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ORIGINAL RESEARCH

Brain injury guidelines for the management of traumatic brain injury: a systematic review and meta-analysis

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Abstract

Objectives The Brain Injury Guidelines (BIG) serve to predict the severity of traumatic brain injuries resulting in radiologic findings. The use of BIG promises significant time and resource savings, over routine neurosurgical consultation and repeat imaging. After more than a decade of validation, studies have demonstrated BIG to reliably predict adverse outcomes. We sought to analyze the existing literature to determine the pooled efficacy of BIG and its variations.

Methods A systematic review and meta-analysis were conducted in accordance with PRISMA guidelines (PROSPERO ID: CRD42023481186). Seven databases were searched, and articles published from inception to October 2025 were included. Pooled sensitivities and specificities were calculated using random effects meta-analysis. The main outcomes of interest were neurologic deterioration, neurosurgical intervention and death. Bias was assessed using a modified PROBAST tool.

Results From the 4,733 studies screened, 47 articles were identified for inclusion, of which 23 studied the original BIG and were suitable for meta-analysis. The remaining 2 used BIG variants, from which, there was insufficient data to conduct meta-analyses. The pooled sensitivity and specificity for BIG1 to rule out neurological deterioration, neurosurgical intervention and death were 98.3% (95%CI 95.7–99.4) and 12.7% (95%CI (1.5–58.7)), 98.7% (95%CI 97.4–99.4) and 14.4%(95%CI 3.3–45.8), and 98.2% (95%CI 96.6–99.1) and 12.8% (95%CI 3.0- 41.0) respectively.

Conclusions BIG is highly sensitive for predicting adverse outcomes among traumatic brain injury patients. BIG may be used to identify patients appropriate for discharge, without further immediate investigations or consultation for their traumatic brain injury. It may also play a role in reducing unnecessary transfers for neurosurgical consultation. BIG specificity is low, however, further study of BIG variants may offer solutions to the BIG's shortcomings.

Keywords Trauma · Traumatic brain injury · Emergency · Neurosurgery

Résumé

Objectifs Les Brain Injury Guidelines (BIG) servent à prédire la gravité des lésions cérébrales traumatiques entraînant des résultats radiologiques. L'utilisation de BIG promet d'importantes économies de temps et de ressources, par rapport à la consultation neurochirurgicale de routine et à l'imagerie répétée. Après plus d'une décennie de validation, des études ont démontré que BIG peut prédire de manière fiable les résultats indésirables. Nous avons cherché à analyser la littérature existante afin de déterminer l'efficacité cumulée de BIG et ses variations.

Méthodes Une revue systématique et une méta-analyse ont été menées conformément aux recommandations de PRISMA (PROSPERO ID : CRD42023481186). Sept bases de données ont été consultées, et des articles publiés depuis le début jusqu'en octobre 2025 ont été inclus. Les sensibilités et spécificités regroupées ont été calculées à l'aide d'une méta-analyse

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à effets aléatoires. Les principaux critères de jugement d'intérêt étaient la détérioration neurologique, l'intervention neurochirurgicale et le décès. Le biais a été évalué à l'aide d'un outil PROBAST modifié.

Résultats Parmi les 6 118 études sélectionnées, 47 articles ont été identifiés pour inclusion, dont 23 étudiaient le BIG original et convenaient à une méta-analyse. Les 2 autres ont utilisé des variantes BIG, à partir desquelles il n'y avait pas suffisamment de données pour effectuer des méta-analyses. La sensibilité et la spécificité poolées pour BIG1 afin d'exclure une détérioration neurologique, une intervention neurochirurgicale et un décès étaient de 98.3 % (IC à 95 % : 95.7–99.4) et 12,7 % (IC à 95 % : 1.5–58.7), 98.7 % (IC à 95 % : 97.4–99.4) et 14,4 % (IC à 95 % : 3.3–45.8), et 98,2 % (IC à 95 % : 96.6–99.1) et 12.8 % (IC à 95 % : 3.0–41.0), respectivement.

Conclusions BIG est très sensible pour prédire les résultats indésirables chez les patients ayant subi un traumatisme crânien. Le BIG peut être utilisé pour identifier les patients dont la sortie est appropriée, sans autres investigations ou consultations immédiates concernant leur lésion cérébrale traumatique. Il peut également jouer un rôle dans la réduction des transferts inutiles pour la consultation neurochirurgicale. La spécificité de BIG est faible, cependant, une étude plus approfondie des variantes de BIG peut offrir des solutions aux lacunes du BIG.

Clinician's capsule

What is known about the topic?
Not all patients with traumatic brain injuries will require further imaging or specialist consultation.

What did this study ask?
This study investigated the cumulative performance of the Brain Injury Guidelines for the management of patients with traumatic brain injuries.

What did this study find?
This study found the Brain Injury Guidelines to be highly sensitive in detecting patients suitable for discharge through a combination of clinical and radiologic factors.

Why does this study matter to clinicians?
Use of the Brain Injury Guidelines offers significant potential for reducing resource utilization by safely allowing a significant proportion of patients with radiologic findings of traumatic brain injury to be discharged.

Introduction

Traumatic brain injury is a frequent indication for emergency department (ED) evaluation and hospital admission. Common practice in many hospitals, has been to obtain a neurosurgical evaluation for any patient with an abnormality on initial CT imaging, despite a substantial proportion of patients not requiring intensive monitoring or intervention [1]. There is need for an outcome prediction and management tool to aid in the discharge of CT positive traumatic brain injury patients directly from the ED [2]. Such an approach would be cost and time effective, by reducing unnecessary transfers and allowing neurosurgical specialists to focus on patients requiring their specialized skillset [3–5].

In 2014, Joseph et al. proposed the Brain Injury Guidelines (BIG) (Table 1), a structured approach to stratifying patients with positive CT findings due to head trauma based on clinical and radiographic criteria to identify those at low risk for adverse outcomes [1]. Patients are divided into three categories (BIG1, BIG2 and BIG3). Management recommendations are made for each category, with BIG1 being appropriate for discharge and, BIG3 requiring expert consultation and hospitalization. Use of BIG would obviate the need for neurosurgical evaluation, admission and potentially transfer in patients at sufficiently low risk of clinical deterioration, requiring a neurosurgical intervention or death.

Much of the criticism towards BIG has been due to small sample sizes in the validation studies [6]. We believe a meta-analysis of all the available data would provide a clearer guidance to many considering BIG implementation. Additionally, several refinements have been made to BIG in hopes of adding data-driven improvements to bolster the consensus derived tool [5, 7–9]. This systematic review and meta-analysis aims to synthesize the existing literature evaluating BIG and its derivatives. We focus on clinically meaningful outcomes including the risk of neurological deterioration, need for neurosurgical intervention and mortality.

Methods

Search strategy and selection criteria

We conducted a systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Guidelines.

The following databases were searched for relevant studies on November 24, 2023: The Cochrane CENTRAL Register of Controlled Trials & Cochrane Database of Systematic Reviews (via Wiley); Embase Classic +Embase (via Ovid 1947 to 2023 November 24, 2023); CINHAL (via EBSCO);

Table 1 BIG criteria reproduced with simplifications from Joseph et al. 2014[1]

Brain Injury Guidelines			
History/Exam:	**BIG 1**	**BIG 2**	**BIG 3**
Neurologic Exam	Normal	Normal	Abnormal
Intoxication	No	Yes	Yes
Coumadin, Aspirin, Plavix (CAMP)	No	No	Yes
CT Findings:			
Skull Fracture	No	Non-displaced	Displaced
Subdural Hemorrhage	≤4 mm	5-7mm	≥8 mm
Epidural Hemorrhage	≤4 mm	5-7mm	≥8 mm
Intraparenchymal Hemorrhage	≤4 mm, 1 location	3-7mm, 2 locations	≥8 mm, >2 locations
Subarachnoid Hemorrhage	Trace	Localized	Scattered
Intraventricular Hemorrhage	No	No	Yes
Management Plan:			
Hospitalization	Observe 6hrs	Yes	Yes
Repeat Head CT	No	No	Yes
Neurosurical Consultation	No	No	Yes

MEDLINE (via Ovid 1946 to November 24, 2023); APA PsycInfo (via Ovid 1987 to November 24, 2023); PubMed; and Web of Science (via ClarivateAnalytics). ClinicalTrials.gov and Google Scholar were searched for grey literature on November 24, 2023. Each database was searched again on October 16, 2024, and October 6, 2025.The search strategies were designed by a librarian (SA) and used text words and relevant indexing on the Brain Injury Guidelines (BIG) for the management of traumatic brain injury. The full search strategy for all databases can be found in Appendix A1. We included studies with patients of all ages, which implemented BIG, or a variant of BIG, on trauma patients and reported any of the outcomes of interest (neurological deterioration, neurosurgical interventions and/or death). We excluded studies that were case reports or conference abstracts.

References and citations of included studies were searched via Web of Science and Scopus (Elsevier) and exported on January 22nd, 2024. Additional citations and references of included studies from the update in October 2024 were searched on March 24, 2025, and again on October 15, 2025.

Data extraction

Using the Covidence systematic review software (Veritas Health Innovation) [10], 2 reviewers (NZ, JG) independently screened, in duplicate, the titles and abstracts of all identified references. The same reviewers assessed the full texts of potentially relevant articles for inclusion. Conflicts were resolved through discussion and consensus.

The main outcome was neurologic deterioration, as defined by the study authors. Neurological deterioration was defined as a focal neurological deficit, abnormal pupillary examination or a GCS score of 12 or less for the original derivation of BIG [1]. Secondary outcomes were neurosurgical intervention and death. Two independent reviewers (NZ, AD) extracted study characteristics (country, number of sites, prospective/retrospective, BIG variant used, and total patients) and outcome data divided by BIG classification from the included studies using a standardized form.

Quality assessment

Quality assessment was completed by two independent reviewers (NZ, AD) using PROBAST, modified to accommodate risk stratification studies by removing by removing some signaling questions from the domain predictors and outcome, and the entire domain analysis as recommended by Cochrane [11]. Conflicts were resolved through discussion and consensus.

Data analysis

Meta-analysis was conducted by extracting the true positives, false positives, true negatives and false negatives from articles for each outcome of interest (neurologic deterioration, neurosurgical intervention and death). We sought to address three clinical questions: safety, utility and danger. Depending on the question of interest, data was divided differently.

For the question of safety, termed BIG-Safety, BIG2 and BIG3 data were pooled together into 2×2 tables for each outcome. This allowed us to compare BIG1 to the remainder of the cohort to assess the safety of discharge compared with the patients destine for admission.

Next, the question of utility, BIG-Utility, was addressed by excluding BIG1 and comparing BIG2 to BIG3 for each outcome in 2×2 tables. This allowed us to compute the tsest characteristics for BIG2 to identify each outcome amongst admitted patients. This was done to assess the safety of admission without transfer to a center with neurosurgical services, representing an option of great potential utility for community, and other non-level 1 trauma, hospitals which would otherwise need to transfer these patients for neurosurgical consultation.

Finally, the question of danger, termed BIG-Danger, was addressed by pooling BIG1 and BIG2 data together to isolate the risk of each outcome amongst solely BIG3 patients. This was meant to give an indication of disease severity in BIG3 patients. When there was overlap of study populations between publications, analyses included the studies that resulted in the most participants.

A bivariate, random effects model (REML) was used to compute summary point estimates for sensitivities and specificities. Heterogeneity was summarized with I^2, τ^2, and Cochran's Q. We summarized findings into forest plots of sensitivities and specificities for eligible studies. Pooled prevalences were made from all studies reporting the relevant outcomes. Analyses were conducted using R 4.6.0 (metafor) and RevMan (https://revman.cochrane.org/) for forest plot generation.

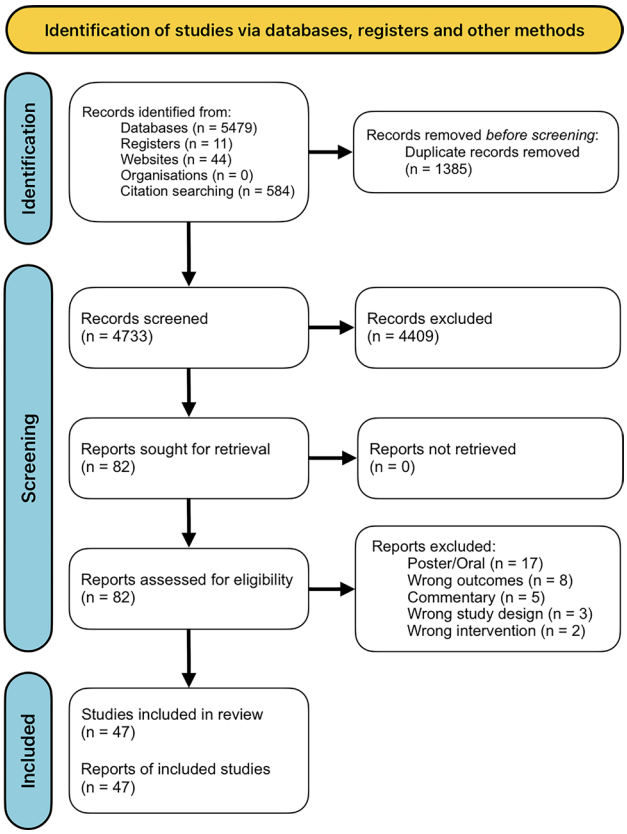


Fig. 1 PRISMA Flowchart

Results

Screening and article selection

After removal of duplicates, 4,733 studies were identified for title and abstract review. Eighty-two studies were selected for full-text review. Thirty-five studies were excluded after full-text review. A total of 47 studies examining the performance of BIG or a BIG variation were identified. Figure 1 displays the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRIMSA) flowchart. Of these, 23 studies [1, 3–5, 7, 8, 12–29] used BIG in an adult population (Table 2), 6 studies [30–35] used BIG in a pediatric population, 14 studies [36–49] used a modified BIG (Khan-mBIG) derived by Khan et al. [7], two studies [8, 50] used an updated BIG (uBIG) derived by Martin et al. [8], one study [5] used a different modified BIG (Ross-mBIG) derived by Ross et al. [5], 3 studies [9, 51, 52] used a pediatric BIG (pBIG) derived by McNickles et al. [9] and the three studies derived other pediatric variations of BIG (kBIG [31], PediBIG [32] and UCD-BIG [34]) (Table S1).

Study characteristics

The baseline characteristics of the 23 studies using the original BIG criteria in adults are summarized in Table 2. The majority were conducted in single, American, level 1 trauma centers with a retrospective design. The remaining 24 studies, summarized in Table S1, were largely of similar design and used other BIG versions or were conducted on pediatric populations. The most common country of study was the United States of America (91%, n=43). The total number of patients was 24,435, with a mean of 592 (standard deviation = 524) patients per study.

Meta-analysis of BIG test characteristics

Of the 47 studies identified, 23 were conducted using the original BIG criteria on 15,423 adult patients and were deemed suitable for meta-analysis. Prospectively recruited patients made up 15.7% (n=2431) of this cohort. There was not sufficient data to meta-analyze the studies using Khan-mBIG, Ross-mBIG, uBIG, pBIG, kBIG, PediBIG, UCD-BIG or BIG in pediatric populations. Additionally, a meta-analysis of prospective BIG studies was also attempted, but

Table 2 Summary table of included study characteristics

Study	Country	Design	No. of Sites	Trauma Centre Level(s)	Total TBI Patients	BIG Version
Joseph et al. 2014a	USA	Retrospective	1	1	1232	BIG
Joseph et al. 2014b	USA	Prospective	1	1	254	BIG
Joseph et al. 2015	USA	Retrospective	1	1	796	BIG
Capron et al. 2017	USA	Retrospective	1	1	340	BIG
Martin et al. 2018	USA	Retrospective	1	3	332	BIG/uBIG
Whetten et al. 2020	USA	Retrospective	1	1	207	BIG
Ross et al. 2020	USA	Retrospective/ Prospective	1	1	590	BIG/Ross mBIG
Marincowitz et al. 2020	UK	Retrospective	3	1	1569	BIG
Khan et al. 2020	USA	Retrospective	3	1,1,3	876	BIG
Delaplain et al. 2020	USA	Retrospective	1	1	461	BIG
Gribell et al. 2021	USA	Retrospective	1	3	49	BIG
Mulari et al. 2021	USA	Retrospective	1	1	214	BIG
Vitale et al. 2022	USA	Retrospective	1	1	354	BIG
Vestlund et al. 2022	Sweden	Retrospective	1	1	533	BIG
Joseph et al. 2022	USA	Prospective	10	1 and 2	2033	BIG
Webb et al. 2023	USA	Retrospective	1	1	1520	BIG
Gallagher et al. 2024	USA	Retrospective	2	1	221	BIG
Morocho et al. 2024	USA	Retrospective	1	2	452	BIG
Southerland et al. 2024	USA	Retrospective	1	1	264	BIG
Tenhoeve et al. 2024	USA	Retrospective	1	1	999	BIG
Chelepy et al. 2025	Australia	Retrospective	1	1	878	BIG
Isidor et al. 2025	USA	Prospective	1	1	144	BIG
Puccio et al. 2025	USA	Retrospective	1	1	1389	BIG

could not be performed because these studies only reported outcomes of BIG1 patients and was underpowered.

All summary test characteristics are summarized in Table 3. The number of studies eligible to assess each clinical question varied. Our first analysis of BIG-Safety analyzed classification into BIG1 to select for safety to discharge (i.e. unlikely to experience any adverse outcome). All test characteristics were obtained using a bivariate random effects model. Eight studies were analyzed for the outcome of neurologic deterioration resulting in a sensitivity and specificity of 98.3% (95%CI 95.7–99.4) and 12.7% (95%CI (1.5–58.7)). The sensitivity and specificity of BIG1 to rule out need for neurosurgical intervention, calculated form 15 studies, was 98.7% (95%CI 97.4–99.4) and 14.4%(95%CI 3.3–45.8), and death, from 14 studies, was 98.2% (95%CI 96.6–99.1) and 12.8% (95%CI 3.0- 41.0). This data is summarized into forest plots seen in Fig. 2.

The second analysis was BIG-Utility, which assessed the safety of classification into BIG2, to rule out adverse outcomes among admitted patients. This was done to assess the safety of avoiding transfer for neurosurgical consultation. The sensitivity and specificity for BIG2 compared with BIG3 to rule out neurologic deterioration was 97.3% (95%CI 94.2–98.8) and 18.7% (95%CI 4.1–55.5), for neurosurgical intervention was 97.7% (95%CI 95.3–98.9) and 16.7% (95%CI 4.0–49.4) and for death was 97.5% (95%CI 94.9–98.8) and 14.2 (95%CI 3.4–43.9). This data was summarized into forest plots seen in Figure S1.

Table 3 Bivariate model summary test characteristics

	BIG 1 for Safety %(95%CI)	I^2	τ^2	X^2 (df)	BIG 2 For Utility %(95%CI)	I^2	τ^2	X^2 (df)	BIG 3 for Danger %(95%CI)	I^2	τ^2	X^2 (df)
Neuro Deterioration:												
Sensitivity:	98.3 (95.7-99.4)	0.00	0.00	7.74 (8) p = 0.46	97.3 (94.2-98.8)	0.17	0.23	7.24 (7) p = 0.40	96.9 (93.2-98.6)	0.31	0.44	9.34 (7) p = 0.23
Specificity:	12.7 (1.5-58.7)	0.97	0.54	107.1 (8) p = 0	18.7 (4.1-55.5)	0.94	0.21	86.8 (7) p = 0	31.9 (7.5-73.1)	0.92	0.10	42.39 (7) p = 0
NSI:												
Sensitivity:	98.7 (97.4-99.4)	0.00	0.00	8.31 (14) p = 0.87	97.7 (95.3-98.9)	0.24	0.47	16.93 (13) p = 0.20	97.7 (95.3-98.9)	0.24	0.48	17.35 (13) p = 0.18
Specificity:	14.4 (3.3 -45.8)	0.97	0.44	218.40 (14) p = 0	16.7 (4.0-49.4)	0.97	0.42	369.15 (13) p = 0	31.3 (9.1-67.5)	0.95	0.16	272.11 (13) p = 0
Death:												
Sensitivity:	98.2 (96.6-99.1)	0.00	0.00	10.23 (13) p = 0.68	97.5 (94.9-98.8)	0.03	0.04	9.42 (9) p = 0.40	97.3 (94.9-98.7)	0.00	0.00	4.68 (9) p = 0.86
Specificity:	12.8 (3.0- 41.0)	0.96	0.73	364.36 (13) p = 0	14.2 (3.4- 43.9)	0.95	0.39	168.31 (9) p = 0	28.6 (8.6-63.2)	0.96	0.21	177.93 (9) p = 0

NSI = Neurosurgical Intervention, df = Degrees of freedom

BIG1 for safety was compute by pooling BIG2 and BIG3 data in 2x2 tables to compare BIG1 classification against the remainder of the cohort. BIG2 for utility was computed by excluding BIG1 patients to assess the performance of BIG2 amongst only the admitted patients, in which case ruling out the need for neurosurgical intervention could save prevent unnecessary transfer to a site with neurosurgical capabilities. Finally, BIG3 for danger was computed by pooling BIG1 and BIG2 data in 2x2 tables to assess prognostic value of adverse outcomes amongst BIG3 patients

The last group analyzed was BIG-Danger, to assess the prognostic value for adverse outcomes when classified as BIG3. The sensitivity and specificity for BIG3 compared with BIG1/2 for neurologic deterioration was 96.9% (95%CI 93.2–98.6) and 31.9 (95%CI 7.5–73.1), for neurosurgical intervention was 99.7% (97.7%CI 95.3–98.9) and 31.3% (95%CI 9.1–67.5) and was 97.3% (95%CI 94.9–98.7) and 28.6% (95%CI 8.6–63.2) for death. This data was summarized into forest plots seen in Figure S2.

Heterogeneity, summarized in Table 3, was mixed. Low variability was consistently present for sensitivity values, while specificity showed high variability across studies. This was true for all measures of heterogeneity.

The number of studies included in each of the analyses were limited due to variations in reported outcomes. A greater number of studies were included in the pooled incidences (Table 4 and S2). Across 14 studies, total of 1,330 patient, only four patients classified as BIG 1 neurologically deteriorated (0.3%). Even fewer, one of 2,142 (0.05%) across 22 studies required a neurosurgical intervention and 3 of 1,397 (0.21%) of 15 studies died. Pooled incidence rates were similar, but marginally higher for BIG 2 patients at 0.74%, 0.59% and 0.54% (neurological deterioration, neurosurgical intervention and death respectively). Pooled incidences in BIG 3 patients were significantly higher, near 10% for all outcomes.

Risk of bias assessment

The risk of bias assessment was done for all studies considered for meta-analysis. It was performed according to a modified PROBAST, summarized in Fig. 3. Nine (38%) of studies were evaluated as low risk of bias, seven (39.4%)

BIG - Safety - Neurological Deterioration

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Joseph 2014	34	1077	0	121	1.00 [0.90, 1.00]	0.10 [0.08, 0.12]
Ross 2020	21	481	0	88	1.00 [0.84, 1.00]	0.15 [0.13, 0.19]
Joseph 2022	232	1500	0	301	1.00 [0.98, 1.00]	0.17 [0.15, 0.19]
Gribbell 2022	4	39	0	6	1.00 [0.40, 1.00]	0.13 [0.05, 0.27]
Morocho 2024	7	337	0	108	1.00 [0.59, 1.00]	0.24 [0.20, 0.29]
Southerland 2024	29	215	0	20	1.00 [0.88, 1.00]	0.09 [0.05, 0.13]

BIG - Safety - Neurosugical Intervention

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Joseph 2014	159	952	0	121	1.00 [0.98, 1.00]	0.11 [0.09, 0.13]
Capron 2017	29	265	0	46	1.00 [0.88, 1.00]	0.15 [0.11, 0.19]
Martin 2018	16	201	0	115	1.00 [0.79, 1.00]	0.36 [0.31, 0.42]
Delaplain 2020	25	354	1	81	0.96 [0.80, 1.00]	0.19 [0.15, 0.23]
Ross 2020	61	441	0	88	1.00 [0.94, 1.00]	0.17 [0.14, 0.20]
Whetten 2020	21	157	0	29	1.00 [0.84, 1.00]	0.16 [0.11, 0.22]
Vestlund 2022	128	397	0	8	1.00 [0.97, 1.00]	0.02 [0.01, 0.04]
Vitale 2022	20	310	0	24	1.00 [0.83, 1.00]	0.07 [0.05, 0.11]
Joseph 2022	280	1452	0	301	1.00 [0.99, 1.00]	0.17 [0.15, 0.19]
Webb 2023	213	1106	0	201	1.00 [0.98, 1.00]	0.15 [0.13, 0.17]
Morocho 2024	28	316	0	108	1.00 [0.88, 1.00]	0.25 [0.21, 0.30]
Southerland 2024	63	181	0	20	1.00 [0.94, 1.00]	0.10 [0.06, 0.15]

BIG - Safety - Death

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Joseph 2015	131	495	0	170	1.00 [0.97, 1.00]	0.26 [0.22, 0.29]
Capron 2017	47	247	0	46	1.00 [0.92, 1.00]	0.16 [0.12, 0.20]
Martin 2018	29	188	1	114	0.97 [0.83, 1.00]	0.38 [0.32, 0.43]
Marincowitz 2019	72	1440	0	57	1.00 [0.95, 1.00]	0.04 [0.03, 0.05]
Delaplain 2020	5	374	0	82	1.00 [0.48, 1.00]	0.18 [0.15, 0.22]
Vestlund 2022	114	411	0	8	1.00 [0.97, 1.00]	0.02 [0.01, 0.04]
Vitale 2022	19	311	0	24	1.00 [0.82, 1.00]	0.07 [0.05, 0.10]
Gribbell 2022	1	42	0	6	1.00 [0.03, 1.00]	0.13 [0.05, 0.25]
Webb 2023	153	1166	2	199	0.99 [0.95, 1.00]	0.15 [0.13, 0.17]
Southerland 2024	24	220	0	20	1.00 [0.86, 1.00]	0.08 [0.05, 0.13]
Tenhoeve 2025	50	781	0	168	1.00 [0.93, 1.00]	0.18 [0.15, 0.20]

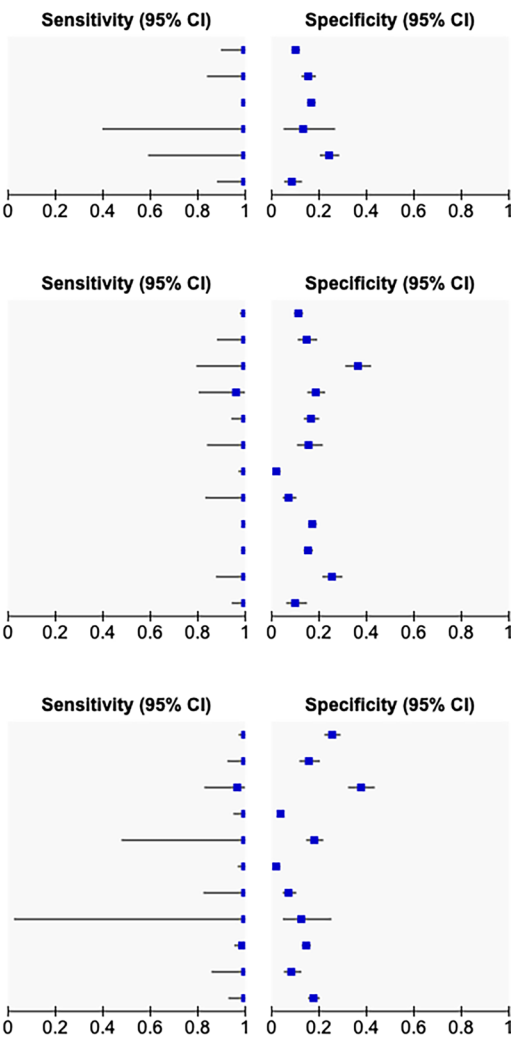


Fig. 2 Forest Plots for BIG1 Safety outcomes

Table 4 Pooled outcome incidence

		Incidence (%)	n	No. Events	No. Studies
BIG 1					
	Neuro Deterioration	0.30	1330	4	14
	Neurosurgical intervention	0.05	2142	1	22
	Death	0.21	1397	3	15
BIG 2					
	Neuro Deterioration	0.74	1349	10	12
	Neurosurgical intervention	0.59	1703	10	17
	Death	0.54	738	4	11
BIG 3					
	Neuro Deterioration	11.40	3940	449	8
	Neurosurgical intervention	12.99	7345	954	15
	Death	9.90	4970	492	11

studies were of uncertain risk due to missing data, and seven (30.4%) studies were deemed to be at high risk of bias. All cases of uncertain bias were due to a lack of definitions (abnormal neurologic examination and/or neurosurgical intervention). High risk of bias occurred due to stated differences in neurosurgical intervention definitions (n=3), restricting the population to a subset of BIG patients (n=2) and expansion of outcomes beyond the emergency department (n=2).

Fig. 3 PROBAST risk of bias summary table

	Risk of Bias			Applicability			Overall	
	1. Participants	2. Predictors	3. Outcome	1. Participants	2. Predictors	3. Outcome	Risk of Bias	Applicability
Joseph et al. 2014a	+	+	+	+	+	+	+	+
Joseph et al. 2014b	+	+	-	+	+	-	-	-
Joseph et al. 2015	+	+	+	+	+	+	+	+
Capron et al. 2017	+	+	+	+	+	+	+	+
Martin et al. 2018	+	+	?	+	+	?	?	?
Whetten et al. 2020	+	?	+	+	?	+	?	?
Ross et al. 2020	+	?	+	+	+	+	?	+
Marincowitz et al. 2020	+	+	-	+	+	-	-	-
Khan et al. 2020	+	+	?	+	+	?	?	?
Delaplain et al. 2020	?	+	-	?	+	+	-	?
Gribell et al. 2021	+	?	?	+	+	?	?	?
Mulari et al. 2021	+	+	?	+	+	+	?	+
Vitale et al. 2022	+	+	+	+	+	+	+	+
Vestlund et al. 2022	+	+	-	+	+	?	-	?
Joseph et al. 2022	+	+	+	+	+	+	+	+
Webb et al. 2023	+	+	+	+	+	+	+	+
Gallagher et al. 2024	-	-	?	+	?	?	-	?
Morocho et al. 2024	+	+	+	+	+	+	+	+
Southerland et al. 2024	-	+	?	?	+	?	-	?
Tenhoeve et al. 2024	?	+	-	?	+	?	-	?
Chelepy et al. 2025	+	+	+	+	+	+	+	+
Isidor et al. 2025	+	+	+	+	+	?	?	+
Puccio et al. 2025	+	?	?	+	?	?	?	?

+ = Low risk of bias, - = High risk of bias, ? = Uncertain

Discussion

Interpretation of findings

BIG represents a potentially useful clinical tool with more than 10 years of consistent validation studies. The robust sensitivities of BIG1 and BIG2 represent safety, allowing for the management of these patients without neurosurgical consultation or repeat imaging. Patients classified as BIG1 are likely appropriate for discharge after a brief period of observation. The original recommendation to observe BIG2 patients for 24 h, without neurosurgical consultation or repeat imaging, is likely also appropriate given the rarity of complications. Additionally, given the low likelihood of neurosurgical intervention, it may be appropriate for patients who originally presented to a hospital without neurosurgical capabilities, to avoid transfer and be observed on location for the remote possibility of clinical deterioration. This meta-analysis provides significantly more confidence in the utility of BIG in the clinical setting.

Comparison to previous studies

To our knowledge, this is the largest and most comprehensive review of BIG criteria to date. A previous review, by Kannan et al. [53] identified only 13 studies, did not purposefully include BIG variants in their search and used radiological deterioration as the primary outcome. While this has been a central outcome in the study of BIG, this is not a patient centered outcome and does not generally dictate care in a stable patient [53]. We chose to focus on patient centered outcomes. Although the previous meta-analysis contains several methodological errors, including the mis-inclusion of a BIG variant, our results are similar with regards to the safe use of BIG to identify patients appropriate for discharge. Where this study offers more is through an analysis of BIG for its use in avoiding immediate transfer when classified as BIG 2 and as a prognostic marker for BIG 3 patients. These outcomes have been highlighted as useful features of BIG, without cumulative analysis until now [54].

Other notable tools for predicting outcomes in traumatic brain injury patients are the Canadian CT Head Rule (CCHR) and the New Orleans Criteria (NOC), both validated for predicting clinically important brain injury and neurosurgical intervention. Meta-analysis of these tools for the outcome of clinically important brain injury shows a sensitivity and specificity of 92.5% and 40.1% for CCHR and 98.3% and 8.5% for NOC [55]. These tools are meant to guide the decision to acquire brain imaging, whereas BIG acts downstream of this decision when imaging results have already been acquired. These tools act well in combination with BIG to more precisely define a clinically important brain injury, using both the clinical evaluation and radiological findings.

Strengths and limitations

This study provides several advantages over previous reviews of the BIG criteria [48, 53, 54]. Our search was more expansive, including the grey literature and non-English sources. This allowed us to uncover more articles for meta-analysis. Additionally, though sub-analyses were not possible, we identified validations of various versions of BIG.

This study contains several limitations. First, most studies were retrospective and there was not enough data to include a subgroup analysis of only prospective studies. Second, there was heterogeneity amongst outcome reporting. Some studies did not explicitly differentiate between death due to traumatic brain injury or other causes and death from transfer to hospice care. Outcome heterogeneity also extended to what was considered a neurosurgical intervention or qualified as neurological deterioration. The absence of outcome definitions caused many studies to be of uncertain risk of bias. Despite this, results were consistent between studies and statistical heterogeneity was low for all sensitivities. Third, several studies only report outcomes on BIG1 patients, limiting available comparisons between groups and causing potential sub-analyses to be underpowered [3, 13, 16, 18, 23]. Fourth, there is very little data on the long-term outcomes after BIG classification. Lastly, BIG has seen relatively little validation outside of the USA and only 9 studies included data from non-level 1 centers, which may limit generalizability.

Clinical implications

The trajectory of traumatic brain injury patients may be significantly altered by the application of BIG. The rigorous validation and consistent effectiveness make BIG a useful tool for the emergency department. BIG 1 and BIG 2 patients can be safely managed without neurosurgical consultation or repeat imaging. This offers a simple and effective method of reducing healthcare resources without compromising patient care. Cost savings may also incentivize adoption of BIG, with the studies to date showing cost reductions of as much as 31% overall [1, 4, 5, 16]. Major barriers to BIG implementation would include the restructuring of community neurosurgical referral care and acceptance of a <1% risk of decompensation among patients admitted for monitoring to hospitals without immediate neurosurgical capabilities. This margin of risk is considered generally acceptable

for discharging other potentially dangerous conditions such as pulmonary embolisms [56]. Although most of the BIG validation has been done in the USA, uBIG saw successful validation in three Canadian hospitals, which improves the likelihood of generalization to Canada [50].

Research implications

Only three articles included in the meta-analysis were comprised of prospectively collected data, this should be prioritized for future studies [1, 5, 16]. Additionally, there are certainly modifications which could simplify or improve BIG. For example, removal of the loss of consciousness criteria, as it does not contribute to classification. The reproduction of BIG seen in Fig. 1 includes this simplification as well as variable groupings for clarity. Multiple studies demonstrate safety when aspirin is removed from BIG [19, 25, 26, 28]. Aspirin use was omitted entirely from Khan-mBIG and uBIG which have seen multiple validations [28, 36, 37, 39–49, 57]. Furthermore, the formal inclusion of direct oral anticoagulants (DOACs) and non-pharmacologic coagulopathies would add clarity for treating patients on modern medications and those with relevant medical conditions [33, 35–46, 50]. Some similar decision tools do not incorporate anticoagulation at all, and this may be a relevant strategy as data on anticoagulation and intracranial hemorrhage evolves [58–60]. Other proposed modifications include clarifying and simplifying the neurological exam, making exceptions for alcohol intoxication and removing epidural hematomas from BIG1 [5, 7, 9, 38, 57]. We encourage future studies to fill these knowledge gaps and prioritize validation in non-level 1trauma centers to improve the applicability of BIG to a wider range of practice settings.

Conclusion

The BIG criteria demonstrate high sensitivity for neurologic deterioration, neurosurgical intervention and death, but are imprecise for some outcomes due to limited events. The risk of adverse outcomes in patients classified as BIG1 is sufficiently low to justify discharge without further testing or consultation. BIG2 patients are at a similarly low risk and may not warrant routine transfers to trauma centers. Classification as BIG3 brings with it significant risk, these patients warrant repeat imaging as well as neurosurgical consultation. With the rising amount of validation for BIG variations and several areas for improvement, it seems reasonable for North American level-1 trauma hospitals to consider adopting the BIG criteria and discuss modifications according to local neurosurgical and trauma specialists.

Appendix

Search details

Databases Searched CINHAL [EBSCO] (November 24, 2023)

#	Query	Limiters/Expanders	Results
S1	(MH "Brain Injuries+") AND (MW "guideline*")	Expanders—Apply equivalent subjects Search modes—Boolean/Phrase	713
S2	TI (brain* N4 injur* N4 guideline*) OR AB (brain* N4 injur* N4 guideline*)	Expanders—Apply equivalent subjects Search modes—Boolean/Phrase	184
S3	S1 OR S2	Expanders—Apply equivalent subjects Search modes—Boolean/Phrase	815
S4	TI ((animal or animals or canine* or cat or cats or dog or dogs or bitch* or feline or hamster* or lamb or lambs or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep*) NOT (human* or patient*))	Expanders—Apply equivalent subjects Search modes—Boolean/Phrase	119,745
S5	S3 NOT S4	Limiters—Publication Date: 20140101- Expanders—Apply equivalent subjects Search modes—Boolean/Phrase	455

Cochrane CENTRAL Register of Controlled Trials [Wiley] (November 24, 2023)

Date Run:	24/11/2023	
Comment:		
ID	Search	Hits

Date Run:	24/11/2023	
#1	(brain* NEAR/4 injur* NEAR/4 guideline*):ti,ab,kw	19
#2	(brain* NEAR/4 injur* NEAR/4 guideline*):ti,ab,kw with Publication Year from 2014 to present, in Trials	15
#3	((animal or animals or canine* or cat or cats or dog or dogs or bitch* or feline or hamster* or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep*) not (human* or patient*)):ti,kw	3959
#4	#2 not #3	15

Embase [Ovid] (November 24, 2023)

Link: Click to run search

The above Jumpstart will only work for users who have access to this specific database.

Database. Embase < 1974 to 2023 November 22 >

#	Query	Results from 24 Nov 2023
1	exp Brain Injury/ and guideline*.hw	4,349
2	(brain* adj4 injur* adj4 guideline*).tw,kf	393
3	1 or 2	4,534
4	limit 3 to yr = 2014-Current	2,799
5	limit 4 to (conference abstract or conference paper or "conference review")	618
6	(animal or animals or bitch or canine* or cat or cats or dog or dogs or feline or hamster* or lamb or lambs or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep* or veterina *).ti,kw,dq,jx. not (human* or patient*).mp	2,078,344
7	5 not 6	614
8	4 not 5	2,181
9	(exp animal/ or exp juvenile animal/ or adult animal/ or animal cell/ or animal tissue/ or nonhuman/ or animal experiment/ or animal model/) not human/	7,451,805
10	6 or 9	7,516,437
11	8 not 10	2,152
12	7 or 11	2,766

Medline [Ovid] (November 24, 2023)

Link: Click to run search

The above Jumpstart will only work for users who have access to this specific database.

Database. Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily < 1946 to November 22, 2023 >

#	Query	Results from 24 Nov 2023
1	exp Brain Injuries/ and guideline*.hw	1,170
2	(brain* adj4 injur* adj4 guideline*).tw,kf	255
3	1 or 2	1,319
4	limit 3 to yr = 2014–2023	604
5	(Animals/ or Models, animal/ or Disease models, animal/) not Humans/	5,139,714
6	((animal or animals or canine* or cat or cats or dog or dogs or bitch* or feline or hamster* or lamb or lambs or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep* or veterina*) not (human* or patient*)).ti,kf,jw	2,627,916
7	5 or 6	5,637,250
8	4 not 7	603
9	("35,358,157" or "28,590,352" or "35,953,341" or "35,953,341" or "26,107,377" or "26,258,312" or "35,078,154" or "37,517,901" or "34,968,784" or "26,107,247" or "35,354,002" or "25,423,541" or "24,662,858" or "35,343,931" or "36,867,721").ui	14
10	8 and 9	14

PsycInfo [Ovid] (November 24, 2023)

Link: Click to run search

The above Jumpstart will only work for users who have access to this specific database.

Database. APA PsycInfo < 1987 to November Week 2 2023 >

#	Query	Results from 24 Nov 2023
1	exp brain injuries/ and guideline*.hw	127
2	(brain* adj4 injur* adj4 guideline*).ti,ab,hw	57
3	1 or 2	167
4	limit 3 to yr = 2014-Current	114
5	(animal not (animal and human)).po	309,519
6	4 not 5	112

PubMed (November 24, 2023)

Search number	Query	Filters	Results
1	brain*[Title/Abstract] AND injur*[Title/Abstract] AND guideline*[Title/Abstract]		3,434
2	((animal[Title] OR animals[Title] OR canine*[Title] OR cat[Title] OR cats[Title] OR dog[Title] OR dogs[Title] OR bitch*[Title] OR feline[Title] OR hamster*[Title] OR lamb[Title] OR lambs[Title] OR mice[Title] OR monkey[Title] OR monkeys[Title] OR mouse[Title] OR murine[Title] OR pig[Title] OR pigs[Title] OR piglet*[Title] OR porcine[Title] OR primate*[Title] OR rabbit*[Title] OR rats[Title] OR rat[Title] OR rodent*[Title] OR sheep*[Title])) NOT (human*[Title] OR patient*[Title])		2,262,871
3	#1 NOT #2		3,386
4	#1 NOT #2	from 2023/11/10—2023/11/24	7

Web Of Science [Clarivate Analytics] (November 24, 2023)

#	Search Query	Results
1	TS = ((brain* Near/4 injur* Near/4 guideline*))	351
2	TS = ((brain* Near/4 injur* Near/4 guideline*)) Timespan: 2014–01-01 to 2023–11-23	235
3	TI = (animal or animals or canine* or cat or cats or dog or dogs or bitch* or feline or hamster* or lamb or lambs or mice or monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or rabbit* or rats or rat or rodent* or sheep*) NOT TI = (human* or patient*)	3,079,268
4	#2 NOT #3	233

Duplication & removal of records

Duplicates were removed by using EndNote's Author/Title/Year duplicate checker, followed by a manual verification of duplicates.

Duplicates were removed using EndNote's Author/Title/Year duplicate checker, followed by a manual verification of duplicates.

Database	Before Duplicate Removal	After Duplicate Removal	% Retained
CINHAL	35	35	100%
Cochrane	2	2	100%
Embase	49	48	98%
Medline	2	2	100%
PsycInfo	7	5	71%
PubMed	10	10	100%
Web Of Science	31	24	77%
Totals	***136***	***126***	**93%**

Other sources

ClinicalTrials.gov

Searched for 'brain injury guidelines' under *Intervention/Treatment* since November 24, 2023. 11 results here: Search for: brain injury guidelines, Study start from 11/24/2023 to 10/16/2024 | Card Results | ClinicalTrials.gov.

Google Scholar

Searched "brain injury guidelines" since November 2023. 52 Results, 44 after deduplication.

Legends

Legend for databases

Legends for Medline (Ovid), Embase (Ovid) & CINAHL are available on our website: http://www.muhclibraries.ca/Documents/Database_Legends.pdf

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s43678-026-01218-y.

Author contributions NZ: Project lead, data collection, data analysis, initial manuscript preparation, JG: Data collection, manuscript revision, SA: Search methods, AD: Data collection, manuscript revision, SS: Supervision, manuscript revision.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Conflicts of interest On behalf of all authors, the corresponding author states that there are no conflicts of interest.

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