Based on a retrospective cohort study, in patients with low grade glioma (WHO Grade II), an approach favouring early resection conferred significant overall survival benefit, when compared to one favouring biopsy and observation.

Clinical Problem: *A 35-year-old female teacher presented after a minor MVA. She is clear of obvious injury, but the CT suggested a left frontal mass. An MRI revealed a left frontal lobe non-enhancing T2 intense lesion suspicious for low grade glioma.*

Clinical Question:
In patients with low-grade glioma (WHO grade II), does early resection confer longer survival, than biopsy and observation?

Search Strategy:
As some of the terms related to this clinical question are poorly encoded / defined in the databases, a broad approach generating concepts related to gliomas (and sub-entities), watchful waiting, and surgical approaches was taken. These were intersected, and further limited to English, last 10 years, and meta-analyses, comparative studies, systematic reviews, or articles on therapy. Additionally, a prognosis filter was applied, but this approach did not yield significantly different results. (For a full description of the search strategy employed, please see Appendix I.)
No meta-analyses or randomized clinical trials were found. The only relevant clinical study found was the following article, a retrospective cohort study comparing two sites with different approaches to low grade gliomas (1). Another article by the same authors examined quality of life outcomes in this same sample (2).

Clinical Bottom Lines:

1. In patients with WHO grade II gliomas, a centre favouring an early resection approach resulted in significantly longer overall survival (OR 0.447 (95% CI 0.231 to 0.864)) when compared to a centre favouring a biopsy and watchful scanning approach.

2. The risk of surgical morbidity (complication or acquired deficit) was not found to differ significantly between groups.

The Evidence:
Design: This was a retrospective population-based parallel cohort study comparing the approaches of two surgical centres in Norway; one centre favoured diagnostic biopsies and a "wait and scan" approach in most of its patients, while the other favoured early and aggressive resection in the majority of its patients.

Patients: 153 patients in two neighbouring catchment areas in Norway were recruited between 1998 and June 2009 inclusive. Patients were 18 or older with histologically verified supratentorial WHO diffuse grade II glioma. All screened patients were retrospectively identified from the pathology databases.

Intervention and Comparison:
Based on geographic location and catchment area (which in Norway, corresponds almost 100% to the hospital attended), patients either underwent biopsy and watchful waiting, or an early resection, in accordance with the preferred practice pattern at either hospital.

Outcomes:
The primary outcome measured was overall survival, followed over a 10 year period. The secondary outcome assessed was surgical morbidity, defined as surgical complications and acquired deficits.

Data:

Table 1: Primary and Secondary Outcome Measures

	Centre Favouring Biopsy and Scan (n=66) N (%)	Centre Favouring Early Resection (n=87) N (%)	Odds Ratio (95% CI)
Primary outcome measure			
Overall Survival- Median, 10y	32 (48%)	59 (68%)	0.447 (0.231 to 0.864)
Secondary outcome measure			***p-value***
Surgical complications	6 (9%)	7 (8%)	*p*=.82
New / worsened neurological deficit	12 (18%)	18 (21%)	*p*=.70
30-day perioperative mortality	1 (2%)	0 (0%)	*p*=.25
Malignant transformation	37 (56%)	31 (37%)	*p*=.02

(Although the inclusion criteria specified grade I and II glioma, only grade II glioma were included.)

Comments:

1. Norway is a small country with a particularly homogeneous population. This may have ramifications for genetic trends in tumours, which was not examined, and for generalizability to other populations.
2. This study leverages a unique geographical phenomenon: There are only 4 Norwegian neurosurgical centres and clearly delineated catchment areas, with universal health care available for all Norwegians. The authors state *"There is almost perfect correlation between site of residence (address) and receipt of treatment in that site's regional neurosurgical centre, which eliminates possible referral bias."*
3. Patients were analysed as having received the treatment favoured by their home hospital (an "intention-to-treat" analysis). An "as-treated" analysis was also conducted, which revealed similar trends.
4. Composite surgical complications were poorly defined.
5. This study did not assess role of genetic / pathology markers in prognostication, such as 1p/q19 deletion.

References:

1. Jakola AS, Myrmel KS, Kloster R, Torp SH, Lindal S, Unsgard G, et al. (2012). Comparison of a strategy favoring early surgical resection vs a strategy favoring watchful waiting in low-grade gliomas. JAMA, 308(18), 1881-8.
2. Jakola AS, Unsgard G, Myrmel KS, Kloster R, Torp SH, Sagberg LM, et al. (2014). Surgical strategies in low-grade gliomas and implications for long-term quality of life. Journal of Clinical Neuroscience, 21, 1304-9.

Key Words: Glioma, Low-grade, Surgery / Resection, Watchful waiting.

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Appendix I: Search Strategy

Ovid MEDLINE

1	exp *Brain Neoplasms/ and exp *Glioma/ and (low-grade$ or (Grade$1 adj2 (I or II or low))).tw.	3844
2	((glioma$ or (glial adj2 cell$ adj2 tumor$)) adj5 (low-grade$ or (Grade$1 adj3 (I or II or low)))).tw.	3056
3	(glioma$ adj4 mixed$).tw.	335
4	((diffuse$ or (Grade$1 adj2 (I or II or low)) or pilocytic$) and astrocytoma$).tw.	4309
5	(oligodendroglioma$ or oligoastrocytoma$).tw.	3341
6	or/1-5	9668
7	Follow-Up Studies/	500603
8	limit 7 to yr="1975 - 2010"	397655
9	Watchful Waiting/	1161
10	Biopsy/	139549
11	(biopsy or biopsies).tw.	286334
12	((Watchful adj5 Wait$) or (Watc$ adj5 Wait$)).tw.	2144
13	((active$ adj3 surveillance$) or (expectant$ adj3 management$) or monitoring$).tw.	320316
14	or/8-13	1043895
15	6 and 14	1748
16	exp Surgical Procedures, Operative/ or Surgical Procedures, Elective/ or Reoperation/ or Perioperative Care/ or Postoperative Care/ or exp Postoperative Period/ or exp Preoperative Care/ or Preoperative Period/ or Intraoperative Period/ or Intraoperative Care/ or Ambulatory Surgical Procedures/ or exp Intraoperative Complications/ or exp Postoperative complications/ or (pre-operativ$ or preoperativ$ or intraoperativ$ or perioperative$ or peri-operative$ or operative$).tw. or su.fs. or surg$.af. or resection.tw. or dissection$.tw. or repair$.tw. or (surg$ or operati$).ti.	4182807
17	6 and 14 and 16	1287
18	limit 17 to english language	1154
19	random$.tw. or randomized controlled trial/	828582
20	18 and 19	30
21	limit 18 to "therapy"	23
22	20 or 21	31
23	"systematic review"/ or meta analysis.mp,pt. or MEDLINE.tw. or systematic review.tw.	143650
24	18 and 23	6
25	**22 or 24** *[first set]*	**35**
26	comparative studies/ or compare$.tw. or (comparing or compared or versus or vs$).tw.	4173682
27	**17 and 26** *[second set]*	**377**
28	exp models, statistical/ or Prognosis/	621253
29	(diagnosed or predictor$ or death).tw.	1000189
30	cohort$.mp.	358116
31	or/28-30 *[Prognosis filter]*	1743039
32	**17 and 31** *[third set]*	**450**