Supplementary

Table S1: Search Strategy

21/10/2021 Embase (3057), Medline via Ovid (1518), and the Cumulative Index of Nursing and Allied Health Literature (CINAHL) (1415)

|  |  |
| --- | --- |
| **Concept and framework** | **Search terms** |
| Incidence | (prevalence:ti,ab,kw OR incidence:ti,ab,kw OR rate:ti,ab,kw OR burden:ti,ab,kw) |
| AND | |
| Paediatric | (child\*:ti,ab,kw OR adolesc\*:ti,ab,kw OR infan\*:ti,ab,kw OR teen\*:ti,ab,kw OR youth:ti,ab,kw OR paediat\*:ti,ab,kw OR pediat\*:ti,ab,kw OR neonat\*:ti,ab,kw) |
| AND | |
| Stroke | stroke:ti,ab,kw |
| AND | |
| Ischaemic | (ischem\*:ti,ab,kw OR ischaem\*:ti,ab,kw OR arter\*:ti,ab,kw OR thromb\*:ti,ab,kw OR infarc\*:ti,ab,kw) |

Supplementary Table S2. Inclusion and exclusion criteria for the systematic review

|  |  |
| --- | --- |
| Inclusion criteria | Exclusion criteria |
| Reported incidence rates of ischaemic stroke in children aged below 20 years of age | Studies that reported the incidence in the adult population, or included adults above 20 years of age in the study population |
| Studies reported in English | Studies reported in languages other than English |
| Studies where full texts were readily available | Studies where full text was not available or were conference abstracts |
| Primary hospital- or population-based incidence studies that reported the incidence of ischaemic stroke, arterial ischaemic stroke, or cerebral venous sinus thrombosis | Reviews, disease-specific or intervention-related incidence rates, research protocols, studies that reported recurrence rates only.  Studies that did not distinguish and report ischaemic incidence rates (such as case reports) |
| Studies could include both genders or of only one gender (e.g. boys only) | - |
| Studies could be from any year of publication (no limit on date) | - |

Table S3: Newcastle-Ottawa quality assessment scale for cohort studies

Note: A study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability

**Selection**

1) Representativeness of the exposed cohort

a) truly representative of the average \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ (describe) in the community ****

b) somewhat representative of the average \_\_\_\_\_\_\_\_\_\_\_\_\_\_ in the community ****

c) selected group of users eg nurses, volunteers

d) no description of the derivation of the cohort

2) Selection of the non exposed cohort

a) drawn from the same community as the exposed cohort ****

b) drawn from a different source

c) no description of the derivation of the non exposed cohort

3) Ascertainment of exposure

a) secure record (eg surgical records) ****

b) structured interview ****

c) written self report

d) no description

4) Demonstration that outcome of interest was not present at start of study

a) yes ****

b) no

**Outcome**

1) Assessment of outcome

a) independent blind assessment ****

b) record linkage ****

c) self report

d) no description

2) Was follow-up long enough for outcomes to occur

a) yes (select an adequate follow up period for outcome of interest) ****

b) no

3) Adequacy of follow up of cohorts

a) complete follow up - all subjects accounted for ****

b) subjects lost to follow up unlikely to introduce bias - small number lost - > \_\_\_\_ % (select an adequate %) follow up, or description provided of those lost ****

c) follow up rate < \_\_\_\_% (select an adequate %) and no description of those lost

d) no statement

# Supplementary of result

## Table 1: Demographic and characteristic of included studies (n=39)

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author | Country | CT and/or MRI  Medical review | Stroke type | Underlying risk factor/aetiology& | Study length/  direction of enquiry | Arterial ischaemic stroke  Incidence rate | | | Cerebral venous sinus thrombosis Incidence rate | | | All ischaemic strokes Incidence rate | | | Quality score |
| <28days | >28 days | All ages | <28 days | >28 days | All ages | <28 days | >28 days | All ages |  |
| Agrawal 200933 | USA | CT/MRI  reviewed | all% | Not reported | 7 years  retrospective |  |  | 2.1 |  |  | 0.3 |  | 1.3 | 2.4 | 5.0 |
| Barnes 200434 | Australia | no CT/MRI  reviewed | all | All risk/ aetiologies &, except thrombophilia | 9 years retrospective |  |  | 1.8 |  |  |  |  |  |  | 5.5 |
| Chiang 201835 | Taiwan | no CT/MRI  no reviewed | all | All risk/ aetiologies &, except thrombophilia | 2 years retrospective |  |  |  |  |  |  |  |  | 2.3 | 6.0 |
| Christerson 201012 | Sweden | CT/MRI  reviewed | first-ever | Arteriopathy, acute infection, and others | 7 years retrospective |  | 0.9 |  |  | 0.1 |  |  | 1.1 |  | 6.5 |
| Chung 200413 | Hong Kong | CT/MRI  no reviewed | first-ever | All risk/ aetiologies &, except thrombophilia | 5 years retrospective |  |  |  |  |  |  |  |  | 1.5 | 6.5 |
| DeVeber 2017^36 | Canada | CT/MRI reviewed | all | All risk/ aetiologies &  Neonate: not reported | 11 years mix | 10.2 |  | 1.7 |  |  |  |  |  |  | 6.0 |
| DeVeber 200137 | Canada | CT/MRI reviewed | all | All risk/ aetiologies &, except cardiac disorder | 6 years prospective |  |  |  | 0.3 | 0.4 | 0.7 |  |  |  | 6.0 |
| Early 199838 | USA | CT/MRI#  reviewed | all | Arteriopathy, chronic conditions, and others | 4 years retrospective |  |  |  |  |  |  |  | 0.6 |  | 6.5 |
| Eeg-Olofsson 19831 | Sweden | CT and angiography  reviewed | all% | Acute infection, cardiac disorder, and others | 10 years prospective |  |  |  |  |  |  |  |  | 0.9 | 4.5 |
| Fink 201939 | Switzerland | CT/MRI  reviewed | all% | Arteriopathy | 17 years retrospective |  | 0.2 | 1.1 |  |  |  |  |  |  | 6.5 |
| Fullerton 20032 | USA | no CT/MRI  no reviewed | first-ever | All risk/ aetiologies &, except arteriopathy and chronic conditions | 10 years retrospective |  |  |  |  |  |  |  |  | 1.2 | 6.0 |
| Gerstl 201940 | Germany | CT/MRI  reviewed | first-ever | All risk/ aetiologies & | 3 years prospective |  |  | 0.4 |  |  |  |  |  |  | 6.0 |
| Giroud 199522 | France | Before 1987: CT  After 1987: CT/MRI  reviewed | first-ever | All risk/ aetiologies &  , except thrombophilia | 9 years prospective |  |  |  |  |  |  |  |  | 7.9 | 6.5 |
| Kleindorfer 200632 | USA | CT/MRI  reviewed | all% | All risk/ aetiologies &, except cardiac condition | 4 years mix |  |  |  |  |  |  |  |  | 3.6 | 4.5 |
| Laugesaar 201041 | Estonia | CT/MRI  reviewed | first-ever | Thrombophilia and chronic condition | 3 years mix |  | 1.6 |  |  | 0.3 |  |  | 1.9 |  | 6.0 |
| Lehman 201824 | USA | CT/MRI  reviewed | all% | All risk/ aetiologies &  except thrombophilia | 4 years retrospective |  |  |  |  |  |  |  |  | 2.7 | 3.5 |
| Krleza 200942 | Croatia | CT/MRI  reviewed | all% | Acute infection, cardiac disorders, chronic conditions, and others | 7 years retrospective |  |  | 0.7 |  |  |  |  |  |  | 5.5 |
| Mallick 201425 | UK | CT/MRI  reviewed | all | Chronic conditions | 1 year prospective |  |  | 1.6 |  |  |  |  |  |  | 4.5 |
| Oh 201243 | Korea | CT/MRI  reviewed | all | Arteriopathy and other aetiologies | 3.5 years retrospective |  |  | 0.2 |  |  |  |  |  |  | 6.0 |
| Rambaud 202044 | France | CT/MRI  reviewed | first-ever | Acute infection, cardiac disorders, chronic conditions, and others | 10 years retrospective |  | 0.6 |  |  |  |  |  |  |  | 6.0 |
| Schoenberg 197845 | USA | no CT/MRI  reviewed | all% | Arteriopathy, cardiac disorders, chronic conditions, and others | 10 years retrospective |  |  | 0.6 |  |  |  |  |  |  | 6.0 |
| Steinlin 200523 | Switzerland | CT/MRI  reviewed | all% | Not reported | 3 years prospective | 0.6 | 1.1 |  | 0.1 | 0.5 |  | 0.7 | 1.5 | 2.1 | 6.5 |
| Surmava 201946 | Canada | CT/MRI  reviewed | first-ever | All risk/ aetiologies &  , except arteriopathy | 1 year retrospective |  |  | 2.2 |  |  | 1.1 |  |  | 3.3 | 5.5 |
| Tuckuviene 201147 | Denmark | CT/MRI  no reviewed | first-ever | Acute infection, cardiac disorders, chronic conditions, and others | 13 years retrospective | 6.1 |  | 1.3 | 0.8 |  | 0.3 | 6.9 |  | 1.6 | 6.5 |
| Ziesmann 201448 | Canada | CT/MRI  reviewed | all | Cardiac disorders | 16 years retrospective | 0.1 |  | 0.4 |  |  |  |  |  |  | 6.5 |
| Tuppin 201449 | France | no CT/MRI  no reviewed | first-ever | Chronic conditions | 2 years  mix |  |  |  |  |  |  |  | 0.5 |  | 4.5 |
| Kristofferson 202050 | Norway | no CT/MRI  reviewed | first-ever | Thrombophilia, acute infection and chronic conditions | 7 years retrospective |  |  |  |  |  | 1.1 |  |  |  | 5.5 |
| Heller 200351 | Germany | CT/MRI  no reviewed | all% | Acute infection, chronic conditions, and others | 7 years prospective |  |  |  | 2.6 | 0.4 |  |  |  |  | 6.0 |
| Hoffman 201152 | USA | CT/MRI#  reviewed | first-ever | Not reported | 6.5 years retrospective |  |  | 10.7 |  |  |  |  |  |  | 6.5 |
| Clive 2020^53 | Canada | CT/MRI  reviewed | first-ever | Neonate: pregnancy smoking | 7 years retrospective | 35.0 |  |  | 3.0 | 3.3 |  | 38.0 |  |  | 6.5 |
| Darmency-Stamboul 2012^54 | France | CT/MRI  reviewed | all% | Neonate: not reported | 8 years retrospective | 22.7 |  |  |  |  |  |  |  |  | 6.5 |
| Martins 2021^55 | Switzerland | CT/MRI  reviewed | first-ever | N Neonate: not reported  not reported | 10 years prospective | 23.5 |  |  |  |  |  |  |  |  | 6.0 |
| Machado 2015^28 | Portugal | CT/MRI  no reviewed | first-ever | Neonate: dehydration | 5 years retrospective | 32.6 |  |  | 7.2 |  |  | 39.8 |  |  | 5.5 |
| Klemme 2017^56 | Germany | CT/MRI  reviewed | first-ever | Neonate: not reported | 1 year prospective | 7.1 |  |  |  |  |  |  |  |  | 3.5 |
| Sorg 2021^57 | Germany | CT/MRI  reviewed | first-ever | Neonate: multiple pregnancies | 2 years prospective | 22.0 |  |  |  |  |  |  |  |  | 6.5 |
| Adami 2016^58 | USA | CT/MRI  reviewed | first-ever | Neonate: childbirth issues | 6 years retrospective | 32.7 |  |  |  |  |  |  |  |  | 6.5 |
| Grunt 2015^27 | Switzerland | CT/MRI  reviewed | first-ever | Neonate: not reported | 11 years prospective | 13.0 |  |  |  |  |  |  |  |  | 6.5 |
| Berfelo 2010^59 | Netherlands | CT/MRI  reviewed | first-ever | Mother cause: preeclampsia, T2Dm, clothing disease and surgeries  Neonate: infections, dehydration, congenital health defect, trauma etc. | 7 years retrospective |  |  |  |  | 1.4-12\* |  |  |  |  | 7 |
| Thrift 200160 | Australia | CT/MRI  reviewed | first-ever | Not reported | 1 year prospective |  |  | 0 |  |  |  |  |  |  | 5 |

\*reported on a range of incidence rates, ^ incidence rate of neonate group reported as 100,000 live- birth, #: unspecific mentioned MRI or CT, &: risk factor group includes: Arteriopathy, thrombophilia, cardiac disorder, chronic conditions (including cancer, sickle cell diseases, metabolic/liver function/renal function etc.), and other non-specific conditions (such as trauma, dehydration and other). In the study reported on neonates, the aetiology was extracted for both maternal and childbirth causes in the neonate group; %: unclear recurrent reported

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## Table 2: Incidence rate of stroke by stroke subtype (first-ever versus all registered, unclear recurrent versus all registered, with recurrent)

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ischemic stroke** | First ever stroke | | | All registered, unclear recurrent | | | All registered strokes, with recurrent | | | p-value\* |
| (all years) | | |  | (all years) |  | (all years) | | |
|  | N. | Incidence rate [95% CI] | I2(%) | N. | Incidence rate [95% CI] | I2(%) | N. | Incidence rate [95% CI] | I2(%) |
| **All ischaemic strokes** | | | | | | | | | | |
| All children | 5 | 2.18 [1.21, 3.94] | 96.61 | 5 | 2.08 [1.43, 3.03] | 85.68 | 1 | 2.30 [2.03, 2.61] | NA | 0.872 |
| Neonates | 2 | 38.57 [27.69-53.72] | 0.00 | 0 | NA | NA | 0 | NA | NA | NA |
| Older children | 3 | 0.97 [0.46-2.04] | 93.75 | 2 | 1.40 [1.16,1.68] | 0.00 | 1 | 0.58 [0.30,1.10] | NA | 0.027 |
| **Arterial ischaemic stroke** | | | | | | | | | | |
| All children | 4 | 1.89 [0.50-7.13] | 99.56 | 5 | 0.80 [0.41, 1.55] | 97.19 | 3 | 1.71 [1.60,1.83] | 0.00 | 0.079 |
| Neonates | 7 | 19.92[12.62-31.44] | 91.55 | 1 | 22.70 [16.05, 32.10] | NA | 1 | 10.20 [8.53, 12.19] | NA | 0 |
| Older children | 3 | 0.91[0.53-1.56] | 82.08 | 0 | NA | NA | 2 | 0.43 [0.08-2.45] | 98.41 | 0.42 |
| **Cerebral venous sinus thrombosis** | | | | | | | | | | |
| All children | 3 | 0.65 [0.24-1.73] | 94.34 | 1 | 0.31[0.20, 0.50] | NA | 1 | 0.67 [0.57-0.79] | NA | 0.01 |
| Neonates | 3 | 5.56 [3.57-8.64] | 0 | 0 | NA | NA | 0 | NA | NA | NA |
| Older children | 2 | 0.14 [0.05-0.37] | 0 | 2 | 0.36 [0.30,0.43] | 0.00 | 1 | 0.38 [0.31, 0.47] | NA | 0.15 |

\*p<0.05: statistically significant

# Results from meta-analysis of pooled incidence rates (per 100,000 persons), by multiple subgroups

### 1.1 Overall ischaemic stroke (live-birth)

Figure S1.1A Overall ischaemic stroke in neonates

Table

Description automatically generated

Figure S1.1B Overall ischaemic stroke in non-neonates (person-year)



Figure S1.1C Overall ischaemic stroke in all children



Figure S1.1D Overall Ischaemic stroke in all children, stratified by CT/MRI usage, by region\*

Chart, box and whisker chart

Description automatically generated

\*all studies that did not report on the use of CT and/or MRI, the older study that used CT only, and the study that did not have medical review by professional were excluded

Figure S1.1E Overall Ischaemic stroke in all children, stratified by CT/MRI usage, by region



\*all studies that did not report on the use of CT and/or MRI, the older study that used CT only, and the study that did not have medical review by professional were excluded

### 1.2 Arterial ischaemic stroke (AIS)

### Figure S1.2A AIS in neonates

Figure S1.2B AIS in non-neonates



Figure S1.2C AIS in all children



### 1.3 Cerebral venous-sinus thrombosis (CVT)

Figure S1.3A CVT in neonates

Diagram

Description automatically generated

Figure S1.3B CVT in non-neonates



Figure S1.3C CVT in all children



# 2.0 Temporal trend in the Log-incidence rates (per 100,000 persons) from the meta-analysis by stroke type

### 2.1 Overall ischaemic stroke

Figure S2.1A Overall ischaemic stroke in neonates

Unable to generate the bubble plot due to low number of included studies (n=2)

Figure S2.1B Overall ischaemic stroke in non-neonatesChart

Description automatically generated

Figure S2.1C Overall ischaemic stroke in all children Chart

Description automatically generated with low confidence

### 2.2 Arterial ischaemic stroke (AIS)

Figure S2.2A AIS in neonates

A picture containing chart

Description automatically generated

Figure S2.2B AIS in non-neonates

Chart, line chart

Description automatically generated

Figure S2.2C AIS in all children

Chart

Description automatically generated

### 2.3 Cerebral venous-sinus thrombosis (CVT)

Figure S2.3A cerebral venous sinus thrombosis (CVT) in neonates\*

Chart

Description automatically generated

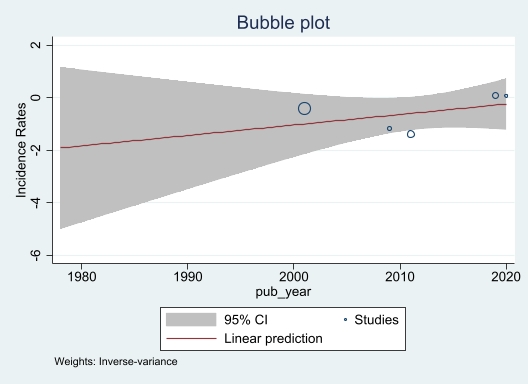
\*The regression was generated from three studies in which one study included data collected over eight years period

Figure S2.3B CVT in non-neonates

Chart, line chart

Description automatically generated

Figure S2.3C CVT in all children



# 3.0 Funnel plots for graphical diagnostics of small-study effects

### 3.1 Overall ischaemic stroke

Figure S3.1A Overall ischaemic stroke in neonates

Chart, line chart

Description automatically generated

Figure S3.1B Overall ischaemic stroke in non-neonates

Chart, line chart, scatter chart

Description automatically generated

Figure S3.1C Overall ischaemic stroke in all children

Chart, line chart

Description automatically generated

### 3.2 Arterial ischaemic stroke

Figure S3.2A AIS in neonates

Chart, scatter chart

Description automatically generated

Figure S3.2B AIS in non-neonates

Chart, line chart

Description automatically generated

Figure S3.2C AIS in all children

Chart, line chart

Description automatically generated

3.1 Cerebral venous-sinus thrombosis (CVT)

Figure S3.3A CVT in neonates

Chart, scatter chart

Description automatically generated

Figure S3.3B CVT in non-neonates

Chart, line chart

Description automatically generated

Figure S3.3C CVT in all children

Chart, line chart, scatter chart

Description automatically generated