TABLE 10.2 TBI and Brain Tumors

Reference	Study Design	Population	Type of TBI	Health Outcomes or Outcome Measures	Results	Adjustments	Comments or Limitations
Annegers et al., 1979	Double cohort	All TBI in Olmsted County, MN, 1935–1974' survived initial trauma; no known pre-existing tumor; comparator data from previous incidence study of brain tumors in Olmsted County	Head injury with LOC, PTA, or skull fracture	Brain tumors	Four brain tumors observed (three astrocytomas, one meningioma); RR (observed/expected) not significant overall or for two tumor types	None	TBI that did not reach medical care uncounted Expected numbers of tumors not adjusted for age or sex to match study population
Burch et al., 1987	Case–control	All brain tumors in Toronto and southern Ontario diagnosed in 1977–1981 and still resident in 1979–1982; of 328 eligible, 247 (75%) participated; comparator, matched hospital controls; of 410 controls asked to participate, 228 (56%) interviewed	Accidents, injuries that involved head (not further specified)	Brain tumors	215 matched pairs analyzed; more cases than controls reported injuries involving head (RR, 2.51; $p \leq 0.0001$), but difference not significant if head injury required medical attention (RR, 1.2; $p = 0.65$)	Matching on basis of sex, area of residence, marital status, ±5 years of birth, date of diagnosis, date of death (if death occurred)	Excluded spongioblastomas, ependymomas, meningiomas, neuroepitheliomas, pituitary adenomas, neurilemmomas. Recall bias, nonparticipation bias noted by authors
Carpenter et al., 1987	Nested case–control	Workers at two nuclear facilities in Oak Ridge, TN, in 1943–1977; cases determined by death certificate; four controls per case	Head injury, self-reported on occupational-medicine pre-employment assessments	Fatal primary malignancy of brain	82 primary brain malignancies: OR, 0.9 (95% CI, 0.2–4.2); for tumors of glial origin: OR, 1.4 (95% CI, 0.3–7.2)	Matched by race, sex, work site, year of birth, year of hire	Misclassification of exposures Outcome assessed by death certificate, excluding those who had not died of primary brain malignancy
Hochberg et al., 1984	Case–control	Cases with glioblastomas from	Severe: resulted in skull fracture or	Glioblasatoma, histologically	Unmatched analysis on 160 cases and 128 controls:	Stratification by age; RR adjusted	Participation bias, recall bias

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		three Boston, one Providence, one Baltimore hospitals; ≥15 years old; 160 of 231 (69%) of eligibles participated; 125 friend controls matched by 5-year age group	concussion, followed by complications (such as coma, intracranial hemorrhage, epilepsy, shock, or long-lasting impairment of memory, hearing, or vision; mild: well-described concussion or brief LOC without other complications	confirmed	overall RR, 2.1 (95% CI, 1.1–4.0); severe RR, 3.8 (95% CI, 1.3–11.0); mild RR, 1.5 (95% CI, 0.7–3.3) Risk increased with age: RR, 10.6 (95% CI, 2.1–53.3) for ≥15 years old at time of TBI	(unknown for what)	
Hu et al., 1998	Case–control	Cases fromsix major hospitals in Heilongjiang Province, China, in 1989–1995; controls from same hospitals with nonneurologic and nonneoplastic disease	History of head trauma by self-report	Histologically confirmed primary gliomas requiring surgery	34 of 218 cases vs 10 of 416 controls reported head trauma; adjusted OR, 4.85 (95% CI, 2.52–9.44)	Matching on age (±5 years), sex, area of residence	Alcohol and skull x rays also found as risk factors
Inskip et al., 1998	Double cohort; Danish population with TBI compared with Danish population without TBI	All Danish residents hospitalized with TBI, 1977–1992 (N = 228,955); comparator, Danish population without history of TBI	Concussion, fractured skull, or other head injury	Intracranial tumors of CNS	Overall SIR, 1.36 (95% CI, 1.20–1.53); ≥1 year PT SIR, 1.15 (95% CI, 0.99–1.32); no difference by cell type	None	
Monteiro et al., 2006	Hospital-based case–control	231 patients 30–65 years old newly diagnosed with	Head injury >1year before diagnosis of brain neoplasm	New diagnosis of primary brain neoplasm,	Association with prior head injury: adjusted OR, 1.49 (95% CI, 1.03–2.15)	Age, sex, education, epilepsy, alcohol	Only 80% of cases confirmed histopathologically,

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		primary brain tumors in 1999–2002, admitted into 10 hospitals in Rio de Janeiro, Brazil; 261 controls matched by age, sex, region of residence from inpatients for conditions other than brain cancer	(cases) or hospitalization (controls) by self-report; hospitalization, amnesia, LOC used as indicators of trauma severity	including cerebral meningiomas, brain cancer, cranial nerve tumors, benign and unspecified brain tumors	By histologic type: glioma (n = 31), OR, 1.30 (95% CI, 0.71–2.35); meningioma (n = 38), OR, 1.63 (95% CI, 0.96–2.75); other with histopathology (n = 15),OR, 1.07 (95% CI, 0.52–2.21); other without histopathology (n = 23), OR, 1.92 (95% CI, 0.99–3.73) As function of severity: hospitalized (n = 15), OR, 0.78 (95% CI, 0.37–1.64); lost consciousness (n = 22), OR, 1.03 (95% CI, 0.55–1.94); amnesia (n = 5), OR, 1.48 (95% CI, 0.38–5.83); any of these (n = 31), OR, 0.93 (95% CI, 0.54–1.60) As function of number of head injuries: 1 (n = 74), OR, 1.29 (95% CI, 0.85–1.96); >1 (n = 28), OR, 3.14 (95% CI, 1.50–6.61; (p trend = 0.004) As function of years since head injury: 1–9 (n = 19), OR, 1.18 (95% CI, 0.73–1.89); 10–19 (n = 27), OR, 1.31 (95% CI, 1.06–1.64); 20–29 (n = 23), OR, 1.07 (95% CI, 0.91–1.27); 30–39	consumption	but nonhistopathologic findings most suggestive; participation rate 94% for cases and 90% for controls; reason for hospitalization for 37.4% of controls was trauma; recall bias cannot be ruled out; information on head injury based on self-reports

Reference	Study Design	Population	Type of TBI	Health Outcomes or Outcome Measures	Results	Adjustments	Comments or Limitations
					(n = 20), OR, 1.09 (95% CI, 0.94–1.26); ≥40 (n = 18), OR, 1.09 (95% CI, 0.96–1.24)		
Nygren et al., 2001	Retrospec-tive population-based cohort	311,006 patients hospitalized for TBI in 1965–1994 from Swedish Inpatient Register (of discharges) without current cancer vs age-, sex- and year-specific incidence rates for Swedish population	Skull trauma that survived hospitalization (ICD-7 801, 853–855; ICD-8 801, 850–854; ICD-9 801, 850–854); considered in three severity groups: concussion, severe without neurosurgery, severe with neurosurgery	Primary brain tumors occurring >1year after trauma through 1995 found by linkage with Swedish Cancer Register, Cause of Death Register, Emigration Register	281 cases of brain tumors (55 meningiomas, 161 primary brain tumors, 65 others) observed in TBI subjects (SIR, 1.0; 95% CI, 0.9–1.2); no relationship for individual types of brain tumor or severity Suggestion of increase in group 30–44 years old at time of TBI: overall, SIR, 1.3 (95% CI, 1.0–1.7); benign meningiomas, SIR, 1.0 (95% CI, 0.5–1.8); primary brain tumors, SIR, 1.4 (95% CI, 1.0–1.8); other, SIR, 1.7 (95% CI, 0.8–3.2) No suggestion of trend with time since trauma (p = 0.69) or increasing age (p = 0.25)	Stratification by age at injury, sex, years after trauma, severity of injury	Record-linkage design permits assembly of large sample, but limited information available on other risk factors; radiation only likely confounder for brain tumors, but no apparent problem in these negative findings; design adopted because of question of reliability of exposure recall in case–control studies of brain-tumor patients; completeness of ascertainment of meningiomas in registry of malignant diagnoses unknown
Phillips et al., 2002	Population-based case–control	200 cases newly diagnosed in January 1995–June 1998, ≥18 years old, histologic confirmation by Cancer Surveillance System at Fred Hutchinson; 400 controls, two per	History of head trauma by self-report; considered "serious" if LOC, went to ED, or hospitalized	Newly diagnosed meningiomas (intracranial); exposures before diagnosis (case applied to two controls) gathered by in-	99 cases, 142 controls with any head trauma: OR, 1.83 (95% CI, 1.28–2.62); mild, OR, 3.23 (95% CI, 1.82–5.71); severe, OR, 1.27 (95% CI, 0.82–1.98); single, OR, 1.51 (95% CI, 0.99–2.29); multiple, OR, 2.75 (95% CI, 1.48–5.08)	Age at diagnosis, sex, skull radiography, CT scanning of head; race, education left out of model when shown to have had no effect	Participation 84% in cases, 55% random-digit dialing controls, 67% in Medicare controls Lack of blinding of interviewers to case or control status

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		case matched on age ± 5 years, sex by RDD or Medicare eligibility lists; all English-speaking residents of three counties in western Washington state with telephone		person interviews	Time before diagnosis: <10 years, OR, 1.39 (95% CI, 0.72–2.68;) 10–19 years, OR, 4.33 (95% CI, 1.28–2.62); ≥20 years, OR, 1.59 (95% CI, 1.09–2.31)		might increase potential for recall bias Cases arising less than 1 year after trauma not excluded, so tumor might have been cause of injuries or found incidentally during workup for TBI Conditional logistic analysis with information on medical, dental exposures to radiation Dose–response relationship for number of head traumas but not expected direction with "severity" of head injury (as defined)
Preston-Martin et al., 1980	Case–control	Cases, women ≤65 years old with intracranial meningiomas identified through cancer registry living in Los Angeles	Head injury >2 years before interview that was medically treated by history	Meningioma, histologically confirmed	185 matched pairs analyzed: OR for head injury treated medically, 2.0 (95% CI, 1.2–3.5)	Matched by sex, race or ethnicity, year of birth (±5 years); by selecting controls from neighborhood, also matched by	189 of 218 (87%) eligible cases interviewed; interviewers not blinded to case–control status

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		County; one matched control per case from neighborhood				socioeconomic status; multivariate logistic regression	Differential recall bias
Preston-Martin et al., 1983	Case–control	Cases, men ≤65 years old with intracranial meningiomas identified through cancer registry living in Los Angeles County; one matched control per case from neighborhood	Head injury >2 years before diagnosis by history; severe head injury defined as LOC or permanent scar	Meningiomas, histologically confirmed	105 matched pairs analyzed with exact binomial test: serious head injury not related to boxing, OR, 1.9 (p = 0.01); boxed as sport, OR, 2.0 (p = 0.03); either boxed or had severe head injury unrelated to boxing, OR, 1.8 (95% CI, 1.1–3.2)	Matched by sex, race or ethnicity, year of birth (±5 years); by selecting controls from neighborhood, also matched by SES; multivariate logistic regression	One-sided tests of significance; differential recall bias
Preston-Martin et al., 1989	Case–control	Cases, men 25–69 years old with glioma or meningioma identified through cancer registry, diagnosed in 1980–1984 in Los Angeles County; one matched neighborhood control per case	Serious head injury >2 years before diagnosis of case that resulted in LOC, dizziness, or medical consultation	Gliomas and meningiomas, histologically confirmed	272 matched pairs (202 glioma, 70 meningiomas) analyzed with exact binomial test For history of serious head trauma ≥20 years before diagnosis: glioma, OR 0.8 (95% CI, 0.5–1.3); meningioma, OR 2.1 (95% CI, 1.1–5.4) For meningiomas only, number of serious head injuries, p for trend = 0.01	Matched by sex, race or ethnicity, year of birth (±5 years); by selecting controls from neighborhood, also matched by SES; multivariate logistic regression	277 of 478 (58%) eligible cases interviewed; differential recall bias less likely with different findings for meningioma and glioma
Preston-Martin et al., 1998	Case–control	Cases from eight centers in six countries (Adelaide, Melbourne, Australia; Grenoble, France; Heidelberg,	Medically treated head injuries; subgroup of serious TBI: medically treated injuries that resulted in LOC,	Gliomas and meningiomas	297 gliomas, 59 meningiomas Glioma: any TBI, males, OR, 1.18 (95% CI, 0.94–1.48), females, OR, 1.03 (95% CI, 0.42–2.55); any serious TBI,	Individual and frequency matching by age and sex; some centers matched on race or geographic	Subject to recall bias; different methods used for matching at different centers

Reference	Study Design	Population	Type of TBI	Health Outcomes or Outcome Measures	Results	Adjustments	Comments or Limitations
		Germany; Toronto, Winnipeg, Canada; Stockholm, Sweden; Los Angeles, US; men, women ≥20 years old with diagnosed glioma or meningioma	PTA, or hospitalization; also recorded participation in sports (differed by region) that could result in TBI; proxy respondents could be used if case or control unavailable		males, OR, 1.13 (95% CI, 0.87–1.48), females, OR, 1.07 (95% CI, 0.74–1.56) Meningioma: any TBI, males, OR, 1.49 (95% CI, 0.86–2.57), females, OR, 0.83 (95% CI, 0.54–1.28); any serious TBI, males, OR, 1.15 (95% CI, 0.57–2.34), females, OR, 0.79 (95% CI, 0.45–1.39) Borderline increase in risk for >1 TBI in men with glioma (OR, 1.52; 95% CI, .00–2.32) but not seen in women or men with meningioma No correlation with sports participation Risk of meningioma in men higher 15-24 years after trauma (OR, 5.35; 95% CI, 1.72–16.62)	region; ORs computed by maximal-likelihood estimates by using both conditional, unconditional logistic regression	
Schlehofer et al., 1992.	Population-based case–control	226 cases in Rhein-Neckar-Odenwald area of Germany with primary brain tumors diagnosed 1987–1988; controls, 418 randomly selected from residential registers	Self-reported history of head injury requiring medical attention; obtained by interview	Primary brain tumors (ICD-9 191, 191.1, 192.0), restricted to gliomas (115), meningiomas (81), acoustic neuromas (30)	For all tumor types: 46 of 226 (20%) vs 113 of 418 (27%); RR, 0.71 (95% CI, 0.5–1.1) For gliomas: 27 cases vs 66 controls; RR, 0.70 (95% CI, 0.4–1.2) For meningiomas: 13 cases vs 39 controls; RR, 0.52 (95%	Age-, sex-matching for controls	418 of 521 (72%) potential controls participated; self-reports of head trauma; no comparisons by severity or number of injuries

Reference	Study Design	Population	Type of TBI	Health Outcomes or Outcome Measures	Results	Adjustments	Comments or Limitations
					CI, 0.3–1.0)		

NOTE: CI = confidence interval, CNS = central nervous system, CT = computed tomography, ED = emergency department, ICD = International Classification of Diseases, LOC = loss of consciousness, OR = odds ratio, PT = posttrauma, PTA = posttraumatic amnesia, RDD = random-digit dialing, RR = relative risk, SES = socioeconomic status, SIR = standardized incidence ratio, TBI = traumatic brain injury.