

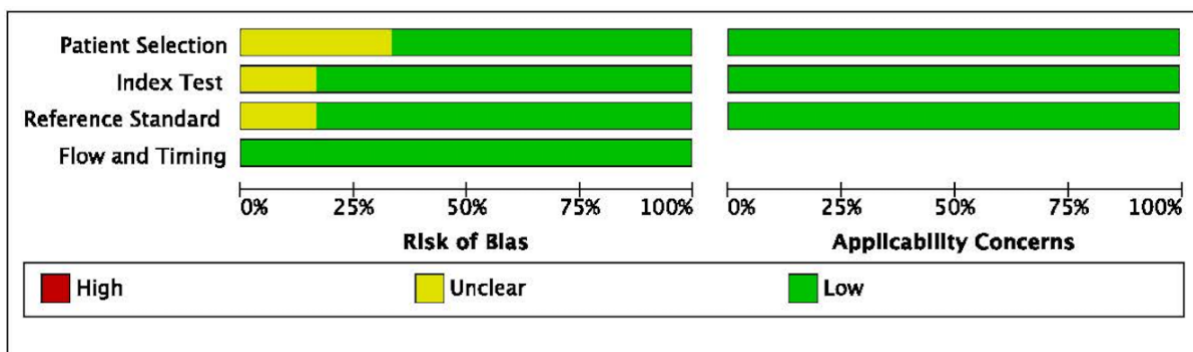
Online Supplemental Data

	<u>Risk of Bias</u>				<u>Applicability Concerns</u>		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Buemi 2019	+	+	+	+	+	+	+
Ellingson 2014	?	+	+	+	+	+	+
Ellingson 2017	+	+	+	+	+	+	+
Pope 2012	+	+	+	+	+	+	+
Rahman 2014	?	?	?	+	+	+	+
Schell 2020	+	+	+	+	+	+	+

<b>- High</b>	<b>? Unclear</b>	<b>+ Low</b>
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Online Fig 1. The results of Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2)



Online Fig 2. Bar graph of QUADAS-2 results of bias and applicability

**Online Table. Study characteristics**

Study	Year	Region*	Period	Total N (BEV/Non-BEV)	Methods	Trial	Definition of recurrence of glioblastoma	Patients' age (year)	Medications	ROI type	ADC type	Outcomes
Pope et al. <sup>9</sup>	2012	US	June, 2006 to February, 2007	97/NA	Retrospective	BRAIN	Histologically confirmed first or second relapse	Mean 54 ± 12 (range, 23–79)	BEV alone or in combination with irinotecan	Volume; CEL	The mean of the lower Gaussian curve (ADC <sub>L</sub> )	6-month PFS PFS OS
Rahman et al. <sup>10</sup>	2014	US	December, 2005 to July, 2012	91/NA	Retrospective	NA	New or increased size of enhancing tumor ([25 % bidimensional products) based on MRI prior to bevacizumab initiation	Mean 56.3 (range, 23–83)	BEV alone (n = 47) BEV plus concurrent chemotherapy (n = 44)	Volume; T2L CEL,	intermediate, and highest peak of the Gaussian curve (ADC-L, ADC-M, and ADC-H)	PFS OS

Ellingson et al. <sup>11</sup>	2014	US	November 15, 2005 to August 31, 2010	89/43	Retrospective	NA	Diagnosed on the basis of clinical data, MRI, and/or histology	BEV: mean 58.0 ± 12 Non-BEV: mean 55.3 ± 9.9	BEV alone or in combination with chemotherapy (carboplatin, irinotecan, etoposide, lomustine)	Volume; CEL	The mean of the upper and lower Gaussian curve (ADC <sub>H</sub> and ADC <sub>L</sub> )	PFS OS
Ellingson et al. <sup>12</sup>	2017	Netherlands	December 11, 2009 to November 10, 2011	42/39	Retrospective	NTR1929	First progression after previous chemoradiotherapy with temozolomide, documented by MRI with at least one bi-dimensionally measurable target lesion with one diameter of at least 10 mm, visible on two or more axial slices 5 mm apart	BEV: 56.3 ± 1.5 Non-BEV: 56.0 ± 1.4	BEV alone (n = 42)	Volume; CEL	The mean of the upper and lower Gaussian curve (ADC <sub>H</sub> and ADC <sub>L</sub> )	OS

Buemi et al. <sup>13</sup>	2019	Italy	December, 2009 to July, 2015	17/NA	Retrospective	NA	Diagnosed on the basis of clinical and imaging data	Median 58.2 (range, 40–81)	BEV alone (n = 4) BEV plus fotemustine (n = 13)	Volume; CEL, T2L	The mean of the upper and lower Gaussian curve (ADC <sub>H</sub> and ADC <sub>L</sub> )	PFS OS
Schell et al. <sup>14</sup>	2020	Netherlands	October, 2011 to April, 2020	242/154	Retrospective	EORTC-26101	Surgically confirmed (operated); must be at least one bi-dimensionally measurable contrast-enhancing lesion with clearly defined margins by MRI scan with minimal diameters of 10mm, visible on 2 or more axial slices 5mm apart, based on MRI scan done	BEV: median 58 (interquartile range, 51–65) Non-BEV: median 60 (interquartile range, 52–66)	BEV alone (at PD: BEV + lomustine) (n = 54) BEV plus lomustine (at PD: salvage treatment at the investigator's best choice) (n = 188)	Volume; CEL	The mean of the lower Gaussian curve (ADC <sub>L</sub> )	PFS OS

within two  
weeks prior to  
randomization  
(non-operated)

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\*Region where the participants were treated

ROI, region-of-interest; ADC, apparent diffusion coefficient; NOS, Newcastle-Ottawa Scale; BEV, patients treated with bevacizumab; Non-BEV, patients treated without bevacizumab; PD, progression disease; CEL, contrast enhanced lesion; T2L, high intensity lesion on T2WI or FLAIR images; PFS, progression-free survival; OS, overall survival