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ELECTRONIC SUPPLEMENTARY MATERIAL

McKinnon NK *et al.*: Ancillary investigations for death determination in infants and children: a systematic review and meta-analysis

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eAppendix 1 PRISMA 2020 checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page P1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	P4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	P5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	P5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	P6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	P6
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	P6
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	P6-7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	P7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	P7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	P7
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	P8
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	P7
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	P7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	N/A
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	P7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	P8
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Prisma diagram, P8
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	N/A
Study characteristics	17	Cite each included study and present its characteristics.	Tables
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Tables
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Tables, P8-13
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	P8-12
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	P8-12
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	P8-12
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	P12-14
	23b	Discuss any limitations of the evidence included in the review.	P13-14
	23c	Discuss any limitations of the review processes used.	P14
	23d	Discuss implications of the results for practice, policy, and future research.	P13-14
OTHER INFORMATION			

Section and Topic	Item #	Checklist item	Location where item is reported
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	P6
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	P6
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	P2
Competing interests	26	Declare any competing interests of review authors.	P2
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

eAppendix 2 Search strategy

Review Protocol: Systematic review of ancillary testing in pediatric neurological determination of death
Review team members: Michaël Chasse, John Basmaji, Nicole McKinnon
Information specialists: Robin Featherstone (2021 pediatrics modification – this search); Risa Shorr (2019 ancillary tests search); Daniela Ziegler (2020 and 2021 updates of the 2019 ancillary tests search)
Search peer reviewer: N/A – conducted for original 2019 search
Date of search: June 26, 2021

Review question: In pediatric patients (≤18 years of age) appearing to meet criteria for neurological determination of death who require ancillary testing, which ancillary test should be performed to complete the neurological determination of death?

Search methods (abstract): We searched MEDLINE, Embase, Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science (Science Citation Index) on June 26, 2021.

Search methods: An information specialist (RF) modified an update search conducted for a systematic review on ancillary testing for adult neurological determination of death[1]. The modified search was verified by content experts. The original ancillary testing systematic review search was peer reviewed according to the PRESS Peer Review of Electronic Search Strategies 2015 Guideline Statement[2]. The search strategy comprised text words and controlled vocabulary terms (e.g. MeSH) combining concepts for neurological death determination, ancillary tests, and pediatric patients. Search filters were applied to exclude animal studies and case reports, and to limit results to references published in English or French.

Search results were managed, and duplicates removed in EndNote X9 (Clarivate). References were uploaded to Covidence for primary (title/abstract) screening.

Search sources: We ran searches in the following electronic databases on June 26, 2021:
- MEDLINE Ovid (1946 to June 25, 2021)
- Embase Ovid (1947 to June 25, 2021)
- Cochrane Central Register of Controlled Trials (CENTRAL; 2021, Issue 5) via EBM Reviews Ovid
- Web of Science (Science Citation Index Expanded--1900-present)

Conference proceedings from the past 3 years (2018-2021) were retrieved by the Embase search, and trial registry records from ClinicalTrials.gov and the World Health Organization's International Clinical Trials Registry Platform (ICTRP) were retrieved by the CENTRAL search. See Appendix 1 for the complete search strategies.

Results of the search: The search retrieved a total of 3601 references and 2632 unique references (duplicates removed).

Difference between the protocol and the review: N/A

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[1] Chassé M, Glen P, Doyle MA, McIntyre L, English SW, Knoll G, Lizé JF, Shemie SD, Martin C, Turgeon AF, Lauzier F. Ancillary testing for diagnosis of brain death: a protocol for a systematic review and meta-analysis. Systematic reviews. 2013 Dec;2(1):1-8.
[2] McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C. PRESS peer review of electronic search strategies: 2015 guideline statement. Journal of clinical epidemiology. 2016 Jul 1;75:40-6. https://doi.org/10.1016/j.jclinepi.2016.01.021

Search summary:

Source	Results (w. duplicates)	Results (unique)
MEDLINE	1,209	1,208
Embase	1,567	1,034
CENTRAL	45	22
Web of Science	780	368
Total:	**3,601**	**2,632**

Database: Ovid MEDLINE(R) ALL 1946 to June 25, 2021
Date search conducted: June 26, 2021
Strategy:

1 Brain Death/ (8908)
2 (cerebral death or absence of neuro$ or cerebr$ circulatory arrest or braindea*).kw,sh,tw. (2169)
3 ((brain* or neurol*) adj3 (dead* or death* or deceas* or arrest* or cease* or cessation* or unarous* or un-arous* or absen* or unresuscit*)).kw,sh,tw. (20932)
4 ((coma* or stupor) adj2 (irreversibl* or depasse* or unrespons* or un-respons* or unresuscit*)).kw,sh,tw. (298)
5 ((unarous* or un-arous*) adj2 (unrespons* or un-respons*)).kw,sh,tw. (2)
6 comatose patient*.kw,sh,tw. (1843)
7 or/1-6 (26726)
8 exp "Sensitivity and Specificity"/ (610911)
9 (sensitiv* or specificity or accurac*).kw,sh,tw. (2188304)
10 (predictive adj3 value*).kw,sh,tw. (119263)
11 ((true adj positive*) or (false adj positive*) or (false adj negative*) or (true adj negative*) or diagnos* determination of death or ((diagnos* or determination) adj2 death)).kw,sh,tw. (89054)
12 (observer adj variation*).kw,sh,tw. (1293)
13 (roc adj curve*).kw,sh,tw. (39623)
14 (likelihood adj3 ratio*).kw,sh,tw. (17127)
15 likelihood function/ (22614)
16 diagnosis, differential/ or exp Diagnostic errors/ (566209)
17 (diagnostic error* or misdiagnos*).kw,sh,tw. (70953)
18 or/8-17 (2974019)
19 four-vessel angiograph*.kw,sh,tw. (134)
20 Technetium Tc 99m Exametazime/ (2966)
21 Tomography, Emission-Computed, Single-Photon/ (31341)
22 (single photon emission computed tomography or single photon emission ct or spect).kw,sh,tw. (34467)
23 Angiography, Digital Subtraction/ (10947)
24 digital subtraction angiograph*.kw,sh,tw. (9018)
25 Positron-Emission Tomography/ (55784)
26 Radionuclide Angiography/ (1188)
27 (Xenon computed tomography or xenon ct).kw,sh,tw. (360)
28 Magnetic Resonance Angiography/ (23711)
29 (magnetic resonance angiography or magnetic resonance perfusion or mr perfusion).kw,sh,tw. (27845)
30 (computed tomography angiography or ct angiography).kw,sh,tw. (27963)
31 (computed tomography perfusion or ct perfusion).kw,sh,tw. (2536)
32 Ultrasonography, Doppler, Transcranial/ (7662)
33 Transcranial Doppler.kw,sh,tw. (8573)
34 ancillary test$.kw,sh,tw. (1649)
35 ((brain or cerebral) adj perfusion).kw,sh,tw. (14049)
36 Electroencephalography/ (150009)
37 (Electroencephalography or eeg).kw,sh,tw. (176796)
38 exp Evoked Potentials/ (119192)
39 (evoked potentials or evoked response).kw,sh,tw. (80756)
40 or/19-39 (448578)
41 7 and 18 (3566)
42 7 and 40 (3317)
43 41 or 42 [Ancillary testing for diagnosis of brain death SR search] (5998)
44 Adolescent/ (2101965)
45 exp Child/ (1982630)
46 Hospitals, Pediatric/ (14101)
47 exp Infant/ (1175377)

48 exp Infant Death/ (7891)
49 exp Infant Mortality/ (30675)
50 exp Infant, Newborn, Diseases/ (179082)
51 exp Infant, Premature, Diseases/ (45411)
52 exp Intensive Care Units, Pediatric/ (23864)
53 Minors/ (2646)
54 exp Pediatrics/ (60334)
55 Premature Birth/ (15787)
56 (adolescen* or boy* or girl* or minors or teen*).tw,kf. (546167)
57 (babies* or baby* or infan* or neo-nat* or neonat* or newborn* or post matur* or postmatur* or pre matur* or prematur* or post nat* or postnat* or pre term* or preterm*).tw,kf. (1020157)
58 (child* or kid or kids or preschool* or school age* or schoolchild* or toddler*).tw,jw,kf. (1599243)
59 ELBW*.tw,kf. (1527)
60 (elementary school* or grade school* or gradeschool* or high school* or highschool* or kindergar* or nursery school* or primary school* or secondary school*).tw,kf. (75085)
61 low birth weight*.tw,kf. (29391)
62 p?ediatric*.tw,jw,kf. (793774)
63 (PICU* or NICU*).tw,kf. (18029)
64 (small* adj2 gestational age).tw,kf. (11416)
65 VLBW*.tw,kf. (4151)
66 or/44-65 [Pediatrics] (4711513)
67 and/43,66 [Pediatrics filter applied to ancillary testing search] (1726)
68 (case reports not review).pt. (2055679)
69 67 not 68 [Exclude case reports] (1435)
70 (exp animals/ or exp animal experimentation/ or exp models animal/ or exp vertebrates/) not (exp humans/ or exp human experimentation/) (4854038)
71 ((ape or apes or animal* or baboon* or beagle* or canine* or cat or cats or cattle or chicken or chickens or chimp* or dog or dogs or feline* or fish or hamster or hamsters or horse or horses or lapin* or macaque* or mouse or mice or nonhuman* or non human* or pig or piglet* or pigs or porcine or rabbit or rabbit or raccoon or raccoons or racehorse or racehorses or rat or rats or rodent* or swine* or sheep or zebrafish*) not (adults or children or human or humans or infants or patient or patients or people or seniors)).ti,kf. (2271901)
72 70 or 71 (5235010)
73 69 not 72 [exclude animal studies] (1377)
74 limit 73 to (english or french) (1209)
75 remove duplicates from 74 [MEDLINE results for export] (1209)

Database: Ovid Embase Classic+Embase 1947 to 2021 June 25
Date search conducted: June 26, 2021
Strategy:
1 brain death/ (15692)
2 (cerebral death or absence of neuro$ or cerebr$ circulatory arrest or braindea*).kw,sh,tw. (3305)
3 ((brain* or neurol*) adj3 (dead* or death* or deceas* or arrest* or cease* or cessation* or unarous* or un-arous* or absen* or unresuscit*)).kw,sh,tw. (67515)
4 ((coma* or stupor) adj2 (irreversibl* or depasse* or unrespons* or un-respons* or unresuscit*)).ti,ab. (424)
5 ((unarous* or un-arous*) adj2 (unrespons* or un-respons*)).kw,sh,tw. (1)
6 comatose patient*.kw,sh,tw. (4580)
7 or/1-6 (77417)
8 "sensitivity and specificity"/ (397350)
9 (sensitiv* or specificity or accurac*).ti,ab. (2614071)
10 (predictive adj3 value*).kw,sh,tw. (180430)
11 ((true adj positive*) or (false adj positive*) or (false adj negative*) or (true adj negative*) or diagnos* determination of death or ((diagnos* or determination) adj2 death)).kw,sh,tw. (171578)
12 (observer adj variation*).kw,sh,tw. (2472)

13 (roc adj curve*).kw,sh,tw. (70839)
14 (likelihood adj3 ratio*).kw,sh,tw. (23789)
15 differential diagnosis/ (403357)
16 Diagnostic errors/ (60268)
17 (diagnostic error* or misdiagnos*).kw,sh,tw. (98236)
18 or/8-17 (3376860)
19 four-vessel angiograph*.kw,sh,tw. (168)
20 hexamethylpropylene amine oxime technetium tc 99m/ (5115)
21 single photon emission computed tomography/ (11969)
22 (single photon emission computed tomography or single photon emission ct or spect).kw,sh,tw. (60288)
23 digital subtraction angiography/ (23726)
24 digital subtraction angiograph*.kw,sh,tw. (25807)
25 positron emission tomography/ (143534)
26 radionuclide ventriculography/ (599)
27 (Xenon computed tomography or xenon ct).kw,sh,tw. (468)
28 magnetic resonance angiography/ (37598)
29 (magnetic resonance angiography or magnetic resonance perfusion or mr perfusion).kw,sh,tw. (41009)
30 (computed tomography angiography or ct angiography).kw,sh,tw. (33665)
31 (computed tomography perfusion or ct perfusion).kw,sh,tw. (4647)
32 transcranial Doppler ultrasonography/ (2331)
33 Transcranial Doppler.kw,sh,tw. (14262)
34 ancillary test$.kw,sh,tw. (2611)
35 ((brain or cerebral) adj perfusion).kw,sh,tw. (21749)
36 electroencephalography/ (128799)
37 (Electroencephalography or eeg).kw,sh,tw. (217839)
38 exp Evoked Potentials/ (78177)
39 (evoked potentials or evoked response).kw,sh,tw. (81960)
40 or/19-39 (616770)
41 7 and 18 (12360)
42 7 and 40 (8045)
43 41 or 42 (18553)
44 limit 43 to embase (8979)
45 exp adolescent/ (1737974)
46 exp child/ (3169513)
47 exp child death/ (28001)
48 exp infant/ (1208707)
49 infant mortality/ (25573)
50 "minor (person)"/ (727)
51 neonatology/ (5119)
52 exp newborn disease/ (1810540)
53 newborn intensive care/ (26754)
54 pediatric hospital/ (26701)
55 pediatric intensive care unit/ (8517)
56 exp pediatrics/ (125788)
57 (adolescen* or boy* or girl* or minors or teen*).tw,kw. (752172)
58 (babies* or baby* or infan* or neo-nat* or neonat* or newborn* or post matur* or postmatur* or pre matur* or prematur* or post nat* or postnat* or pre term* or preterm*).tw,kw. (1338325)
59 (child* or kid or kids or preschool* or school age* or schoolchild* or toddler*).tw,kw. (2070481)
60 ELBW*.tw,kw. (2225)
61 (elementary school* or grade school* or gradeschool* or high school* or highschool* or kindergar* or nursery school* or primary school* or secondary school*).tw,kw. (98172)
62 low birth weight*.tw,kw. (39331)
63 p?ediatric*.tw,kw. (635439)

64 (PICU* or NICU*).tw,kw. (34260)
65 (small* adj2 gestational age).tw,kw. (15676)
66 VLBW*.tw,kw. (5736)
67 or/45-66 [Pediatrics] (6134420)
68 and/44,67 [Pediatrics filter applied to ancillary testing search] (2465)
69 (case report/ or (case adj1 (report or study)).ti.) not review.pt. (2722423)
70 68 not 69 [Exclude case reports] (1915)
71 (exp animals/ or exp animal experimentation/ or exp models animal/ or exp vertebrates/) not (exp humans/ or exp human experimentation/) (5915331)
72 ((ape or apes or animal* or baboon* or beagle* or canine* or cat or cats or cattle or chicken or chickens or chimp* or dog or dogs or feline* or fish or hamster or hamsters or horse or horses or lapin* or macaque* or mouse or mice or nonhuman* or non human* or pig or piglet* or pigs or porcine or rabbit or rabbit or raccoon or raccoons or racehorse or racehorses or rat or rats or rodent* or swine* or sheep or zebrafish*) not (adults or children or human or humans or infants or patient or patients or people or seniors)).ti. (2661264)
73 71 or 72 (6277041)
74 70 not 73 [exclude animal studies] (1794)
75 (Conference Abstract or Conference Paper or Conference Review).pt. (4887732)
76 74 and 75 (45)
77 limit 76 to yr="2018-2021" (1)
78 74 not 75 [exclude conference proceedings] (1749)
79 77 or 78 [add proceedings from last 3 yrs] (1750)
80 limit 79 to (english or french) (1575)
81 remove duplicates from 80 [Embase results for export] (1567)

Database: EBM Reviews - Cochrane Central Register of Controlled Trials May 2021
Date search conducted: June 26, 2021
Strategy:
1 Brain Death/ (84)
2 (cerebral death or absence of neuro$ or cerebr$ circulatory arrest or braindea*).af. (134)
3 ((brain* or neurol*) adj3 (dead* or death* or deceas* or arrest* or cease* or cessation* or unarous* or un-arous* or absen* or unresuscit*)).af. (1545)
4 ((coma* or stupor) adj2 (irreversibl* or depasse* or unrespons* or un-respons* or unresuscit*)).ti,ab. (6)
5 ((unarous* or un-arous*) adj2 (unrespons* or un-respons*)).af. (0)
6 comatose patient*.af. (268)
7 or/1-6 (1849)
8 exp "Sensitivity and Specificity"/ (16749)
9 (sensitiv* or specificity or accurac*).ti,ab. (92662)
10 (predictive adj3 value*).af. (17206)
11 ((true adj positive*) or (false adj positive*) or (false adj negative*) or (true adj negative*) or diagnos* determination of death or ((diagnos* or determination) adj2 death)).af. (5681)
12 (observer adj variation*).af. (2482)
13 (roc adj curve*).af. (3320)
14 (likelihood adj3 ratio*).af. (1072)
15 likelihood function/ (335)
16 diagnosis, differential/ or exp Diagnostic errors/ (4381)
17 (diagnostic error* or misdiagnos*).af. (1199)
18 or/8-17 (115656)
19 four-vessel angiograph*.af. (3)
20 Technetium Tc 99m Exametazime/ (101)
21 Tomography, Emission-Computed, Single-Photon/ (1027)
22 (single photon emission computed tomography or single photon emission ct or spect).af. (2453)
23 Angiography, Digital Subtraction/ (228)
24 digital subtraction angiograph*.af. (540)

25 Positron-Emission Tomography/ (1007)
26 Radionuclide Angiography/ (64)
27 (Xenon computed tomography or xenon ct).af. (27)
28 Magnetic Resonance Angiography/ (451)
29 (magnetic resonance angiography or magnetic resonance perfusion or mr perfusion).af. (983)
30 (computed tomography angiography or ct angiography).af. (1791)
31 (computed tomography perfusion or ct perfusion).af. (325)
32 Ultrasonography, Doppler, Transcranial/ (452)
33 Transcranial Doppler.af. (1287)
34 ancillary test$.af. (44)
35 ((brain or cerebral) adj perfusion).af. (1320)
36 Electroencephalography/ (4761)
37 (Electroencephalography or eeg).af. (11126)
38 exp Evoked Potentials/ (3231)
39 (evoked potentials or evoked response).af. (4767)
40 or/19-39 (23806)
41 7 and 18 (180)
42 7 and 40 (170)
43 41 or 42 [Ancillary testing for diagnosis of brain death SR search] (308)
44 Adolescent/ (107543)
45 exp Child/ (57412)
46 Hospitals, Pediatric/ (209)
47 exp Infant/ (32372)
48 exp Infant Death/ (71)
49 exp Infant Mortality/ (547)
50 exp Infant, Newborn, Diseases/ (6465)
51 exp Infant, Premature, Diseases/ (3237)
52 exp Intensive Care Units, Pediatric/ (1059)
53 Minors/ (10)
54 exp Pediatrics/ (697)
55 Premature Birth/ (1497)
56 (adolescen* or boy* or girl* or minors or teen*).tw. (39434)
57 (babies* or baby* or infan* or neo-nat* or neonat* or newborn* or post matur* or postmatur* or pre matur* or prematur* or post nat* or postnat* or pre term* or preterm*).tw. (75795)
58 (child* or kid or kids or preschool* or school age* or schoolchild* or toddler*).tw. (140462)
59 ELBW*.tw. (271)
60 (elementary school* or grade school* or gradeschool* or high school* or highschool* or kindergar* or nursery school* or primary school* or secondary school*).tw. (9646)
61 low birth weight*.tw. (4059)
62 p?ediatric*.tw. (36585)
63 (PICU* or NICU*).tw. (3645)
64 (small* adj2 gestational age).tw. (1044)
65 VLBW*.tw. (992)
66 or/44-65 [Pediatrics] (316178)
67 and/43,66 [Pediatrics filter applied to ancillary testing search] (48)
68 remove duplicates from 67 [CENTRAL results for export] (45)

Database: Web of Science Core Collection: Science Citation Index Expanded (SCI-EXPANDED) --1900-present
Date search conducted: June 26, 2021
Strategy:

# 12	**780**	(#10 NOT #11) *AND* **LANGUAGE:** (English OR French) *Indexes=SCI-EXPANDED Timespan=All years*
# 11	**2,838,076**	(TI=((ape or apes or animal* or baboon* or beagle* or canine* or cat or cats or cattle or chicken or chickens or chimp* or dog or dogs or feline* or fish or hamster or hamsters or horse or horses or lapin* or macaque* or mouse or mice or nonhuman* or "non human*" or pig or piglet* or pigs or porcine or rabbit or rabbit or raccoon or raccoons or racehorse or racehorses or rat or rats or rodent* or swine* or sheep or zebrafish*) not (adults or children or human or humans or infants or patient or patients or people or seniors))) *AND* **LANGUAGE:** (English OR French) *Indexes=SCI-EXPANDED Timespan=All years*
# 10	**819**	(#8 NOT #9) *AND* **LANGUAGE:** (English OR French) *Indexes=SCI-EXPANDED Timespan=All years*
# 9	**280,970**	(TI=("case report" or "case study")) *AND* **LANGUAGE:** (English OR French) *Indexes=SCI-EXPANDED Timespan=All years*
# 8	**847**	#7 AND #6 *Indexes=SCI-EXPANDED Timespan=All years*
# 7	**2,718,488**	(TS=(adolescen* or boy* or girl* or minors or teen* or babies* or baby* or infan* or "neo nat*" or neonat* or newborn* or "post matur*" or postmatur* or "pre matur*" or prematur* or "post nat*" or postnat* or "pre term*" or preterm* or child* or kid or kids or preschool* or "school age*" or schoolchild* or toddler* or ELBW* or "elementary school*" or "grade school*" or gradeschool* or "high school*" or highschool* or kindergar* or "nursery school*" or "primary school*" or "secondary school*" or "low birth weight*" or pediatric* or pediatric* or PICU* or NICU* or (small* NEAR/2 "gestational age") or VLBW*)) *AND* **LANGUAGE:** (English OR French) *Indexes=SCI-EXPANDED Timespan=All years*
# 6	**4,475**	#5 OR #4 *Indexes=SCI-EXPANDED Timespan=All years*
# 5	**2,122**	#3 AND #1 *Indexes=SCI-EXPANDED Timespan=All years*
# 4	**3,020**	#2 AND #1 *Indexes=SCI-EXPANDED Timespan=All years*
# 3	**240,482**	(TS=("four vessel angiograph*" or "single photon emission computed tomography" or "single photon emission ct" or spect or "digital subtraction angiograph*" or "Xenon computed tomography" or "xenon ct" or "magnetic resonance angiography" or "magnetic resonance perfusion" or "mr perfusion" or "computed tomography angiography" or "ct angiography" or "computed tomography perfusion" or "ct perfusion" or "transcranial doppler" or "ancillary test*" or ((brain or cerebral) NEAR/1 perfusion) or electroencephalography or eeg or "evoked potentials" or "evoked response")) *AND* **LANGUAGE:** (English OR French) *Indexes=SCI-EXPANDED Timespan=All years*

# 2	**3,284,384**	(TS=(sensitiv* or specificity or accurac* or (predictive NEAR/3 value*) or (true NEAR/1 positive*) or (false NEAR/1 positive*) or (false NEAR/1 negative*) or (true NEAR/1 negative*) or "diagnos* determination of death" or ((diagnos* or determination) NEAR/2 death) or (observer NEAR/1 variation*) or (roc NEAR/1 curve*) or (likelihood NEAR/3 ratio*) or "differential diagnosis" or "diagnostic error*" or misdiagnos*)) *AND* **LAN GUAGE:** (English OR French) *Indexes=SCI-EXPANDED Timespan=All years*
# 1	**22,767**	(TS=("cerebral death" or "absence of neuro*" or "cerebr* circulatory arrest" or braindea* or ((brain* or neurol*) NEAR/3 (dead* or death* or deceas* or arrest* or cease* or cessation* or unarous* or "un arous*" or absen* or unresuscit*)) or ((coma* or stupor) NEAR/2 (irreversibl* or depasse* or unrespons* or "un respons*" or unresuscit*)) or ((unarous* or "un arous*") NEAR/2 (unrespons* or "un-respons*")) or "comatose patient*")) *AND* **LANGUAGE:** (English OR French) *Indexes=SCI-EXPANDED Timespan=All years*

eTable 1 Risk of bias assessment using the Quality Assessment Tool for Diagnostic Accuracy Studies Version 2.0 (QUADAS-2) tool

	Risk of Bias				Applicability Concerns		
	Patient selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Ashwal 1977	?	?	?	O	O	O	O
Ashwal 1979	?	?	O	O	O	O	O
Ashwal 1989	X	?	?	O	O	O	O
Ashwal 1993	X	?	?	X	O	O	O
Blanot 2016	X	X	?	X	O	X	O
Bode 1988	O	?	?	O	O	?	O
Coker 1987	X	X	X	X	O	X	O
Duyu 2000	X	?	?	?	O	?	O
Erbengi 1990	?	X	O	?	O	O	O
Erbengi 1991	O	X	O	O	O	O	O
Fackler 1988	O	?	?	?	O	O	O
Flowers 2000	X	X	X	?	O	O	O
Furgiuele 1984	X	X	O	?	O	?	O
Gencpinar 2015	?	?	?	X	O	O	O
Goh 2004	O	?	?	?	O	?	O
Hindy-Francois	X	X	?	O	O	X	O
Holzman 1983	X	O	X	X	O	O	O
Jalili 1994	O	?	O	O	O	?	O
Kahveci 2002	X	X	O	?	O	O	O
Kraft 2006	X	X	?	O	O	O	O
Laurin 1989	O	?	?	?	O	?	O

Mohandas 1971	X	?	?	X	O	O	O
Newell 1989	X	?	?	O	O	O	O
Okuyaz 2004	X	?	X	O	O	O	O
Okuyaz 2006	X	?	X	O	O	O	O
Parker 1995	X	?	?	?	O	O	O
Pistoia 1991	X	?	?	O	O	O	O
Powers 1989	?	X	?	?	O	X	O
Qian 1998	O	X	?	O	O	X	O
Riggs 2017	O	X	O	O	O	X	O
Rodriguez 2002	X	X	?	X	X	X	O
Ruiz-Garcia 2000	?	X	?	X	O	O	O
Ruiz-Lopez 1999	?	X	O	O	O	X	O
Schober 1987	?	?	?	?	O	O	O
Schwartz 1984	?	?	?	?		O	
Steinhart 1985	?	X	O	?	O	X	O
Thompson 1987	?	X	O	?	O	X	O
Tribolet 1977	?	?	?	?	O	O	O
Wilson 1993	?	?	?	X	O	O	?

O: low risk of bias, ?: unclear risk of bias, X: high risk of bias

eTable 2 Number of studies for each combination of radiopharmaceutical and criteria of interpretation

	Criteria of interpretation		
	Flow	Parenchyma (planar)	Parenchyma (SPECT)
^{99m}Tc -Diethylenetriamine pentaacetate (DTPA)	5		
^{99m}Tc-pertechnetate	4		
^{99m}Tc-glucoheptonate (GHA)	1		
^{99m}Tc-unspecified or multiple	2		
^{99m}Tc-hexamethylpropyleneamine oxime (HMPAO)	1	4	5
^{123}I-iodoamphetamine (^{123}I-IMP)		1	

eTable 3 Individual and pooled sensitivity and specificity for Imaging Ancillary Investigations

ANCILLARY INVESTIGATION (n = # of studies)	STUDY PATIENT # (N)	DNC CONFIRMED or SUSPECTED	CONFOUNDERS	SENSITIVITY (95% high density interval)	SPECIFICITY (95% high density interval)
4 vessel cerebral angiogram	Schwartz 1984	Suspected	PHB (*n* = 4)	1.00	-
	Fackler 1988	Confirmed	PHB (*n* = 8)	1.00	-
CT Angiography	Duyu 2000	Confirmed	NR	1.00	-
FLOW (n = 13)					
^{99m}Tc-DTPA	Erbengi 1990	Suspected	No	0.80	-
	deTribolet 1977	Suspected	No	1.00	-
	POOLED (*N* =7)	SUSPECTED		0.87 (0.53 to 0.99)	-
	Erbengi 1991	Confirmed	No	1.00	-
	Ruiz-Garcia 2000	Confirmed	Unclear, injury listed as "other" (*n* = 5)	0.92	-
	Schober 1987	Confirmed	PHB (*n* = 6), thiopental (*n* = 1), hypothermia (*n* = 1)	1.00	-
	POOLED (*N* = 93)	CONFIRMED		0.92 (0.86 to 0.97)	-
^{99m}Tc-glucoheptonate	Holzman 1983	Suspected	NR	0.89	0.67
^{99m}Tc-Pertechnetate	Ashwal 1977	Suspected	PHB (*n* = 2)	1.00	1.00
	Schwartz 1984	Suspected	Hypothermia (*n* = 1)	1.00	-
	Thompson 1986	Suspected	Hypothermia, PHB (*n* = 2)	0.60	1.00
	POOLED (*N* = 30)	SUSPECTED		0.91 (0.77 to 0.99)	0.97 (0.65 to 1.00)
	Flowers 2000	Confirmed	No	1.00	-

^{99m}Tc-RP unspecified	Coker 1986	Suspected	No	0.98	1.0
	Ashwal 1993	Confirmed	No	0.90	-
^{99m}Tc-HMPAO	Laurin 1989	Suspected	Hypothermia (*n* = 2), PHB (*n* = 3)	1.00	1.00
FLOW (n = 8)	POOLED (*N* = 116)	SUSPECTED		0.95 (0.89 to 0.98)	0.88 (0.67 to 0.98)
FLOW (n = 5)	POOLED (*N* = 133)	CONFIRMED		0.94 (0.88 to 0.97)	-
PARENCHYMAL UPTAKE (n = 10)					
^{99m}Tc-HMPAO Planar	Laurin 1989	Suspected	Hypothermia (*n* = 2), PHB (*n* = 3)	1.00	1.00
	Wilson 1993	Suspected	No	1.00	1.00
	Kraft 2006	Suspected	NR	1.00	-
	POOLED (*N* = 27)	SUSPECTED		0.99 (0.87 to 1.00)	0.97 (0.65 to 1.00)
	Parker 1995	Confirmed	Neuromuscular blockade (*n* = 3), PHB (*n* = 1)	0.87	-
	Schober 1987	Confirmed	Hypothermia (*n* = 1), PHB (*n* = 2)	1.00	-
	POOLED (*N* = 38)	CONFIRMED		0.89 (0.77 to 0.97)	-
^{99m}Tc-HMPAO SPECT	Erbengi 1990	Suspected	No	1.00	-
	Erbengi 1991	Confirmed	No	1.00	-
	Kahveci 2002	Confirmed	No	1.00	-
	Okuyaz 2004	Confirmed	No	1.00	-
	POOLED (*N* = 15)	CONFIRMED		0.99 (0.83 to 1.00)	-
UPTAKE (*n* = 4)	POOLED (*N* = 31)	SUSPECTED		0.99 (0.89 to 1.00)	0.97 (0.65 to 1.00)
UPTAKE (*n* = 5)	POOLED (*N* = 53)	CONFIRMED		0.92 (0.83 to 0.98)	-

^{123}I-IMP†	Schober 1987	Confirmed	Hypothermia (*n* = 1)	1.00	-
TCD	Blanot 2016	Confirmed	Unclear, injury listed as "other" (*n* = 3)	1.00	-
	Bode 1988	Confirmed	No	0.89	-
	Gencpinar 2015	Confirmed	No	0.72	-
	POOLED (*N* = 70)	CONFIRMED		0.91 (0.83 to 0.97)	
	Newell 1989	Suspected	NR	1.00	-
	Powers 1989	Suspected	No	1.00	-
	Qian 1998	Confirmed*	No	0.82	0.88
	Rodriguez 2002	Confirmed*	No	1.00	0.86
	POOLED (*N* = 79)	SUSPECTED		0.91 (0.77 to 0.98)	0.88 (0.77 to 0.95)
Xenon CT	Ashwal 1989 (*N* = 21)	Suspected	No	0.90	1.0
	Thompson 1986 (*N* = 9)	Suspected	Hypothermia, PHB (*n* = 2)	0.60	1.0
	POOLED (*N* = 30)	SUSPECTED		0.81 (0.57 to 0.94)	0.99 (0.83 to 1.0)
	Pistoia 1991	Confirmed	No	0.83	-

† ^{123}I-IMP is a lipophilic RP, however only the ^{99m}Tc-RP studies were included in the pooled analysis.
* Denotes a case-controlled study. Included in analysis with studies involving suspected DNC.

DNC: death determination by neurologic criteria, DTPA: Diethylenetriamine pentaacetate, HMPAO: hexamethylpropyleneamine oxime, IMP: iodoamphetamine, NR: not recorded, RP: radiopharmaceutical, SPECT: single photon emission computed tomography, PHB: phenobarbital, TCD: transcranial doppler.

eTable 4 Individual and pooled sensitivity and specificity for non-imaging ancillary investigations

ANCILLARY INVESTIGATION (*n* = # of studies)	STUDY PATIENT # (N)	DNC SUSPECTED or CONFIRMED	CONFOUNDERS	SENSITIVITY (95% high density interval)	SPECIFICITY (95% high density interval)
BAEP	Erbgeni 1991	Confirmed	No	0.86	-
	Goh 2004	Confirmed	NR	1.00	-
	POOLED (*N* = 8)	CONFIRMED		0.88 (0.56 to 0.99)	-
	Steinhart 1985	Confirmed*	No	0.90	1.00
BAEP + SSEP	Ruiz-Garcia 2000	Confirmed	Unclear, injury listed as transoperative complications (*n* = 2)	0.93	-
	Ruiz-Lopez 1999	Confirmed	Unclear, injury listed as "other" (*n* = 5)	0.88	-
	POOLED (*N* = 158)	CONFIRMED		0.92 (0.87 to 0.96)	-
Bispectral Index	Okuyaz 2006	Confirmed	No	1.00	-
Carotid artery doppler ultrasonography	Jalili 1994	Suspected	No	0.71	1.00
Cranial sector ultrasound	Furgiuele 1984	Suspected	NR	1.00	-
EEG	Ashwal 1993	Confirmed	No	0.85	-
	Fackler 1988	Confirmed	PHB (*n* = 8)	0.85	-
	Goh 2004	Confirmed	NR	0.62	-
	Mohandas 1971	Confirmed	No	0.40	-
	Okuyaz 2004	Confirmed	No	1.00	-
	Parker 1995	Confirmed	PHB (*n* = 1)	1.00	-
	Ruiz-Garcia 2000	Confirmed	Unclear, injury listed as transoperative complications (*n* = 2)	0.91	-

ANCILLARY INVESTIGATION (*n* = # of studies)	STUDY PATIENT # (N)	DNC SUSPECTED or CONFIRMED	CONFOUNDERS	SENSITIVITY (95% high density interval)	SPECIFICITY (95% high density interval)
	POOLED (*N* = 231)	CONFIRMED		0.87 (0.82 to 0.91)	-
	Ashwal 1977	Suspected	PHB (*n* = 2)	0.89	0.50
	Ashwal 1979 (	Suspected	No	0.00	-
	Ashwal 1989	Suspected	No	1.00	1.00
	Furgiuele 1984	Suspected	NR	1.00	-
	Holzman 1983	Suspected	NR	0.92	1.00
	Thompson 1986	Suspected	Yes, PHB + hypothermia (*n* = 2)	1.00	1.00
	POOLED (*N* = 68)	SUSPECTED		0.88 (0.78 to 0.96)	0.96 (0.82 to 1.00)
Ophthalmic US of the central retina	Riggs 2017	Suspected	No	0.92	-

* Denotes a case-controlled study. Included in analysis with studies involving suspected DNC.

BAEP: brainstem auditory evoked potentials, DNC: death determination by neurologic criteria, EEG: electroencephalography, NR: not recorded, PHB: phenobarbital, SSEP: somatosensory evoked potentials.