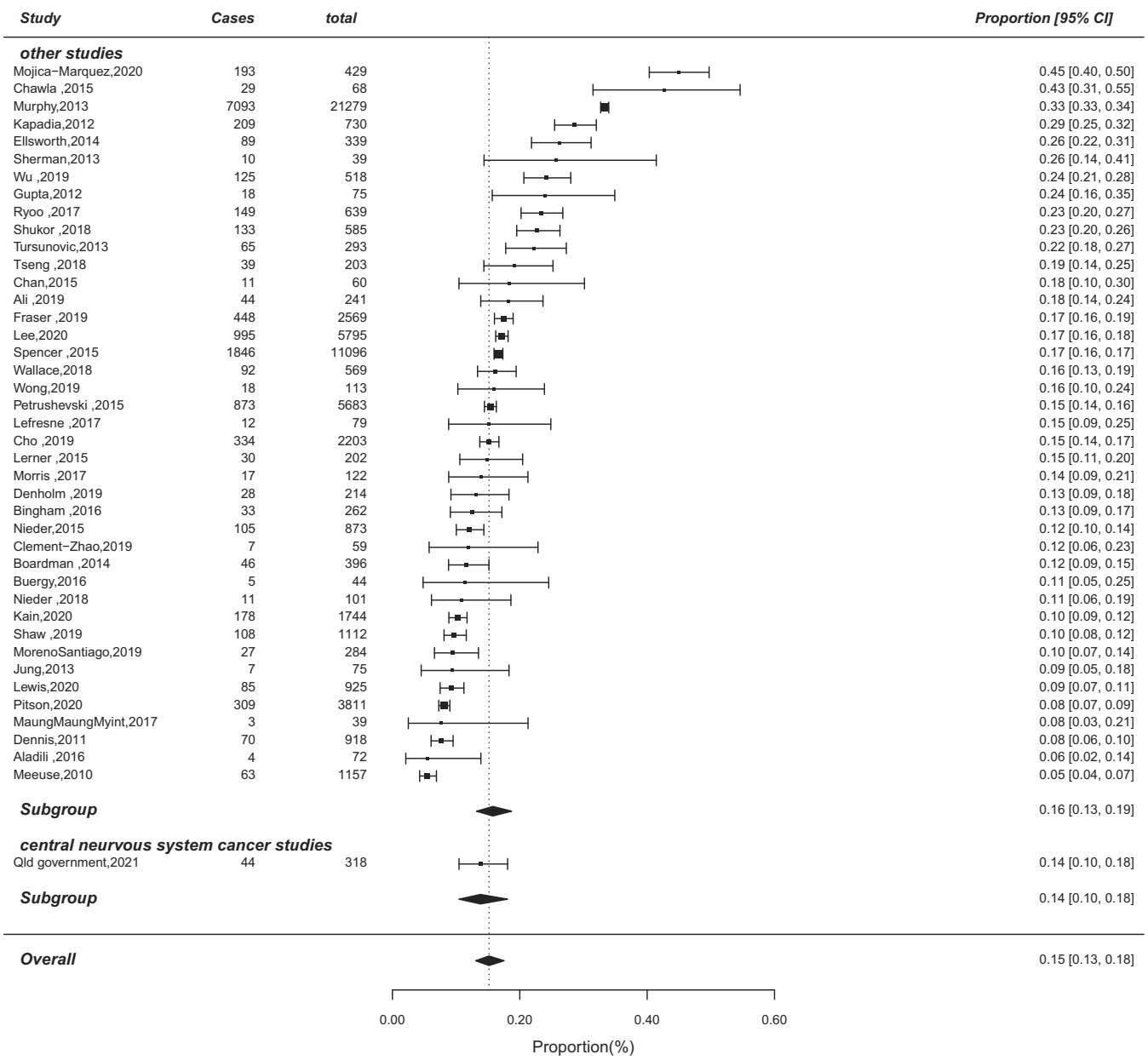

Fig. G17. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in central nervous system cancer studies vs. other studies. The central nervous system cancer subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.70, $p = 0.404$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

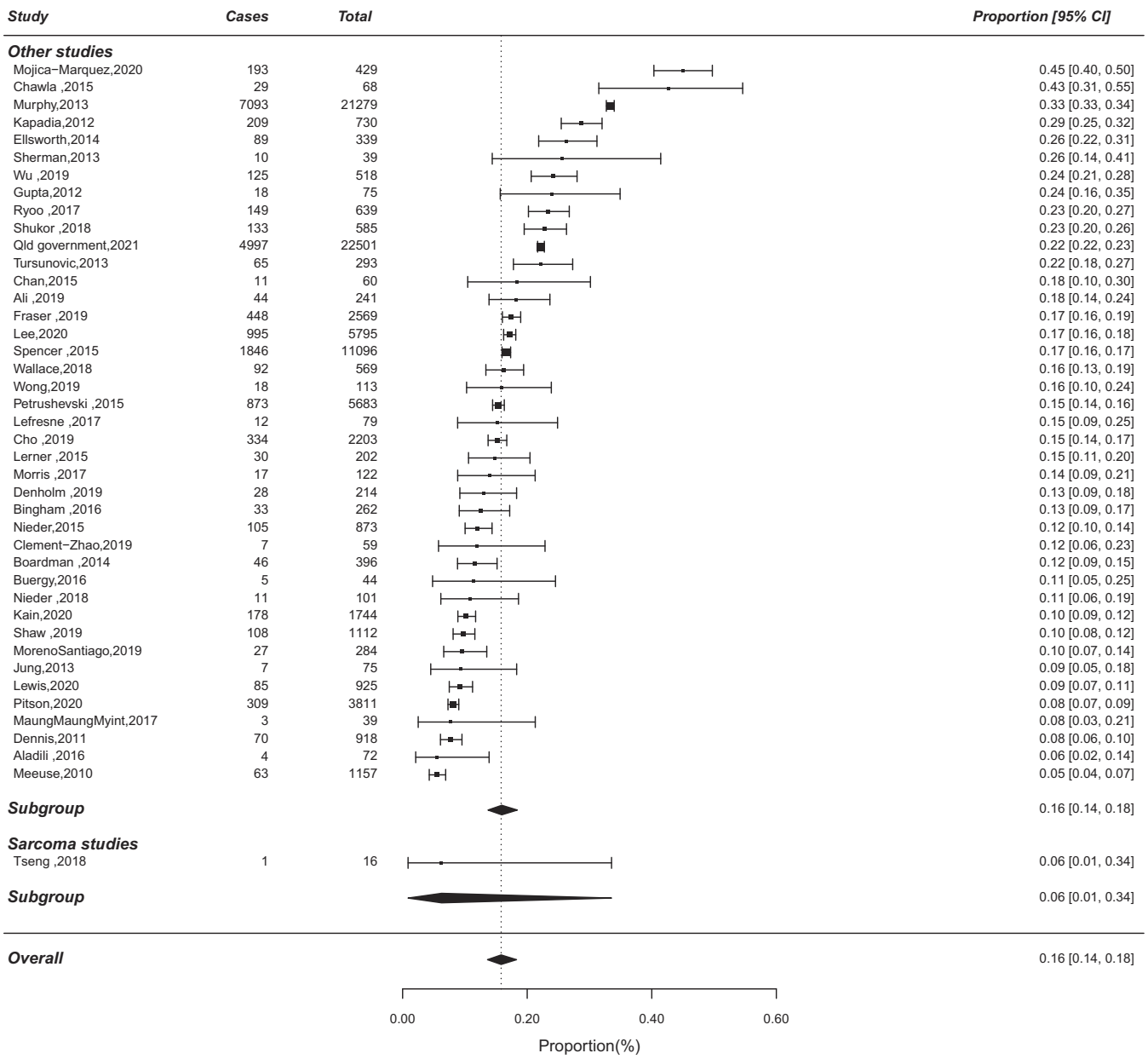

Fig. G18. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in sarcoma studies vs. other studies. The sarcoma subgroup did not significantly modify the overall summary effect proportion (QM(1) = 1.01, $p = 0.315$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

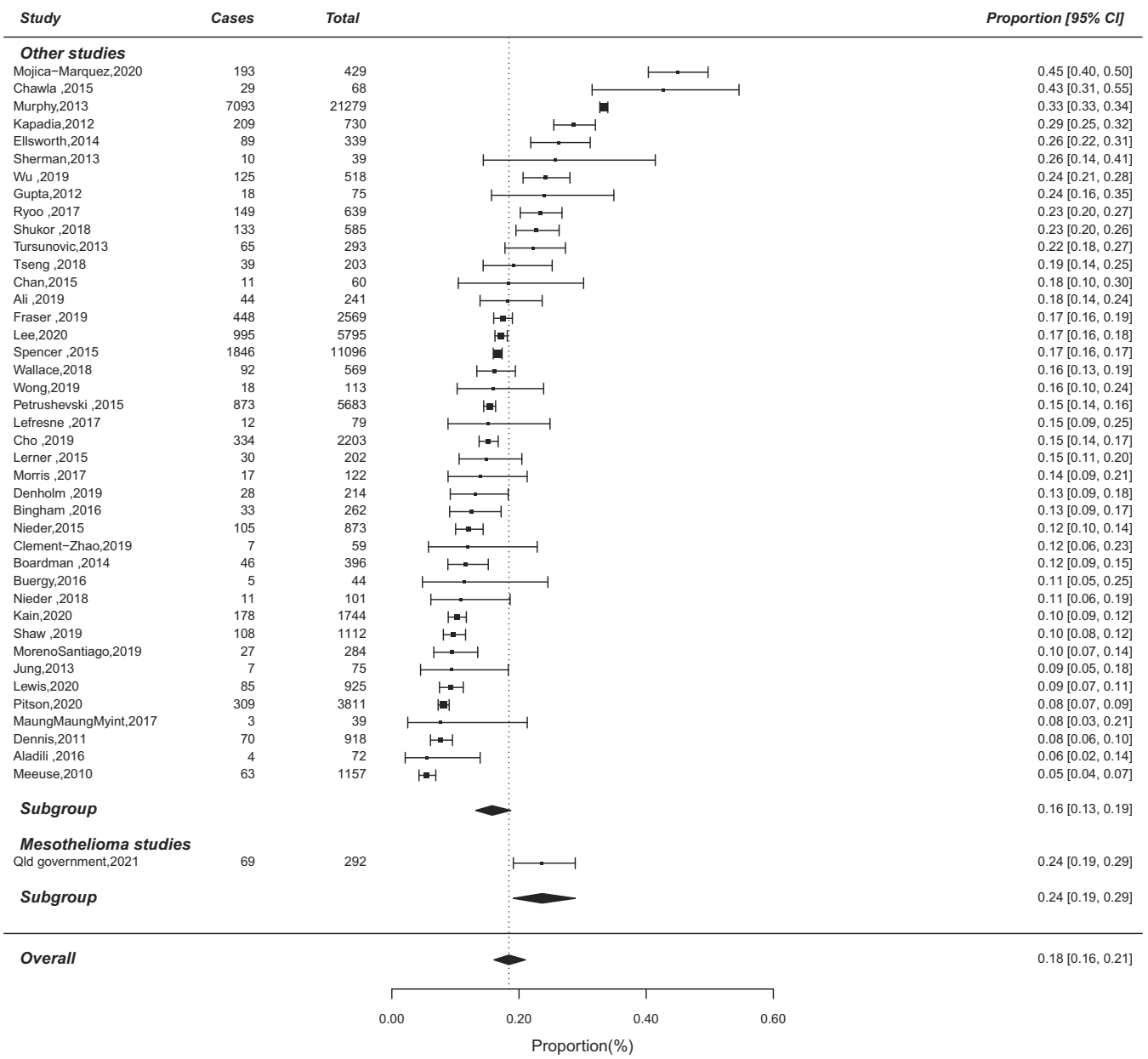

Fig. G19. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in mesothelioma studies vs. other studies. The mesothelioma subgroup did significantly raise the overall summary effect proportion (QM(1) = 8.89, p = 0.003). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

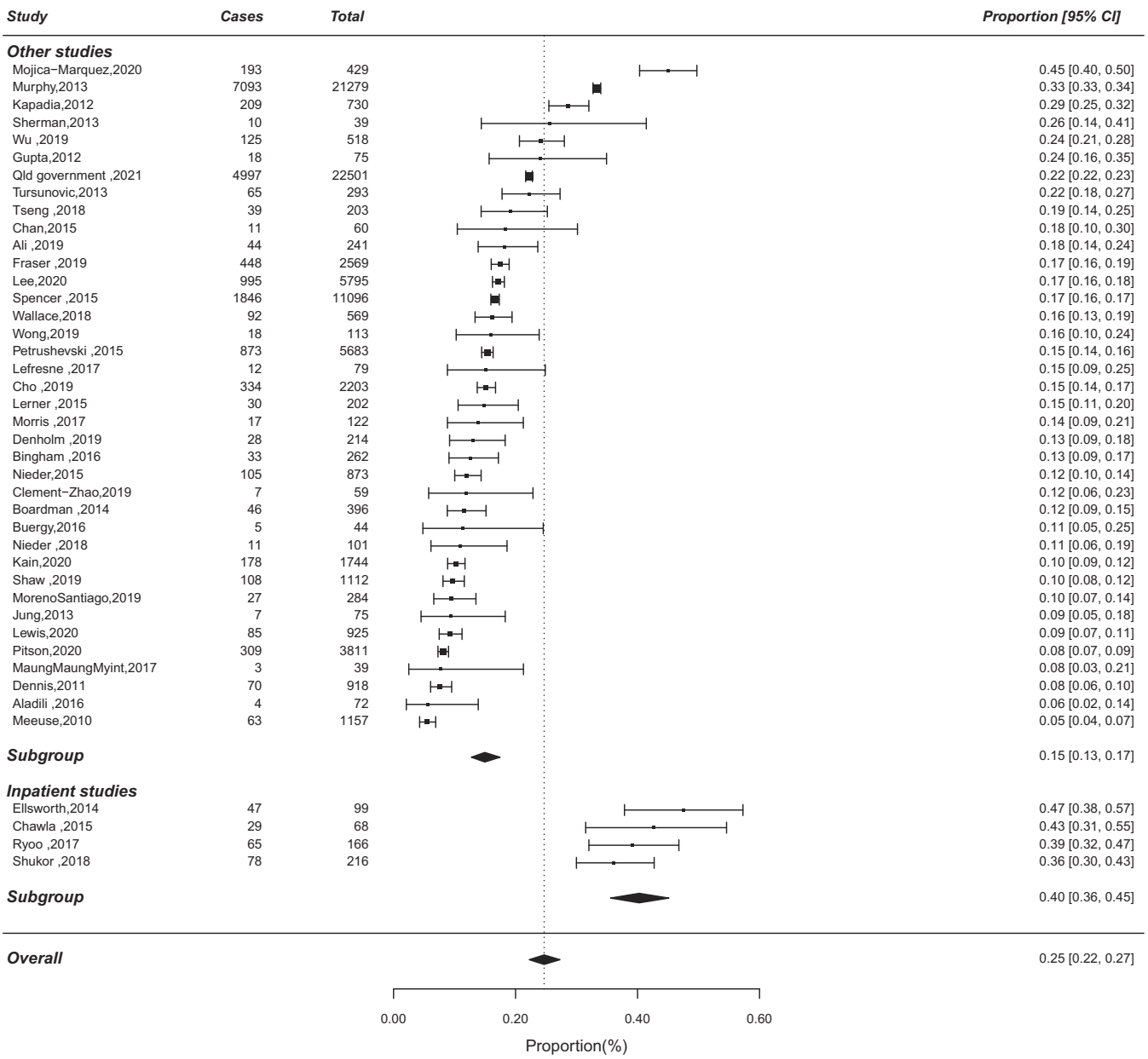

Fig. G20. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of inpatients vs. other studies. The inpatient studies subgroup did significantly raise the overall summary effect proportion (QM(1) = 92.27, $p < 0.001$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

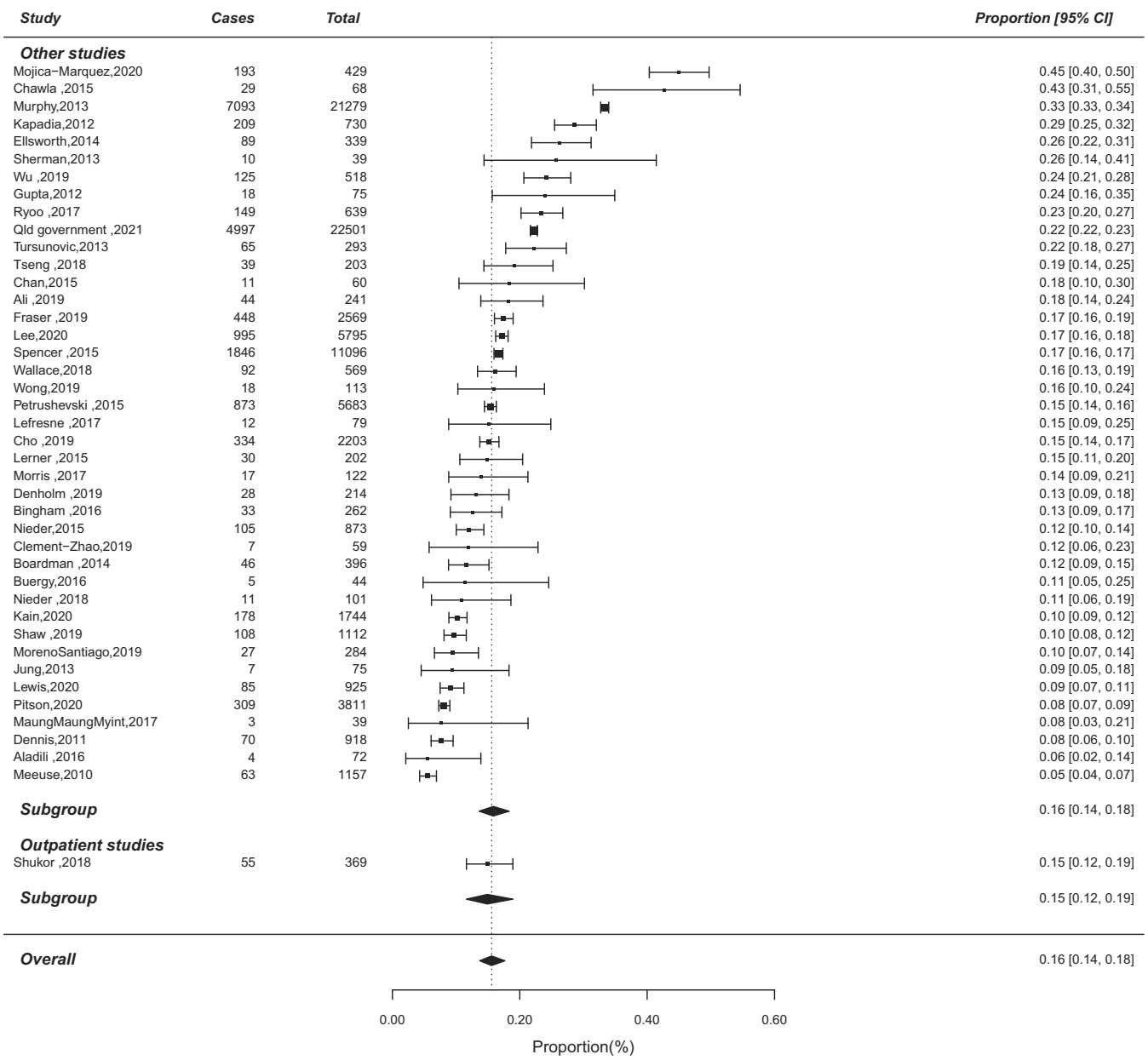

Fig. G21. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of outpatients vs. other studies. The outpatient subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.16, p = 0.690). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

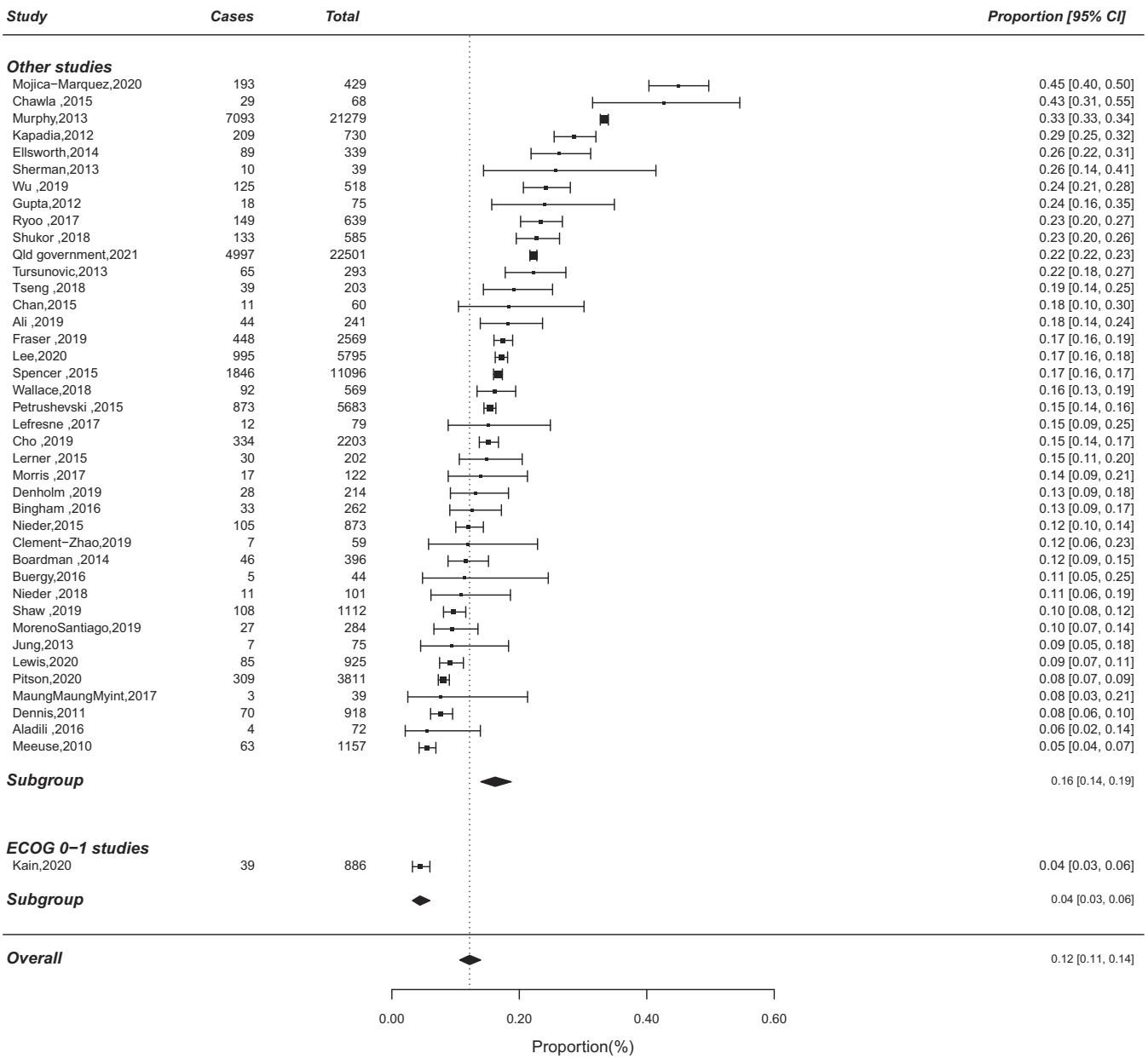

Fig. G22. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients with Eastern Cooperative Oncology Group performance score 0–1 vs. other studies. The Eastern Cooperative Oncology Group performance score 0–1 subgroup did significantly lower the overall summary effect proportion (QM (1) = 56.68, $p < 0.001$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia, ECOG = Eastern Cooperative Oncology Group performance score.

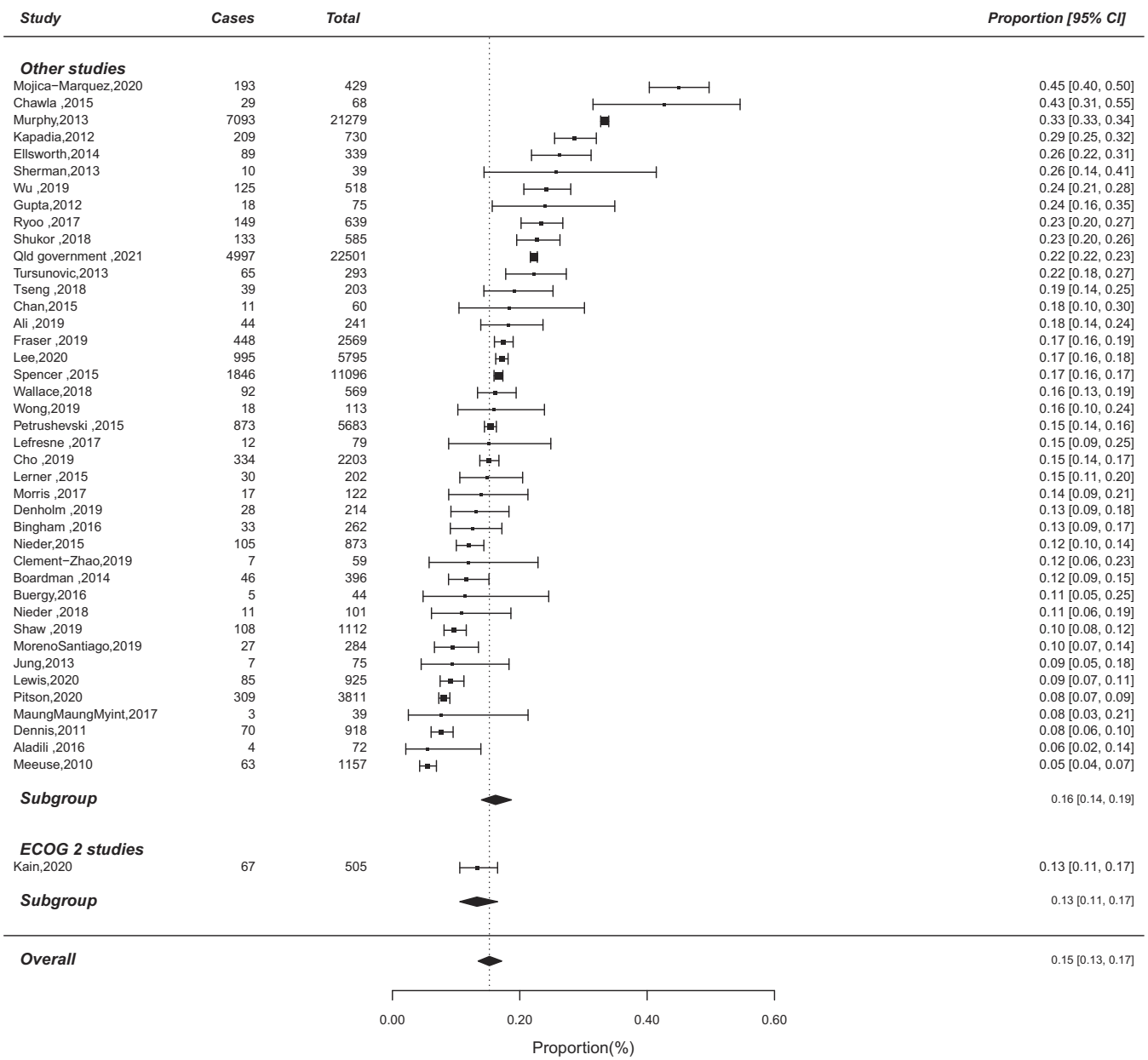

Fig. G23. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients with Eastern Cooperative Oncology Group performance score 2 vs. other studies. The Eastern Cooperative Oncology Group performance score 2 subgroup did not significantly modify the overall summary effect proportion (QM (1) = 2.05, $p = 0.153$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia, ECOG = Eastern Cooperative Oncology Group performance score.

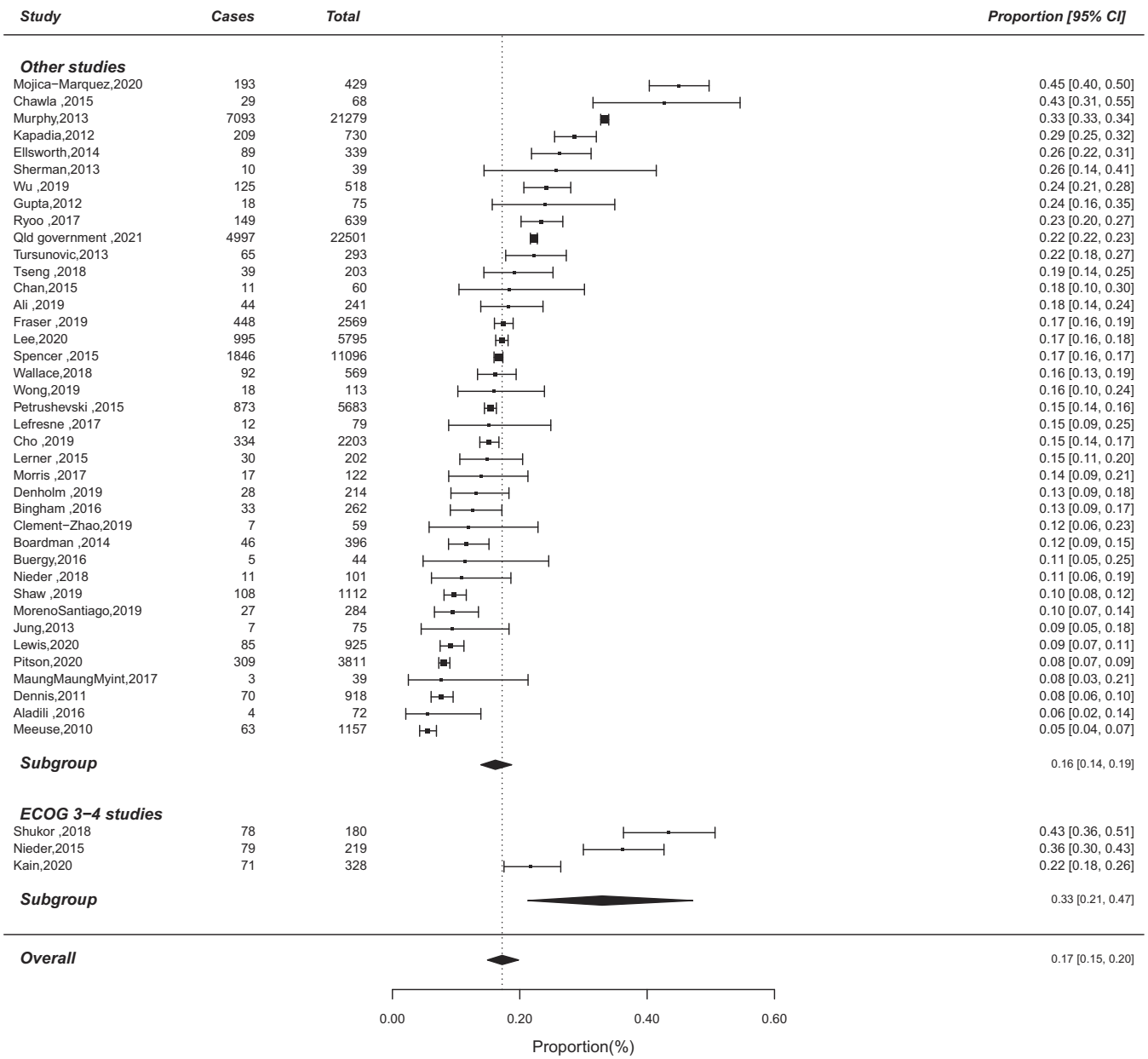

Fig. G24. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients with Eastern Cooperative Oncology Group performance score 3–4 vs. other studies. The Eastern Cooperative Oncology Group performance score 3–4 subgroup did significantly raise the overall summary effect proportion (QM (1) = 8.70, p = 0.003). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia, ECOG = Eastern Cooperative Oncology Group performance score.

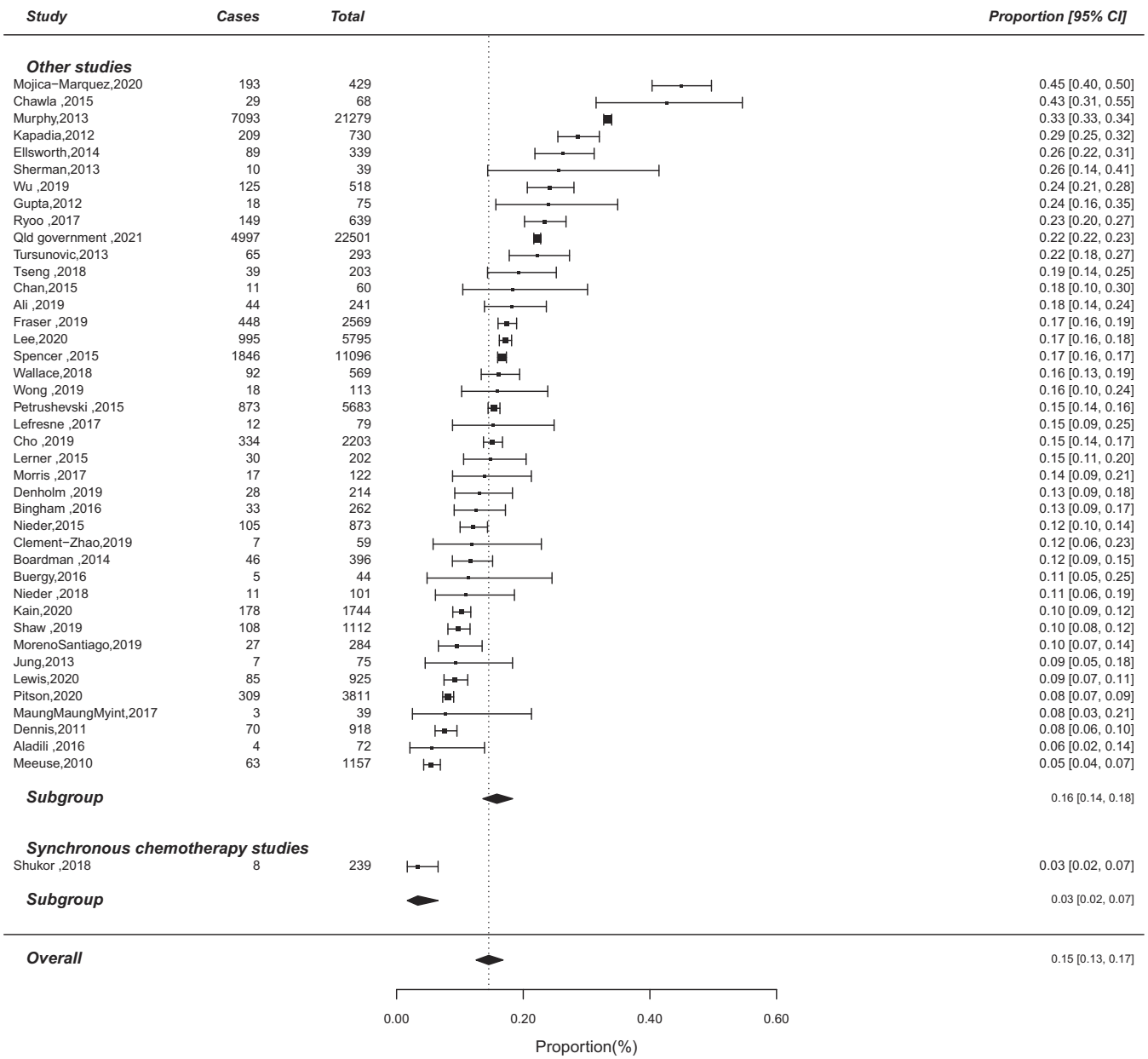

Fig. G25. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients getting synchronous chemotherapy vs. other studies. The synchronous chemotherapy subgroup did significantly lower the overall summary effect proportion (QM(1) = 20.66, $p < 0.001$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

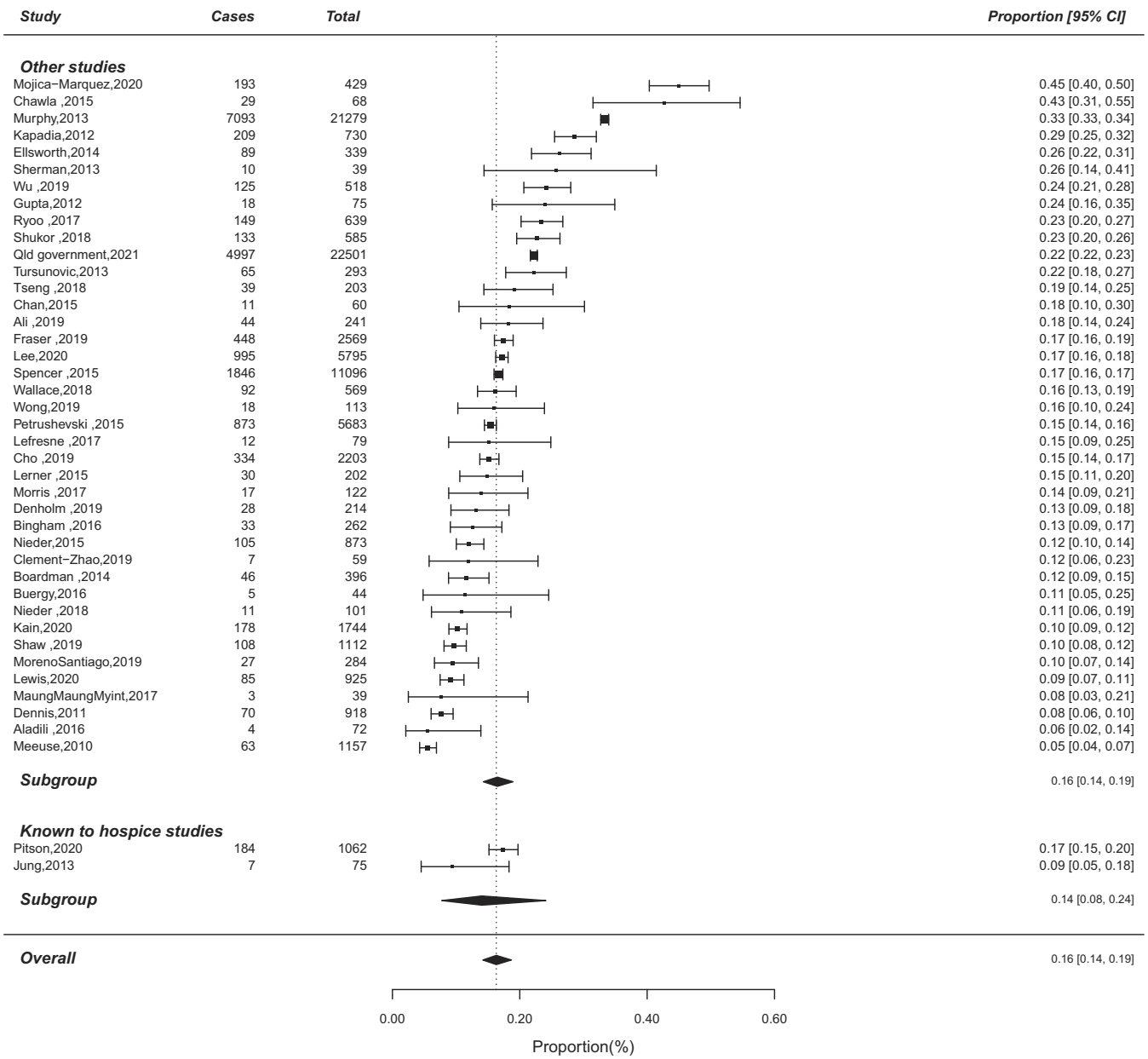

Fig. G26. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients known to hospice vs. other studies. The known to hospice subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.28, $p = 0.559$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

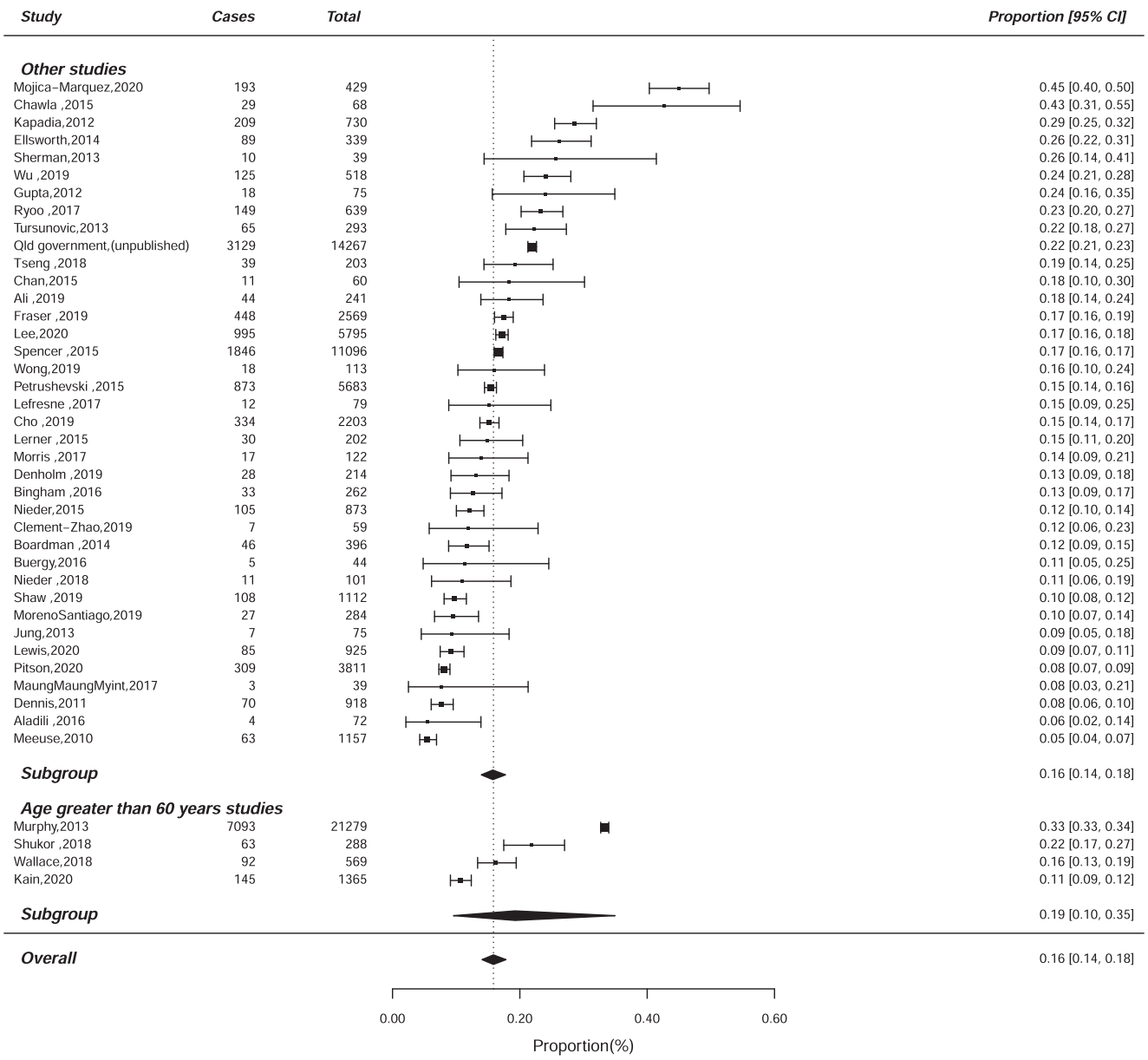

Fig. G27. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients greater than 60 years of age vs. other studies. The greater than 60 years of age subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.63, p = 0.429). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

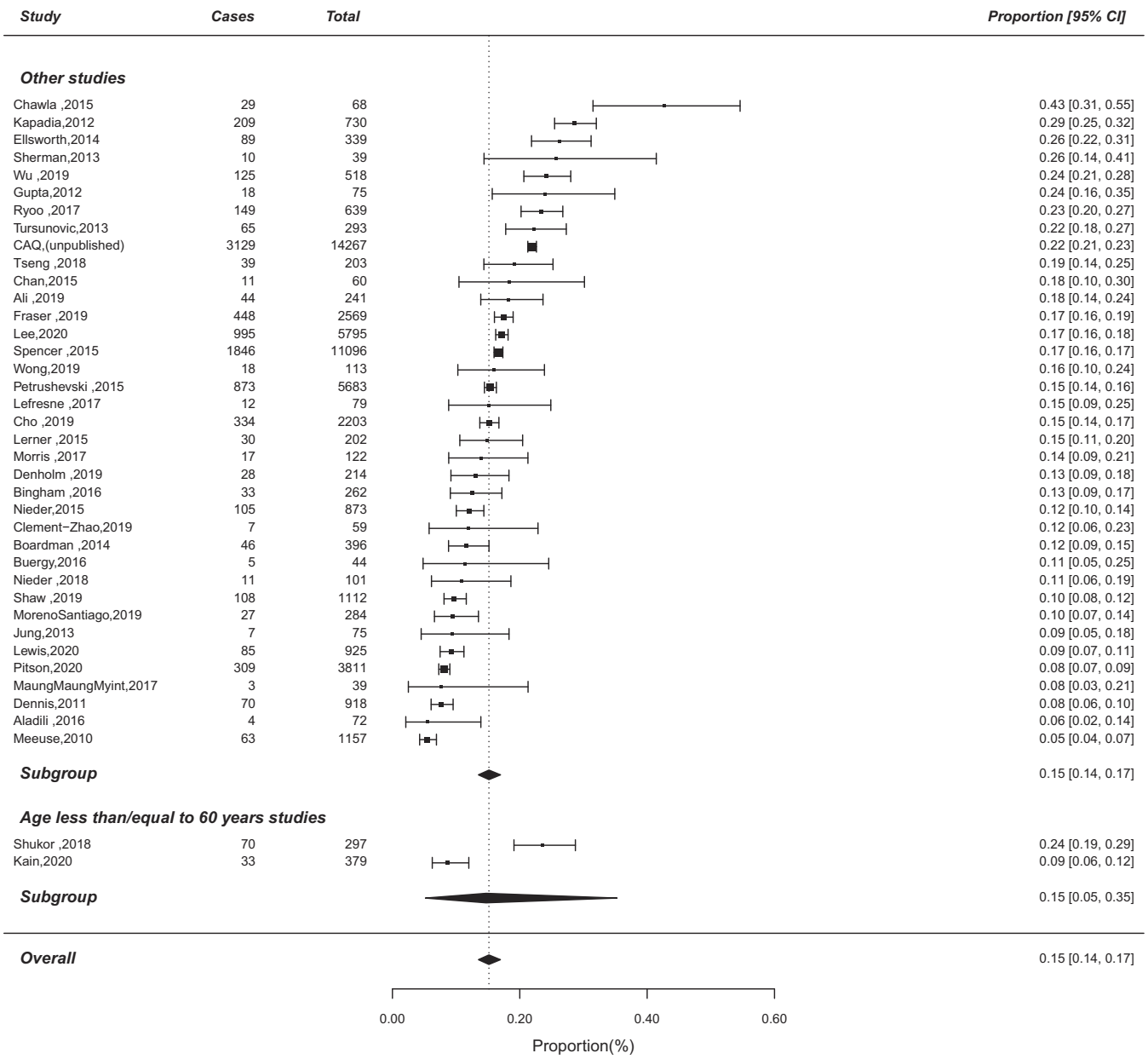

Fig. G28. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients </= 60 years of age vs. other studies. The </= 60 years of age subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.00, p = 0.96). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

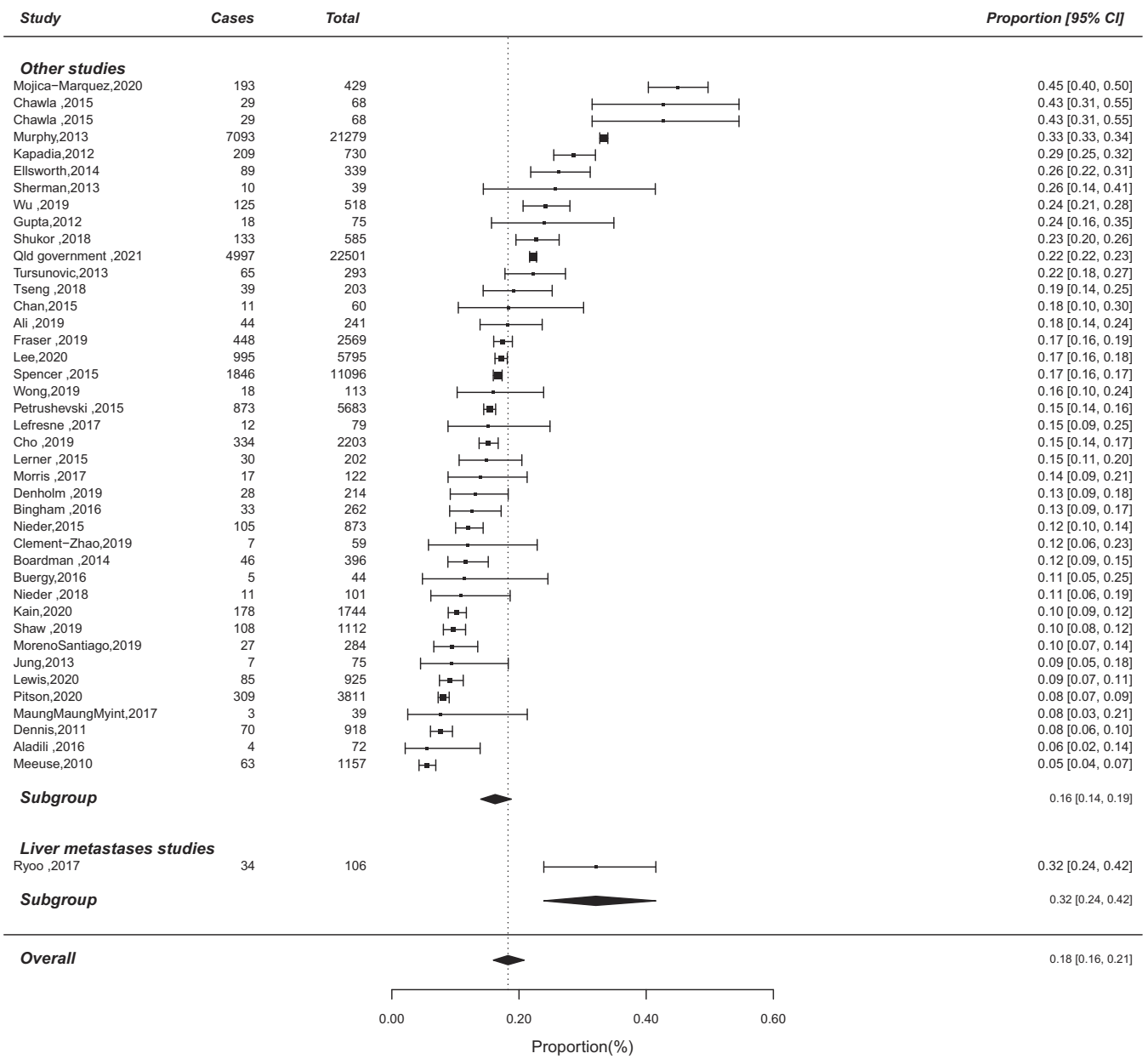

Fig. G29. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients with liver metastases vs. other studies. The liver metastases subgroup did significantly raise the overall summary effect proportion (QM(1) = 14.96, $p < 0.001$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

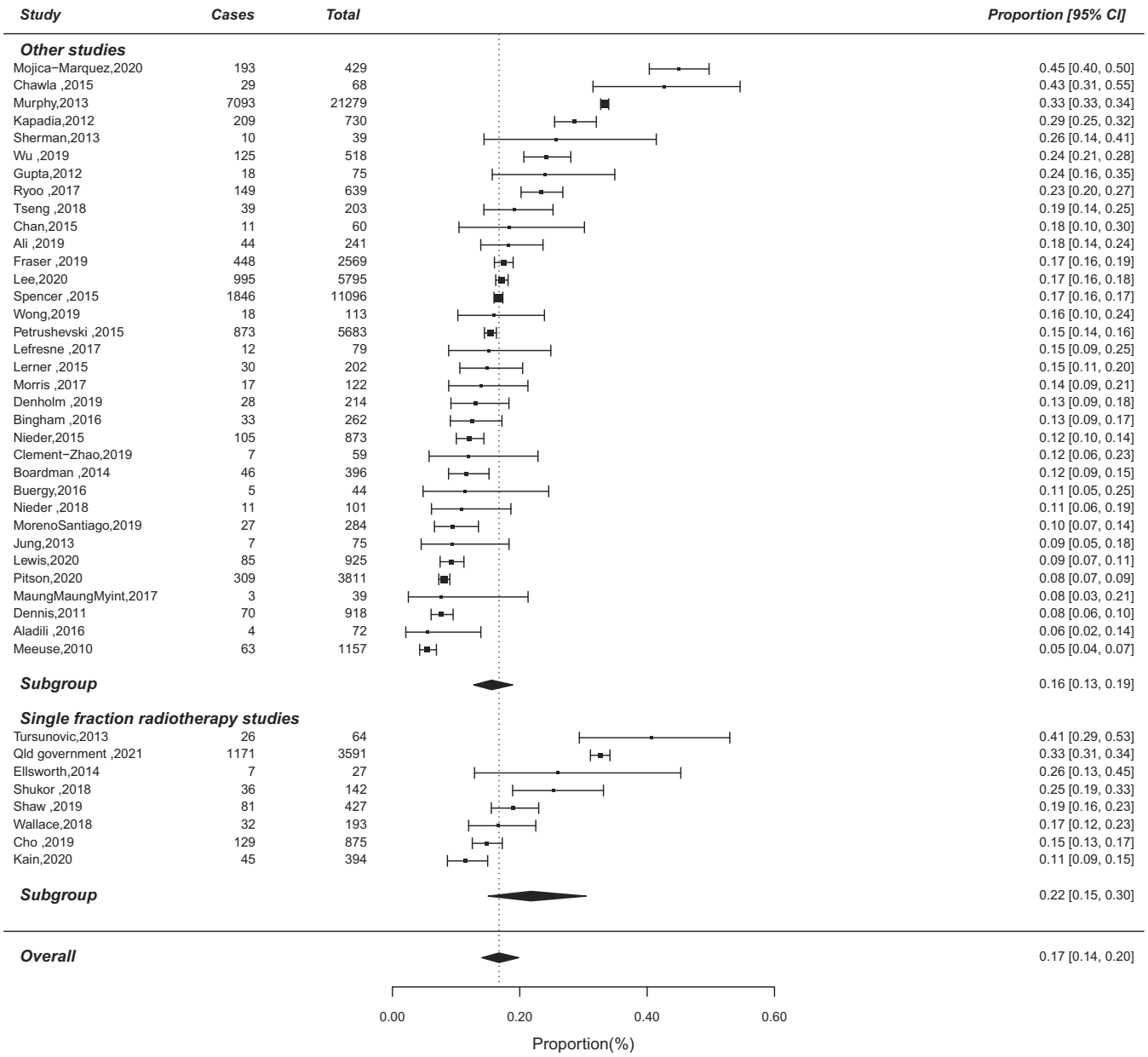

Fig. G30. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients getting single fraction treatments vs. other studies. The single fraction subgroup did not significantly modify the overall summary effect proportion (QM(1) = 3.11, $p = 0.078$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

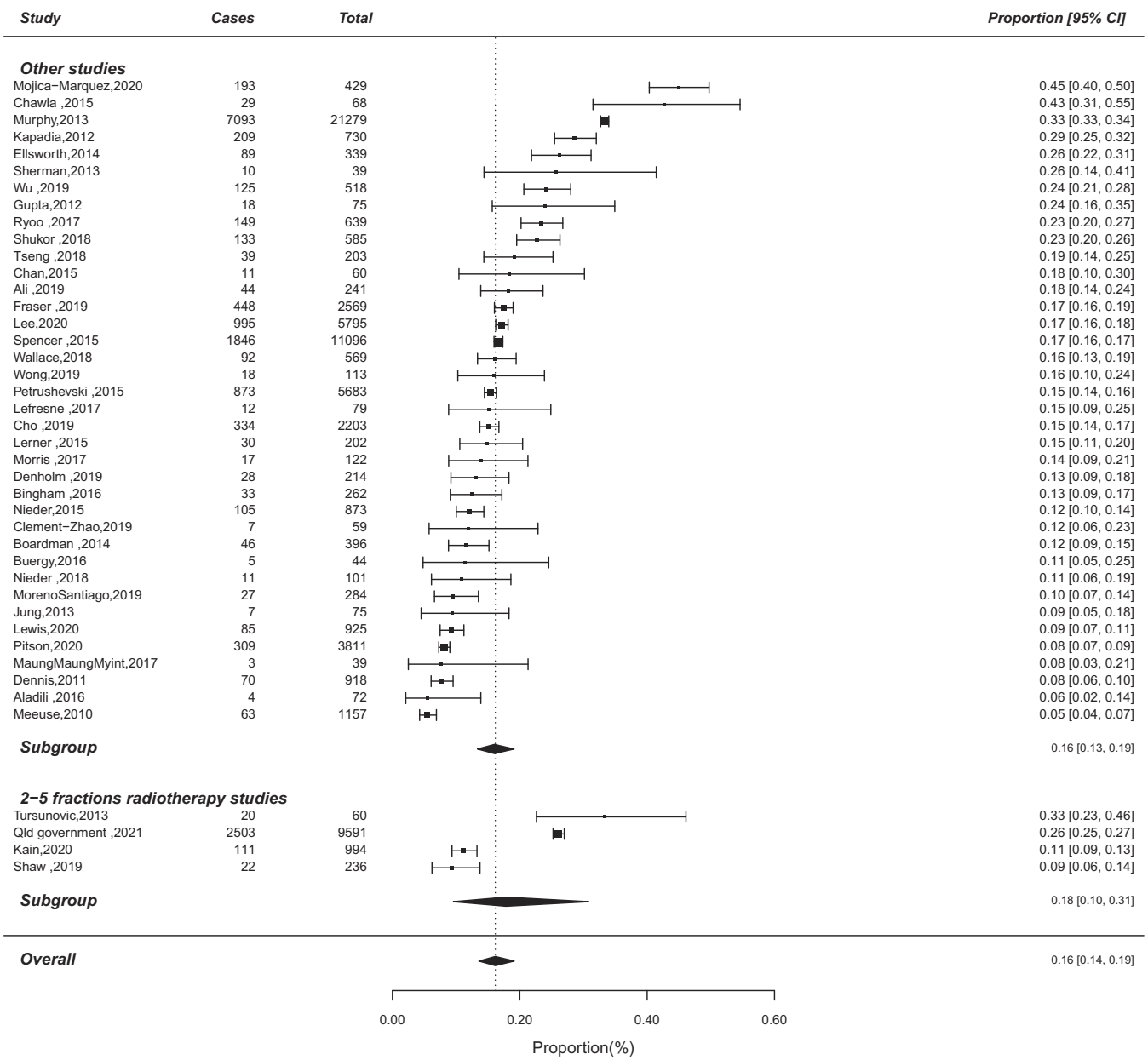

Fig. G31. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients getting a 2–5 fraction treatments vs. other studies. The 2–5 fraction treatment subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.10, p = 0.749). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

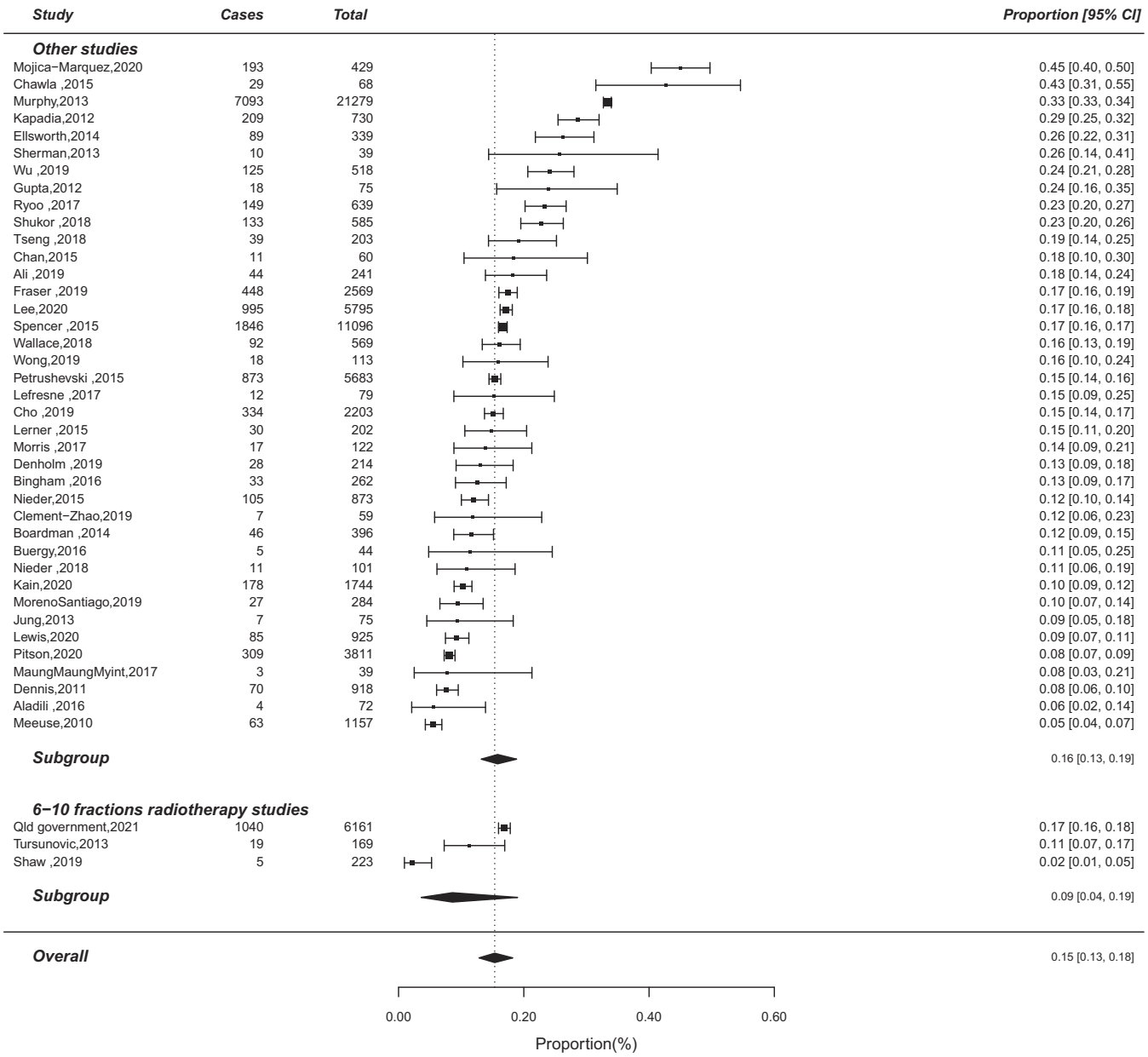

Fig. G32. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients getting 6–10 fraction treatments vs. other studies. The 6–10 fraction treatment subgroup did not significantly modify the overall summary effect proportion (QM(1) = 1.34, p = 0.246). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

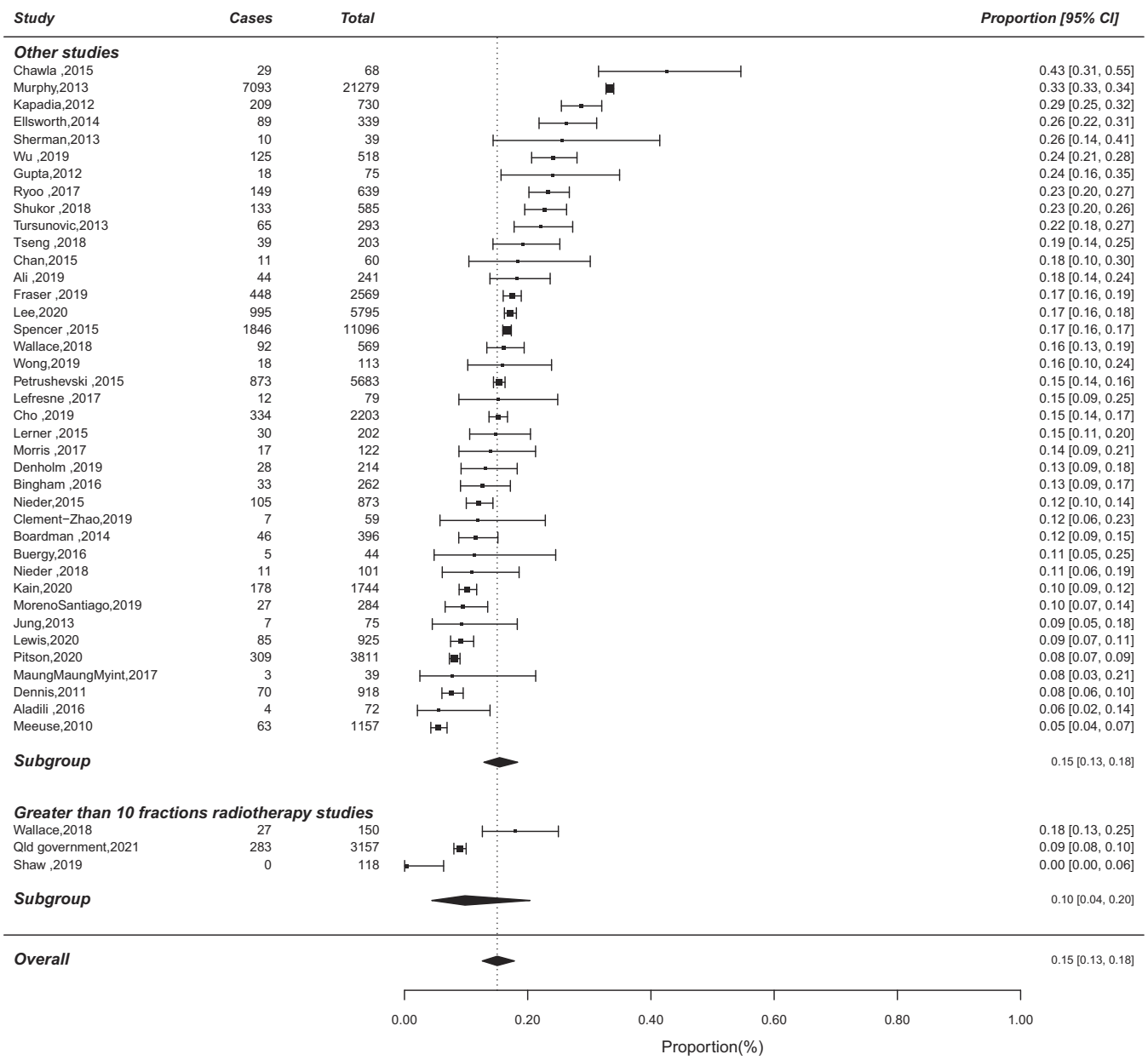

Fig. G33. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients getting more than 10 fraction treatments vs. other studies. The > 10 fraction treatment subgroup did not significantly modify the overall summary effect proportion (QM(1) = 1.06, $p = 0.304$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

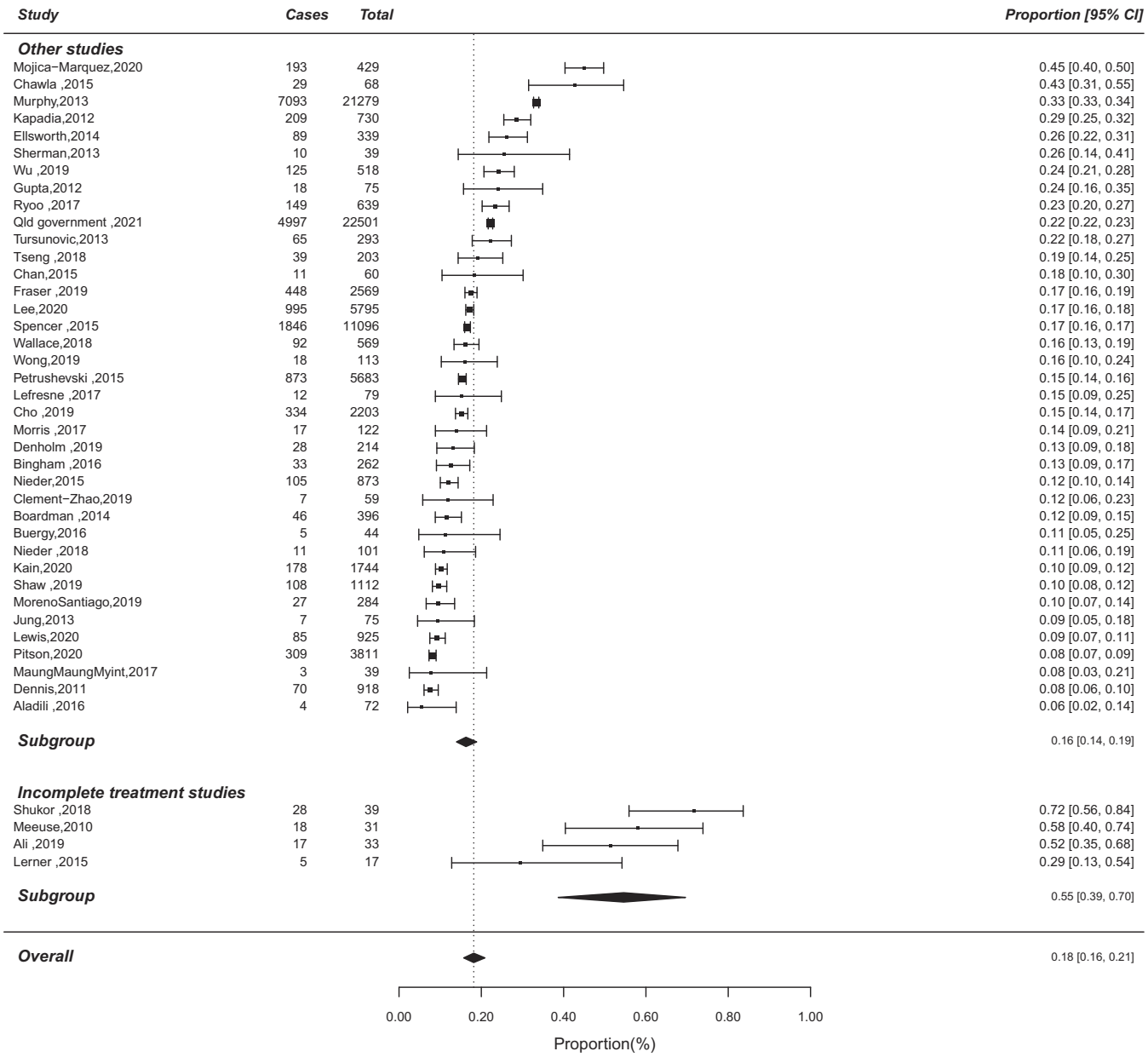

Fig. G34. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients not completing treatment vs. other studies. The incomplete treatment subgroup did significantly raise the overall summary effect proportion (QM(1) = 26.51, $p < 0.001$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

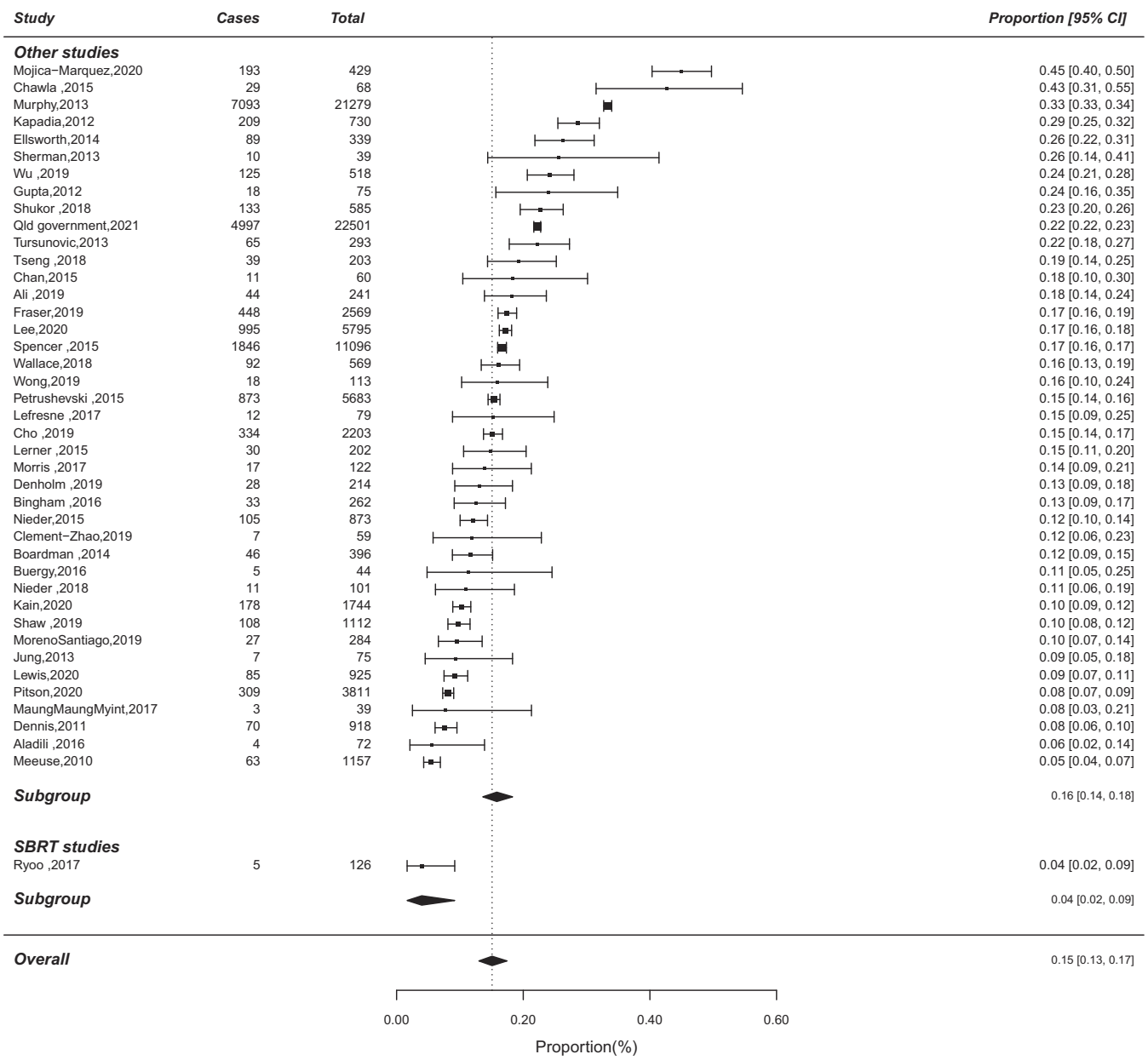

Fig. G35. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients getting stereotactic body radiotherapy for brain metastases vs. other studies. The stereotactic body radiotherapy for brain metastases treatment subgroup did significantly lower the overall summary effect proportion (QM (1) = 10.54, $p = 0.001$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia, SBRT = stereotactic body radiotherapy.

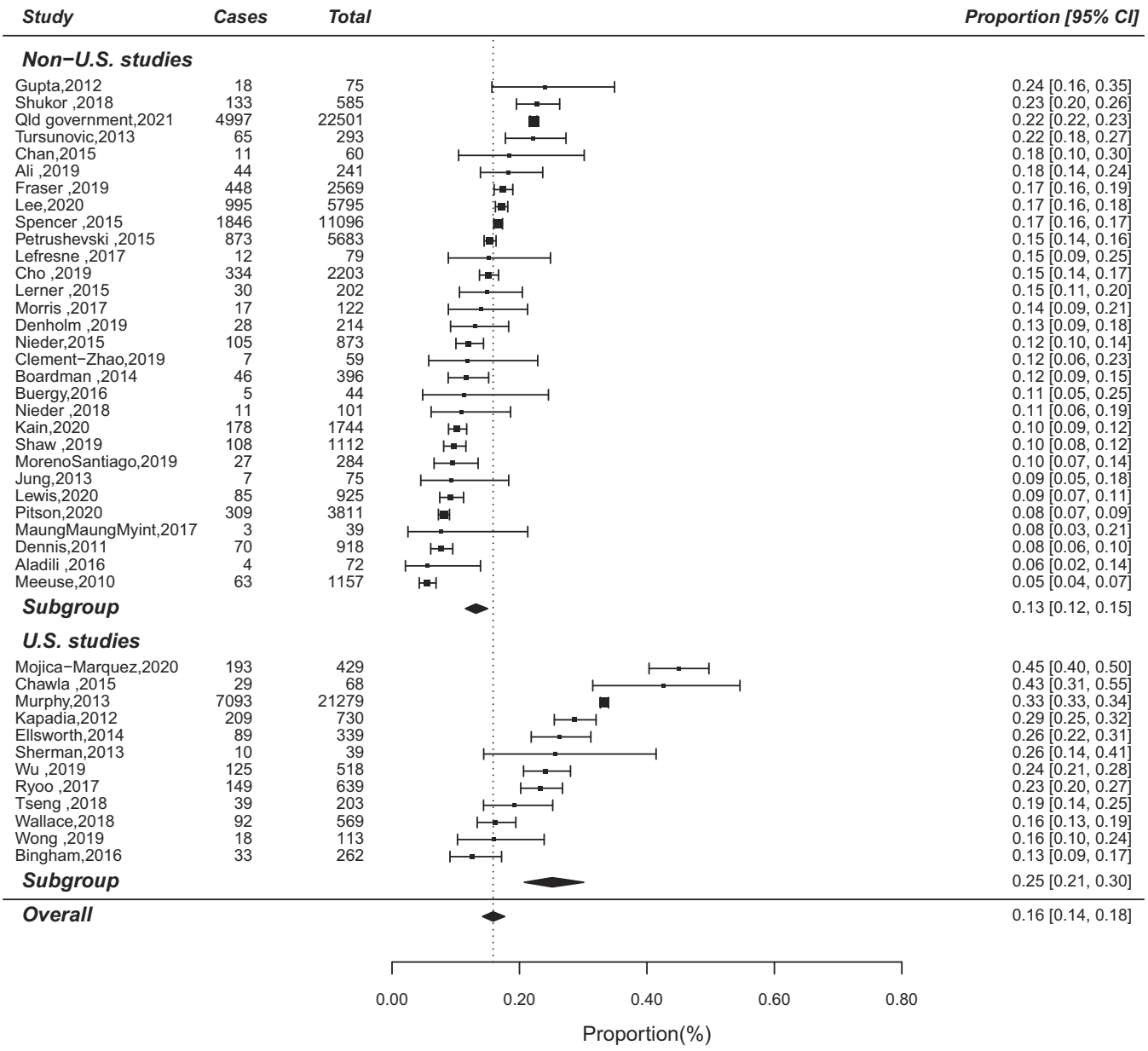

Fig. G36. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies of patients in the United States of America vs. other studies. The United States subgroup did significantly raise the overall summary effect proportion (QM(1) = 28.70, $p < 0.001$). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia, U.S. = United States of America.

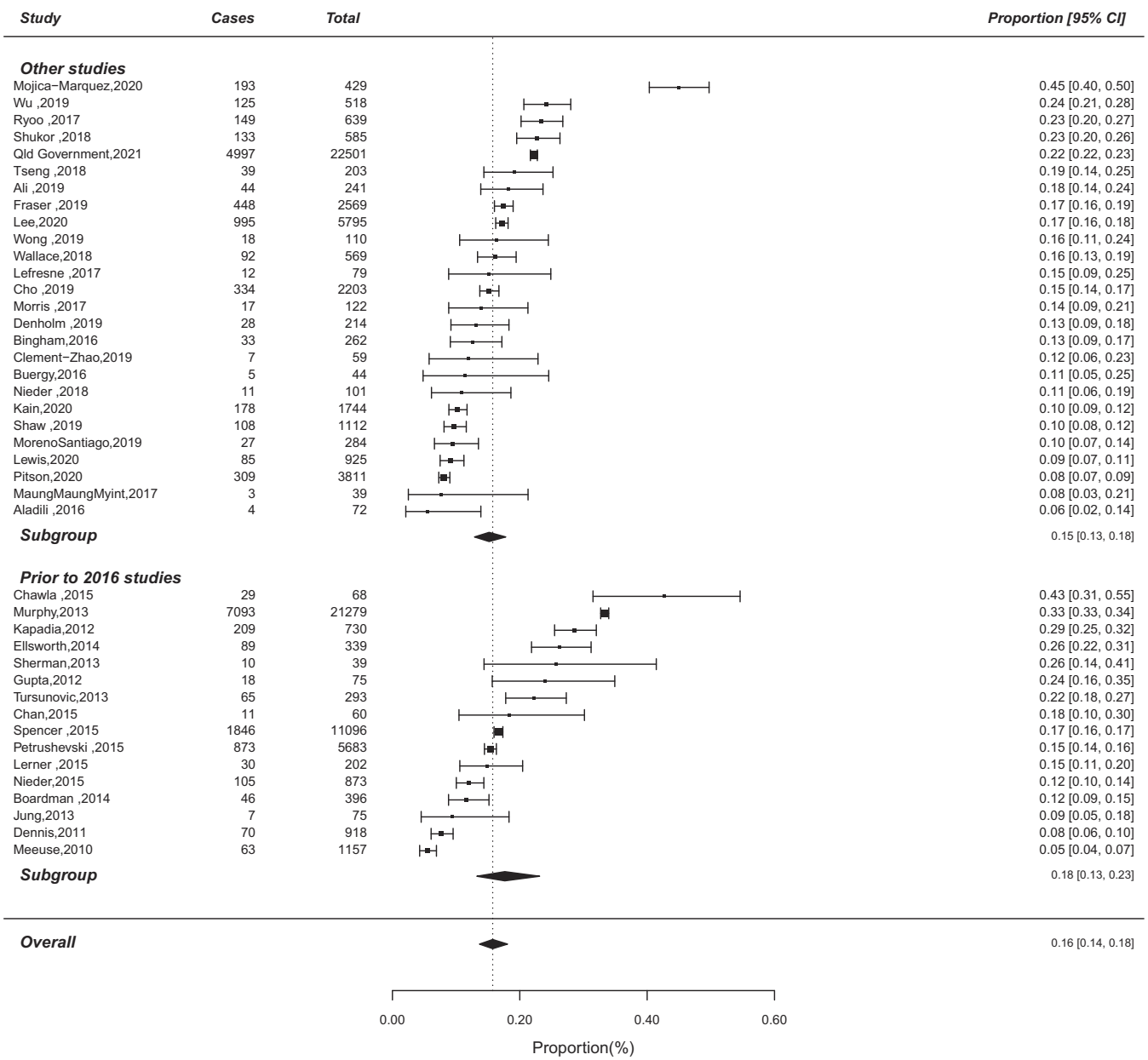

Fig. G37. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies prior to year 2016 vs. other studies. The prior to year 2016 subgroup did not significantly modify the overall summary effect proportion (QM(1) = 0.85, p = 0.358). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

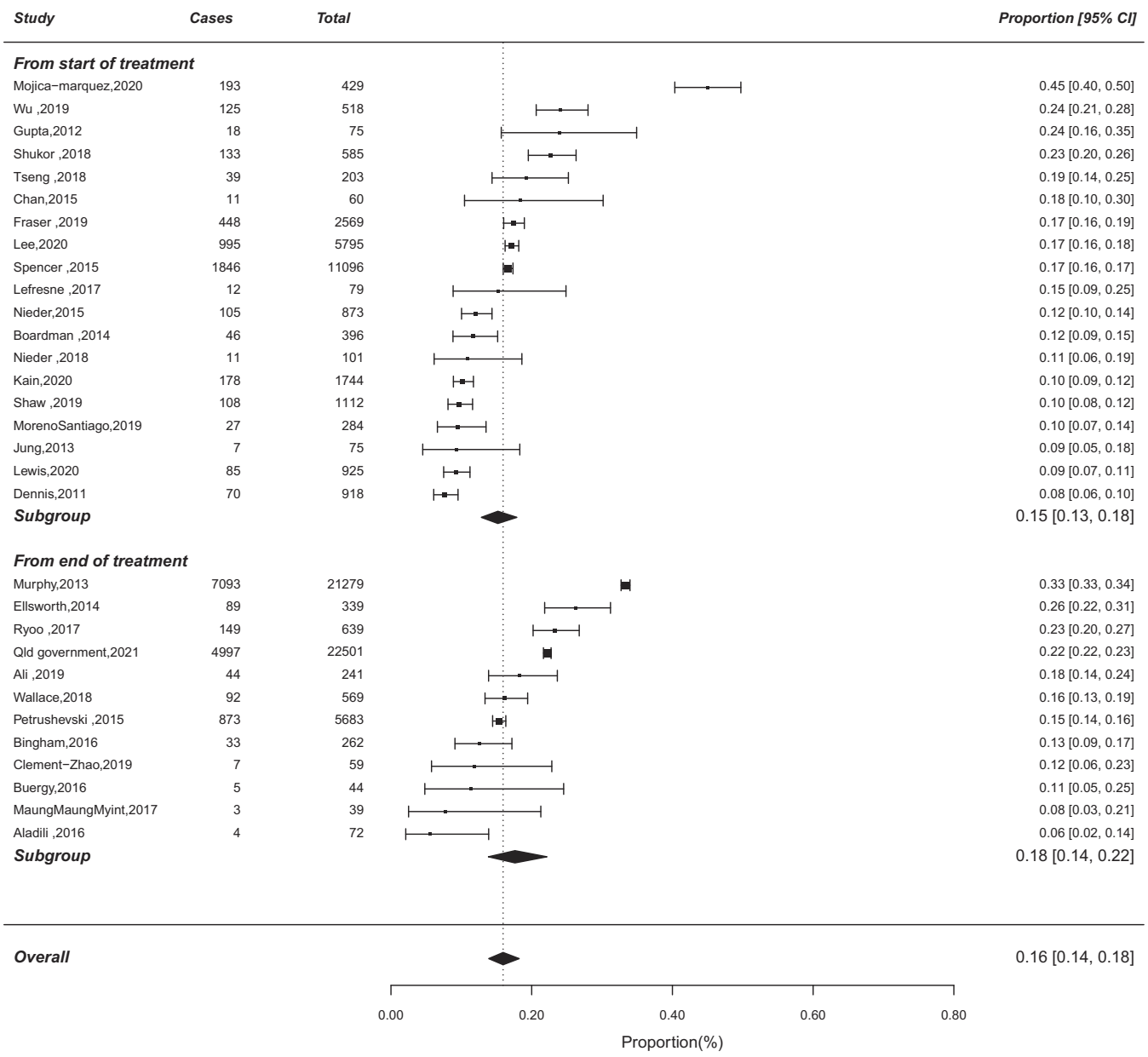

Fig. G38. Forest plot of subgroup analysis: 30-day mortality rate after palliative radiotherapy in studies measuring 30 days from end of patients' treatment vs. studies measuring from the beginning of their treatment. The measuring from end of treatment subgroup did not significantly modify the overall summary effect proportion (QM (1) = 0.73, p = 0.392). Cases indicate the number of patients that died within 30-days of their palliative radiotherapy, Total indicates the number of patients getting palliative radiotherapy, and proportion indicates the proportion of patients dying within 30-days of palliative radiotherapy (cases/total). Abbreviations CI = confidence intervals (horizontal lines), ■ = 30-day mortality rate of study), ◆ = subgroup effect; overall summary effect proportion (dotted vertical line), Qld = Queensland, Australia.

Appendix H

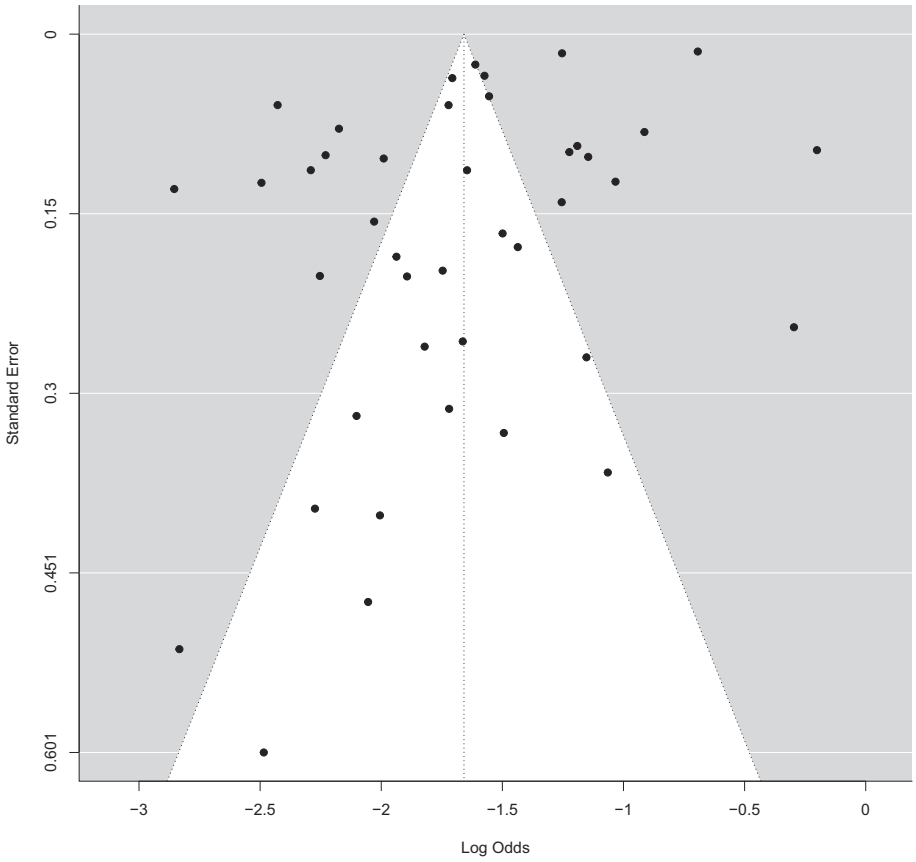

Fig. H1. Funnel plot displaying study standard error as a measure of precision. Heterogeneity is illustrated, but asymmetry and therefore small study bias is unclear.

References

[1] World Health Organization RG. Cancer. Published 2018. Accessed January 26, 202https://www.who.int/news-room/fact-sheets/detail/cancer.

[2] Queensland Government. End of Life Cancer Care 30 Day Mortality Rates for Queenslanders Receiving Palliative Radiation Therapy Indicators of Safe, Quality Cancer Care Delivered by Public and Private Services.; 2021. https://cancerallianceqld.health.qld.gov.au.

[3] Lutz S, Berk L, Chang E, Chow E, Hahn C, Hoskin P, et al. Palliative radiotherapy for bone metastases: an ASTRO evidence-based guideline. Int J Radiat Oncol Biol Phys 2011;79:965–76. https://doi.org/10.1016/j.ijrobp.2010.11.026.

[4] Loblaw DA, Mitera G, Ford M, Laperriere NJ. A 2011 updated systematic review and clinical practice guideline for the management of malignant extradural spinal cord compression. Int J Radiat Oncol Biol Phys 2012;84:312–7. https://doi.org/10.1016/j.ijrobp.2012.01.014.

[5] Linskey ME, Andrews DW, Asher AL, Burri SH, Kondziolka D, Robinson PD, et al. The role of stereotactic radiosurgery in the management of patients with newly diagnosed brain metastases: a systematic review and evidence-based clinical practice guideline. J Neurooncol 2010;96:45–68. https://doi.org/10.1007/s11060-009-0073-4.

[6] Van Lonkhuijzen L, Thomas G. Palliative radiotherapy for cervical carcinoma, a systematic review. Radiother Oncol 2011;98:287–91. https://doi.org/10.1016/j.radonc.2011.01.009.

[7] Cameron MG, Kersten C, Vistad I, van Helvoirt R, Weyde K, Undseth C, et al. Palliative pelvic radiotherapy for symptomatic rectal cancer–a prospective multicenter study. Acta Oncol (Madr) 2016;55:1400–7. https://doi.org/10.1080/0284186X.2016.1191666.

[8] Chow E, Zeng L, Salvo N, Dennis K, Tsao M, Lutz S. Update on the systematic review of palliative radiotherapy trials for bone metastases. Clin Oncol 2012;24:112–24. https://doi.org/10.1016/j.clon.2011.11.004.

[9] Tseng YD, Krishnan MS, Sullivan AJ, Jones JA, Chow E, Balboni TA. How radiation oncologists evaluate and incorporate life expectancy estimates into the treatment of palliative cancer patients: a survey-based study. Int J Radiat Oncol Biol Phys 2013;87:471–8. https://doi.org/10.1016/j.ijrobp.2013.06.2046.

[10] Chow E, Davis L, Panzarella T, Hayter C, Szumacher E, Loblaw A, et al. Accuracy of survival prediction by palliative radiation oncologists. Int J Radiat Oncol Biol Phys 2005;61:870–3. https://doi.org/10.1016/j.ijrobp.2004.07.697.

[11] ASTRO. "'Choosing wisely'" campaign. Accessed January 17, 2021. https://www.astro.org/uploadedFiles/Main_Site/News_and_Media/News_Releases/2013/ASTRO ChoosingWisely List_FINAL_092313.pdf.

[12] Gripp S, Mjartan S, Boelke E, Willers R. Palliative radiotherapy tailored to life expectancy in end-stage cancer patients. Cancer 2010;116:3251–6. https://doi.org/10.1002/cncr.25112.

[13] Park KR, Lee CG, Tseng YD, Liao JJ, Reddy S, Bruera E, et al. Palliative radiation therapy in the last 30 days of life: a systematic review. Radiother Oncol 2017;125:193–9. https://doi.org/10.1016/j.radonc.2017.09.016.

[14] Department of Health. *Improving Outcomes: A Strategy for Cancer.*; 2011. Accessed January 17, 2021. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/213785/dh_123394.pdf.

[15] Earle CC, Park ER, Lai B, Weeks JC, Ayanian JZ, Block S. Identifying potential indicators of the quality of end-of-life cancer care from administrative data. J Clin Oncol 2003;21:1133–8. https://doi.org/10.1200/JCO.2003.03.059.

[16] Earle CC, Landrum MB, Souza JM, Neville BA, Weeks JC, Ayanian JZ. Aggressiveness of cancer care near the end of life: Is it a quality-of-care issue? J Clin Oncol 2008;26:3860–6. https://doi.org/10.1200/JCO.2007.15.8253.

[17] Barbera L, Seow H, Sutradhar R, Chu A, Burge F, Fassbender K, et al. Quality indicators of end-of-life care in patients with cancer: What rate is right? J Oncol Pract 2015;11:e279–87. https://doi.org/10.1200/JOP.2015.004416.

[18] Wallington M, Saxon EB, Bomb M, Smittenaar R, Wickenden M, McPhail S, et al. 30-day mortality after systemic anticancer treatment for breast and lung cancer in England: a population-based, observational study. Lancet Oncol 2016;17:1203–16. https://doi.org/10.1016/S1470-2045(16)30383-7.

[19] Lees K. Audit of 30 day mortality following palliative radiotherapy. | The Royal College of Radiologists. Vols. 1-3. Accessed January 17, 2021. https://www.rcr.ac.uk/audit/audit-30-day-mortality-following-palliative-radiotherapy.

[20] Kutzko JH. Protocol: Defining the expected 30 day mortality for patients undergoing palliative radiotherapy: a systematic review. National Institute for Health Research: PROSPERO International prospective register of systematic reviews. Published 20Accessed January 26, 2021. https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=181567.

[21] Innovation VH. Covidence systematic review software. www.covidence.org.

[22] Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Rev Esp Cardiol (Engl Ed) 2021;74:790–9. https://doi.org/10.1016/J.REC.2021.07.010.

[23] J.AC. Sterne M.A. Hernán B.C. Reeves J. Savović N.D. Berkman M. Viswanathan et al. ROBINS-I: A tool for assessing risk of bias in non-randomised studies of interventions i4919 10.1136/bmj.i4919.

[24] Viechtbauer W. Conducting meta-analyses in R with the metafor. J Stat Softw 2010;36:1–48. https://doi.org/10.18637/jss.v036.i03.

[25] Meeuse JJ, Van Der Linden YM, Van Tienhoven G, Gans ROB, Leer JWH, Reyners AKL. Efficacy of radiotherapy for painful bone metastases during the last 12 weeks of life: results from the dutch bone metastasis study. Cancer 2010;116:2716–25. https://doi.org/10.1002/cncr.25062.

[26] Shapiro SS, Wilk MB. An analysis of variance test for normality (complete samples). Biometrika 1965;52:591–611. https://doi.org/10.1093/biomet/52.3-4.591.

[27] Lipsey, M., Wilson, D. (2001). Practical meta-analysis - IDoStatistics. Accessed February 4, 2021. https://idostatistics.com/lipsey-wilson-2001-practical-meta-analysis-2001/.

[28] Barendregt JJ, Doi SA, Lee YY, Norman RE, Vos T. Meta-analysis of prevalence. J Epidemiol Community Health 2013;67:974–8. https://doi.org/10.1136/jech-2013-203104.

[29] Wang N. (PDF) How to conduct a meta-analysis of proportions in R: A comprehensive tutoriall. doi:10.13140/RG.2.2.27199.00161

[30] DerSimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986;7:177–88. https://doi.org/10.1016/0197-2456(86)90046-2.

[31] Higgins JPT, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med 2002;21:1539–58. https://doi.org/10.1002/sim.1186.

[32] Wong K, Hwang L, Liu KX, Lee HJ, Olch AJ. Vulnerable populations receiving palliative radiation in a children's hospital: reporting on the underreported. Int J Radiat Oncol 2019;105:E451. https://doi.org/10.1016/j.ijrobp.2019.06.1497.

[33] Murphy JD, Nelson LM, Chang DT, Mell LK, Le Q-T-T. Patterns of care in palliative radiotherapy: a population-based study. J Oncol Pract 2013;9:e220–7. https://doi.org/10.1200/JOP.2012.000835.

[34] Wallace AS, Fiveash JB, Williams CP, Kvale E, Pisu M, Jackson BE, et al. Choosing wisely at the end of life: use of shorter courses of palliative radiation therapy for bone metastasis. Int J Radiat Oncol Biol Phys 2018;102:320–4. https://doi.org/10.1016/j.ijrobp.2018.05.061.

[35] Viechtbauer W, Cheung M-L. Outlier and influence diagnostics for meta-analysis. Res Synth Methods 2010;1:112–25. https://doi.org/10.1002/jrsm.11.

[36] Card N. *Applied meta-analysis for social science research.*; 2015. Accessed January 23, 2021. https://books.google.com/books?hl=en&lr=&id=GC42CwAAQBAJ&oi=fnd&pg=PR1&ots=_e0xDJuOms&sig=q_GfKUMu2kRgO3TMImWSfaWF6LQ.

[37] Hunter JP, Saratzis A, Sutton AJ, Boucher RH, Sayers RD, Bown MJ. In meta-analyses of proportion studies, funnel plots were found to be an inaccurate method of assessing publication bias. J Clin Epidemiol 2014;67:897–903. https://doi.org/10.1016/j.jclinepi.2014.03.003.

[38] Yu H-HM, Lutz ST, Johnstone PA. Palliative radiotherapy (PRT) at end of life (EOL): Benchmarks for a proposed metric. *https://doi.org/101200/jco20143231_suppl119*. 2014;32(31_suppl):119-119. doi:10.1200/JCO.2014.32.31_SUPPL.119.

[39] Kapadia NS, Mamet R, Zornosa C, Niland JC, D'Amico TA, Hayman JA. Radiation therapy at the end of life in patients with incurable nonsmall cell lung cancer. Cancer 2012;118:4339–45. https://doi.org/10.1002/cncr.27401.

[40] Fraser I, Lefresne S, Regan J, Berthelet E, Chooback N, Ho C, et al. Palliative thoracic radiotherapy near the end of life in lung cancer: a population-based analysis. Lung Cancer 2019;135:97–103. https://doi.org/10.1016/j.lungcan.2019.02.024.

[41] Dennis K, Wong K, Zhang L, Culleton S, Nguyen J, Holden L, et al. Palliative radiotherapy for bone metastases in the last 3 months of life: Worthwhile or futile? Clin Oncol 2011;23:709–15. https://doi.org/10.1016/j.clon.2011.05.004.

[42] Cho CKJ, Sunderland K, Pickles T, Bachand F, Chi KN, Tyldesley S. A Population-based study of palliative radiation therapy for bone metastases in patients dying of prostate cancer. Pract Radiat Oncol 2019;9:e274–82. https://doi.org/10.1016/j.prro.2019.01.002.

[43] Ellsworth SG, Alcorn SR, Hales RK, McNutt TR, Deweese TL, Smith TJ. Patterns of care among patients receiving radiation therapy for bone metastases at a large academic institution. Int J Radiat Oncol Biol Phys 2014;89:1100–5. https://doi.org/10.1016/j.ijrobp.2014.04.028.

[44] Petrushevski AN, Gabriel GS, Hanna TP, Allen S, Allison RW, Barton MB. Factors affecting the use of single-fraction radiotherapy for the palliation of bone metastases in Australia. Clin Oncol 2015;27:205–12. https://doi.org/10.1016/j.clon.2014.11.027.

[45] Morris M, O'Donovan T, Ofi B, Flavin A. A Rapid Access Palliative Clinic to reduce waiting time for palliative radiotherapy in a Regional Cancer Centre in Ireland. Int J Integr Care 2017;17:158. https://doi.org/10.5334/ijic.3466.

[46] Spencer K, Morris E, Dugdale E, Newsham A, Sebag-Montefiore D, Turner R, et al. 30 Day mortality in adult palliative radiotherapy - a retrospective population based study of 14,972 treatment episodes. Radiother Oncol 2015;115:264–71. https://doi.org/10.1016/j.radonc.2015.03.023.

[47] Nieder C, Angelo K, Dalhaug A, Pawinski A, Haukland E, Norum J. Palliative radiotherapy during the last month of life: predictability for referring physicians and radiation oncologists. Oncol Lett 2015;10:3043–9. https://doi.org/10.3892/ol.2015.3656.

[48] Wu SY, Singer L, Boreta L, Garcia MA, Fogh SE, Braunstein SE. Palliative radiotherapy near the end of life. BMC Palliat Care 2019;18. https://doi.org/10.1186/s12904-019-0415-8.

[49] Nieder C, Dalhaug A, Haukland E, Engljähringer K. Patient-reported symptom burden, rate of completion of palliative radiotherapy and 30-day mortality in two groups of cancer patients managed with or without additional care by a multidisciplinary palliative care team. Anticancer Res 2018;38:2271–5. https://doi.org/10.21873/anticanres.12471.

[50] Denholm M, Cooper S, Malek A, Rubasingham J, Mithra S, Tsang D. Audit of 30-day mortality following palliative radiotherapy at Southend University Hospital. Clin Oncol 2019;31:e3. https://doi.org/10.1016/j.clon.2019.09.026.

[51] Shukor SA, Bustam AZ. Palliative radiotherapy for advanced cancer: Are we giving it to the right patient at the right time? Med J Malaysia 2018;73:190–6.

[52] Shaw R, Parikh O, Chatten N. An audit of 30 and 90 day mortality following radiotherapy. Clin Oncol 2019;31:e1–2. https://doi.org/10.1016/j.clon.2019.09.022.

[53] Clément-Zhao A, Luu M, Bibault J-E, Daveau C, Kreps S, Jaulmes H, et al. Effective delivery of palliative radiotherapy: a prospective study. Cancer/Radiotherapie 2019;23:365–9. https://doi.org/10.1016/j.canrad.2018.09.006.

[54] Boardman A, Clements H, Kellett D, Mitchell C, Board R. The Assessment of deaths after radiotherapy is an essential part of service evaluation - results of a 30 day mortality audit of patient deaths after palliative radiotherapy. Clin Oncol 2014;26:807. https://doi.org/10.1016/j.clon.2014.09.005.

[55] Chawla S, Easterly C, Tenjarla S, Herman A. Inpatients who received palliative radiation therapy: status survey. Int J Radiat Oncol 2015;93:E470. https://doi.org/10.1016/j.ijrobp.2015.07.1747.

[56] Toole M, Lutz S, Johnstone PAS. Radiation oncology quality: aggressiveness of cancer care near the end of life. J Am Coll Radiol 2012;9:199–202. https://doi.org/10.1016/j.jacr.2011.11.006.

[57] Ali A, Song YP, Mehta S, Mistry H, Conroy R, Coyle C, et al. Palliative radiation therapy in bladder cancer—Importance of patient selection: a retrospective multicenter study. Int J Radiat Oncol Biol Phys 2019;105:389–93. https://doi.org/10.1016/j.ijrobp.2019.06.2541.

[58] Jung H, Sinnarajah A, Enns B, Voroney J-P, Murray A, Pelletier G, et al. Managing brain metastases patientswith and without radiotherapy: Initial lessons from a team-based consult service through a multidisciplinary integrated palliative oncology clinic. Support Care Cancer 2013;21:3379–86. https://doi.org/10.1007/s00520-013-1917-1.

[59] Lee SF, Luk H, Wong A, Ng CK, Wong FCS, Luque-Fernandez MA. Prediction model for short-term mortality after palliative radiotherapy for patients having advanced cancer: a cohort study from routine electronic medical data. Sci Rep 2020;10:5779. https://doi.org/10.1038/s41598-020-62826-x.

[60] Tseng YD, Gouwens NW, Lo SS, Halasz LM, Spady P, Mezheritsky I, et al. Use of radiation therapy within the last year of life among cancer patients. Int J Radiat Oncol Biol Phys 2018;101:21–9. https://doi.org/10.1016/j.ijrobp.2018.01.056.

[61] Sherman A, DiPetrillo TA, Leonard KL. Does palliative radiation improve performance status? Int J Radiat Oncol 2013;87:S566–7. https://doi.org/10.1016/j.ijrobp.2013.06.1503.

[62] Santiago DCM, Varela MV, Gonzalez MA, Giralt J. EP-1633 Profile of patients who die in the first 30 days after palliative radiotherapy in our center. Radiother Oncol 2019;133:S880–1. https://doi.org/10.1016/s0167-8140(19)32053-5.

[63] Lerner A, Phillips I, Ezhil V. Early mortality following radiotherapy – meeting standards and improving patient selection. Clin Oncol 2015;27:S5–6. https://doi.org/10.1016/j.clon.2015.04.021.

[64] Bingham BS, Dvorak T, Morris CG, Yeung AR. Thirty-day mortality rate in oncology patients treated with palliative radiotherapy. *J Clin Oncol.* 2016;34(26_suppl):172-172. doi:10.1200/jco.2016.34.26_suppl.172.

[65] Aladili Z, Kearns DJ, Chan O. 146 Retrospective audit of treatment outcomes from palliative thoracic radiotherapy – a single centre experience. Lung Cancer 2016;91:S53. https://doi.org/10.1016/s0169-5002(16)30163-5.

[66] Lefresne S, Olson R, Cashman R, Kostuik P, Jiang WN, Levy K, et al. Prospective analysis of patient reported symptoms and quality of life in patients with incurable lung cancer treated in a rapid access clinic. Lung Cancer 2017;112:35–40. https://doi.org/10.1016/j.lungcan.2017.07.033.

[67] Kain M, Bennett H, Yi M, Robinson B, James M. 30-day mortality following palliative radiotherapy. J Med Imaging Radiat Oncol 2020;64:570–9. https://doi.org/10.1111/1754-9485.13073.

[68] Buergy D, Siedlitzki L, Boda-Heggemann J, Wenz F, Lohr F. Overall survival after reirradiation of spinal metastases - independent validation of predictive models. Radiat Oncol 2016;11. https://doi.org/10.1186/S13014-016-0613-Y.

[69] Gupta K, Faivre-Finn C, Burt P, Chittalia A, Harris M, Lee L, et al. PO-0744 is 14 day mortality a useful measure of palliative radiotherapy efficacy in lung cancer. Radiother Oncol 2012;103:S288–9.

[70] Pitson G, Matheson L, Garrard B, Eastman P, Rogers M. Population-based analysis of radiotherapy and chemotherapy treatment in the last month of

life within regional Australia. Intern Med J 2020;50:596–602. https://doi.org/10.1111/imj.14377.
[71] Ryoo JJ, Batech M, Zheng C, Kim RW, Gould MK, Kagan AR, et al. Radiotherapy for brain metastases near the end of life in an integrated health care system. Ann Palliat Med 2017;6:S28–38. https://doi.org/10.21037/apm.2017.03.04.
[72] Tursunovic A, Schytte T, Hansen O. *Use of palliative radiotherapy in lung cancer during the last weeks of the life*. Vol 29.; 2013.
[73] Chan C, Faivre-Finn C, Bayman N, Burt PA, Chittalia AZ, Harris MA, et al. 150: A re-audit of mortality rates after palliative radiotherapy for lung cancer from a single UK radiotherapy centre. Lung Cancer 2015;87:S54.
[74] Maung Maung Myint Y, Watkins S, Howard H, Jackson T. 128: 90-day mortality after radical radiotherapy and 30-day mortality after high dose palliative radiotherapy in lung cancer patients at the University Hospitals Birmingham. Lung Cancer 2017;103:S58.
[75] Lewis TS, Kennedy JA, Price GJ, Mee T, Woolf DK, Bayman NA, et al. Palliative lung radiotherapy: higher dose leads to improved survival? Clin Oncol 2020;32:674–84. https://doi.org/10.1016/j.clon.2020.05.003.
[76] Mojica-Márquez AE, Rodríguez-López JL, Patel AK, Ling DC, Rajagopalan MS, Beriwal S. External validation of life expectancy prognostic models in patients evaluated for palliative radiotherapy at the end-of-life. Cancer Med 2020;9:5781–7. https://doi.org/10.1002/cam4.3257.
[77] Guadagnolo BA, Liao KP, Elting L, Giordano S, Buchholz TA, Shih YCT. Use of radiation therapy in the last 30 days of life among a large population-based cohort of elderly patients in the United States. J Clin Oncol 2013;31:80–7. https://doi.org/10.1200/JCO.2012.45.0585.
[78] Grendarova P, Sinnarajah A, Trotter T, Card C, Wu JSY. Variations in intensity of end-of-life cancer therapy by cancer type at a Canadian tertiary cancer centre between 2003 and 2010. Support Care Cancer 2015;23:3059–67. https://doi.org/10.1007/s00520-015-2676-y.
[79] Burton A, Altman DG. Missing covariate data within cancer prognostic studies: a review of current reporting and proposed guidelines. Br J Cancer 2004;91:4–8. https://doi.org/10.1038/sj.bjc.6601907.
[80] Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC. Trends in the aggressiveness of cancer care near the end of life. J Clin Oncol 2004;22:315–21. https://doi.org/10.1200/JCO.2004.08.136.
[81] Gupta K, Faivre-Finn C, Burt P, Coote J, Chittalia A, Harris M, et al. 157 Mortality rates after palliative radiotherapy for lung cancer from a single UK radiotherapy centre. Lung Cancer 2012;75:S51–2.
[82] Anshushaug M, Gynnild MA, Kaasa S, Kvikstad A, Grønberg BH. Characterization of patients receiving palliative chemo- and radiotherapy during end of life at a regional cancer center in Norway. Acta Oncol (Madr) 2015;54:395–402. https://doi.org/10.3109/0284186X.2014.948061.
[83] Tiwana MS, Barnes M, Kiraly A, Olson RA. Utilization of palliative radiotherapy for bone metastases near end of life in a population-based cohort Cancer palliative care. BMC Palliat Care 2016;15. https://doi.org/10.1186/s12904-015-0072-5.
[84] Matter-Walstra KW, Achermann R, Rapold R, Klingbiel D, Bordoni A, Dehler S, et al. Cancer-related therapies at the end of life in hospitalized cancer patients from four swiss cantons: SAKK 89/09. Oncology 2014;88:18–27. https://doi.org/10.1159/000367629.
[85] Zhang Z, Gu XL, Chen ML, Liu MH, Zhao WW, Cheng WW. Use of palliative chemo- and radiotherapy at the end of life in patients with cancer: a retrospective cohort study. Am J Hosp Palliat Med 2017;34:801–5. https://doi.org/10.1177/1049909116653733.
[86] Angelo K, Norum J, Dalhaug A, et al. Development and validation of a model predicting short survival (death within 30 days) after palliative radiotherapy. Anticancer Res 2014;34.
[87] Kress MAS, Jensen RE, Tsai HT, Lobo T, Satinsky A, Potosky AL. Radiation therapy at the end of life: a population-based study examining palliative treatment intensity. Radiat Oncol 2015;10. https://doi.org/10.1186/s13014-014-0305-4.
[88] Benson KRK, Aggarwal S, Carter JN, von Eyben R, Pradhan P, Prionas ND, et al. Predicting survival for patients with metastatic disease. Int J Radiat Oncol Biol Phys 2020;106:52–60. https://doi.org/10.1016/j.ijrobp.2019.10.032.
[89] Morden NE, Chang C-H, Jacobson JO, Berke EM, Bynum JPW, Murray KM, et al. The care span: End-of-life care for medicare beneficiaries with cancer is highly intensive overall and varies widely. Health Aff 2012;31:786–96. https://doi.org/10.1377/hlthaff.2011.0650.
[90] White N, Reid F, Harris A, Harries P, Stone P, Thompson Coon Jo. A systematic review of predictions of survival in palliative care: How accurate are clinicians and who are the experts? PLoS ONE 2016;11:e0161407. https://doi.org/10.1371/journal.pone.0161407.
[91] Krishnan MS, Epstein-Peterson Z, Chen YH, Tseng YD, Wright AA, Temel JS, et al. Predicting life expectancy in patients with metastatic cancer receiving palliative radiotherapy: The TEACHH model. Cancer 2014;120:134–41. https://doi.org/10.1002/cncr.28408.
[92] Chow E, Abdolell M, Panzarella T, Harris K, Bezjak A, Warde P, et al. Predictive model for survival in patients with advanced cancer. J Clin Oncol 2008;26:5863–9. https://doi.org/10.1200/JCO.2008.17.1363.
[93] Zucker A, Tsai CJ, Loscalzo J, Calves P, Kao J. The NEAT predictive model for survival in patients with advanced cancer. Cancer Res Treat 2018;50:1433–43. https://doi.org/10.4143/crt.2017.223.
[94] Sperduto PW, Chao ST, Sneed PK, Luo X, Suh J, Roberge D, et al. Diagnosis-specific prognostic factors, indexes, and treatment outcomes for patients with newly diagnosed brain metastases: a multi-institutional analysis of 4,259 patients. Int J Radiat Oncol Biol Phys 2010;77:655–61. https://doi.org/10.1016/j.ijrobp.2009.08.025.
[95] Rades D, Fehlauer F, Schulte R, Veninga T, Stalpers LJA, Basic H, et al. Prognostic factors for local control and survival after radiotherapy of metastatic spinal cord compression. J Clin Oncol 2006;24:3388–93. https://doi.org/10.1200/JCO.2005.05.0542.
[96] Nieder C, Tollali T, Yobuta R, Reigstad A, Flatoy LR, Pawinski A. Palliative thoracic radiotherapy for lung cancer: what is the impact of total radiation dose on survival? J Clin Med Res 2017;9:482–7. https://doi.org/10.14740/jocmr2980w.
[97] Käsmann L, Janssen S, Schild SE, Rades D. Impact of the radiation dose on survival after radiochemotherapy for small-cell lung cancer. Anticancer Res 2016;36:1089–92.
[98] Morin L, Beaussant Y, Aubry R, Fastbom J, Johnell K. Aggressiveness of end-of-life care for hospitalized individuals with cancer with and without dementia: a nationwide matched-cohort study in France. J Am Geriatr Soc 2016;64:1851–7. https://doi.org/10.1111/jgs.14363.
[99] B. Zhang K.B. Adelson S. Velji J. Rimar P. Longley B. Keane et al. Characterization of aggressive interventions within 30 days of death in lung cancer patients at Smilow Cancer Hospital (SCH) J Clin Oncol. 32 30_suppl 2014 20 20 10.1200/jco.2014.32.30_suppl.20.
[100] Li D, Prigerson HG, Kang J, Maciejewski PK. Impact of radiation therapy on aggressive care and quality of life near death HHS public access. J Pain Symptom Manag 2017;53:25–32. https://doi.org/10.1016/j.jpainsymman.2016.08.011.
[101] Nieder C, Mannsåker B, Pawinski A, Haukland1 E. Polypharmacy in older patients ≥70 years receiving palliative radiotherapy. Anticancer Res 2017;37:795–800. https://doi.org/10.21873/anticanres.11379.
[102] Futagami M, Yokoyama Y, Sato T, et al. Palliative care for patients with gynecologic cancer in Japan: A Japan Society of Gynecologic Palliative Medicine (JSGPM) Survey. Asian Pacific J Cancer Prev 2016;17:4637–42. https://doi.org/10.22034/APJCP.2016.17.10.4637.
[103] Clément-Zhao, A.; Luu, M.; Bibault, J. E.; Daveau, C.; Kreps, S.; Jaulmes, H.; Dessard-Diana, B.; Housset, M.; Giraud, P.; Durdux C. Abstracts of the MASCC/ISOO Annual Meeting 2018: Effective achievement of palliative radiotherapy: A prospective study. *Support Care Cancer*. Published online 2018:39-364. doi:10.1007/s00520-018-4193-2.
[104] Huang J, Wai ES, Lau F, Blood PA. Palliative radiotherapy utilization for cancer patients at end of life in British Columbia: retrospective cohort study. BMC Palliat Care 2014;13. https://doi.org/10.1186/1472-684X-13-49.
[105] Gallais Sérézal I, Beaussant Y, Rochigneux P, Tournigand C, Aubry R, Lindelöf B, et al. End-of-life care for hospitalized patients with metastatic melanoma in France: a nationwide, register-based study. Br J Dermatol 2016;175:583–92. https://doi.org/10.1111/bjd.14631.
[106] Dennis K, Zhang L, Holden L, Jon F, Barnes E, Tsao M, et al. Functional interference due to pain following palliative radiotherapy for bone metastases among patients in their last three months of life. World J Oncol 2011;2:47–52. https://doi.org/10.4021/wjon290w.
[107] Becerra AZ, Probst CP, Fleming FJ, Xu Z, Aquina CT, Justiniano CF, et al. Patterns and yearly time trends in the use of radiation therapy during the last 30 days of life among patients with metastatic rectal cancer in the United States From 2004 to 2012. Am J Hosp Palliat Care 2018;35:336–42.
[108] Patel A, Dunmore-Griffith J, Lutz S, Johnstone PAS. Radiation therapy in the last month of life. Reports Pract Oncol Radiother 2014;19:191–4. https://doi.org/10.1016/j.rpor.2013.09.010.
[109] Caussa L, Hijal T, Michon J, Helfre S. Role of palliative radiotherapy in the management of metastatic pediatric neuroblastoma: a retrospective single-institution study. Int J Radiat Oncol Biol Phys 2011;79:214–9. https://doi.org/10.1016/j.ijrobp.2009.10.031.
[110] Spencer K, Le Calvez K, Hall P, Velikova G, Henry A, Morris E, et al. Fractionation and early mortality in palliative radiotherapy: insights from the national radiotherapy dataset. Clin Oncol 2019;31:e14. https://doi.org/10.1016/j.clon.2019.09.039.
[111] Varma S, Friedman DL, Stavas MJ. The role of radiation therapy in palliative care of children with advanced cancer: clinical outcomes and patterns of care. Pediatr Blood Cancer 2017;64. https://doi.org/10.1002/pbc.26359.
[112] Sun DS, Lee JS, Lee OK, Kim HK. The features of palliative radiation therapy for advanced cancer patients in hospice care. *Palliat Med*. 2018;32 (1 Supp:237-238. Accessed August 22, 2021. http://ovidsp.ovid.com/ovidweb.cgi?T=JS&CSC=Y&NEWS=N&PAGE=fulltext&D=emexa&AN=622331185.
[113] Nieder C, Haukland E, Mannsåker B, Pawinski A, Dalhaug A. Early palliative radiation therapy in patients with newly diagnosed cancer: reasons, clinical practice, and survival. Pract Radiat Oncol 2015;5:e537–42. https://doi.org/10.1016/j.prro.2015.02.008.
[114] Berger B, Ankele H, Bamberg M, Zips D. Patients who die during palliative radiotherapy: status surveySterbefälle unter palliativer Radiotherapie: Statuserhebung. Strahlentherapie und Onkol 2014;190:217–20. https://doi.org/10.1007/s00066-013-0471-6.
[115] Cassidy V, Perlow H, Awerbuch AW, Kwon D, Quintana J, Griggs J, et al. Determination of physician effectiveness in adjusting palliative radiation fractionation for patients near the end of life. Int J Radiat Oncol 2018;102:e438–9. https://doi.org/10.1016/j.ijrobp.2018.07.1274.
[116] Panoff J, Simoneaux RV, Shah N, Scott M, Buchsbaum JC, Johnstone PAS, et al. Radiation therapy at end of life in children. J Palliat Med 2015;18:167–9. https://doi.org/10.1089/jpm.2014.0219.

[117] M.S. Tiwana M. Barnes A. Kiraly S. Miller D. Hoegler I. Olivotto et al. Palliative radiotherapy for bone metastases: Population-based utilization near end of life in a Canadian province J Clin Oncol. 32 15_suppl 2014 9523 9523 10.1200/jco.2014.32.15_suppl.9523

[118] Olson RA, Tiwana MS, Barnes M, Kiraly A, Beecham K, Miller S, et al. Use of single- versus multiple-fraction palliative radiation therapy for bone metastases: population-based analysis of 16,898 courses in a Canadian Province. Int J Radiat Oncol Biol Phys 2014;89():1092–9.

[119] Lee SF, Wong FCS. 30-day mortality in palliative radiotherapy. Ann Oncol 2019;30:v662. https://doi.org/10.1093/annonc/mdz261.004.

[120] Pitson G, Matheson L, Eastman P, Rogers M. MA19.11 population based analysis of end of life treatment patterns in thoracic malignancies. J Thorac Oncol 2019;14:S329–30. https://doi.org/10.1016/j.jtho.2019.08.663.

[121] Alcorn SR, Hales RK, Smith TJ, McNutt TR, Cheng MJ, Dy SM, et al. Patterns of fractionation of palliative radiation therapy: a single-institution experience. Int J Radiat Oncol 2013;87:S562. https://doi.org/10.1016/j.ijrobp.2013.06.1490.

[122] S.R. Alcorn T.J. Smith T.R. McNutt M.J. Cheng S.M. Dy R.K. Hales et al. Patterns of palliative radiation near the end of life: a single-institution retrospective analysis J Clin Oncol. 31 15_suppl 2013 9636 9636 10.1200/jco.2013.31.15_suppl.9636.

[123] Hwang L, Hwang J, Olch AJ, Wong K. Pediatric palliative radiation: single institution practice patterns and end of life outcomes. Int J Radiat Oncol 2018;102:e442. https://doi.org/10.1016/j.ijrobp.2018.07.1282.

[124] Fraser IM, Regan J, Lefresne S, Olson RA. Palliative radiation therapy near the end of life in lung cancer patients: a population-based analysis. Int J Radiat Oncol 2018;102:e661. https://doi.org/10.1016/j.ijrobp.2018.07.1791.

[125] Morris M, O'Donovan T, Ofi B, Flavin A. EP-1405: A Rapid Access Palliative Radiotherapy Clinic to reduce waiting time in a Regional Cancer Centre. Radiother Oncol 2017;123:S751. https://doi.org/10.1016/s0167-8140(17)31840-6.

[126] Lopez AN, Bingham B, Strickler S, Dvorak T, Morris CG, Yeung AR. 30- and 90-day mortality rates in patients treated with curative or palliative radiation therapy. Int J Radiat Oncol 2017;99:E558. https://doi.org/10.1016/j.ijrobp.2017.06.1941.

[127] Wu SY, Singer L, Garcia MA, Fogh SE, Braunstein SE. Factors associated with palliative radiotherapy in the last 30 days of life. *J Clin Oncol*. 2017;35(31_suppl):84. doi:10.1200/JCO.2017.35.31_suppl.84.

[128] Witztum A, Wu S, Gennatas E, Valdes G, Solberg T, Braunstein S. PO-0884 predicting 30-day mortality for palliative radiotherapy. Radiother Oncol 2019;133:S466–7. https://doi.org/10.1016/s0167-8140(19)31304-0.

[129] Nieder C. Palliative radiotherapy (PRT) during the last month of life: a constant sorrow even in a dedicated PRT facility with research focus on this endpoint. Radiother Oncol 2015;115:284. https://doi.org/10.1016/j.radonc.2015.04.017.

[130] Hall G, Crellin A, Turner R, Franks K, Johnson C, Sebag-Montefiore D. 2035 POSTER early mortality after 40,670 courses of external beam radiotherapy in unselected patients. Eur J Cancer 2011;47:S198–9. https://doi.org/10.1016/s0959-8049(11)70993-5.

[131] Spencer, K; Morris, E; Dugdale, E; Newsham, A; Sebag-Montefiore, D; Turner, R; Hall, G; Crellin A. 30-day mortality in adult palliative radiotherapy: a retrospective population based study of 14 972 treatment episiodes. 2015;21(4):205.

[132] Wallace AS, Keene KS, Kvale E, Williams C, Pisu M, Partridge E, et al. Palliating bone mets at the end of life: are we choosing wisely? Int J Radiat Oncol Biol Phys 2017;99:S220. https://doi.org/10.1016/j.ijrobp.2017.06.541.

[133] Nieder C, Marienhagen K, Dalhaug A, Aandahl G, Haukland E, Pawinski A. Prognostic models predicting survival of patients with brain metastases: integration of lactate dehydrogenase, albumin and extracranial organ involvement. Clin Oncol (R Coll Radiol) 2014;26:447–52. https://doi.org/10.1016/j.CLON.2014.03.006.

[134] Nieder C, Dalhaug A, Pawinski A, Haukland E, Mannsåker B, Engljähringer K. Palliative radiotherapy with or without additional care by a multidisciplinary palliative care team in patients with newly diagnosed cancer: a retrospective matched pairs comparison. Radiat Oncol 2015;10. https://doi.org/10.1186/S13014-015-0365-0.

[135] Nieder C, Andratschke N, Angelo K, Haukland E, Grosu AL. Development of a score predicting survival after palliative reirradiation. J Oncol 2014;2014:1–7. https://doi.org/10.1155/2014/128240.

[136] Jones A Joshua, Lutz T Stephen, Chow Edward, Johnstone A Peter. Palliative radiotherapy at the end of life: a critical review. CA Cancer J Clin 2014;64(5):296–310. https://doi.org/10.3322/caac.21242. In this issue.