



# BMJ Open Trend of cerebral aneurysms over the past two centuries: need for early screening

Arjun Burlakoti <sup>1,2</sup> Jaliya Kumaratilake,<sup>2</sup> Jamie Taylor,<sup>3</sup> Maciej Henneberg <sup>2,4</sup>

**To cite:** Burlakoti A, Kumaratilake J, Taylor J, *et al.* Trend of cerebral aneurysms over the past two centuries: need for early screening. *BMJ Open* 2024;**14**:e081290. doi:10.1136/bmjopen-2023-081290

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<https://doi.org/10.1136/bmjopen-2023-081290>).

Received 24 October 2023  
Accepted 14 February 2024



© Author(s) (or their employer(s)) 2024. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

<sup>1</sup>Human Anatomy, University of South Australia, Adelaide, South Australia, Australia

<sup>2</sup>School of Biomedicine, Faculty of Health and Medical Sciences, Adelaide Medical School, The University of Adelaide, Adelaide, South Australia, Australia

<sup>3</sup>South Australia Medical Imaging, Royal Adelaide Hospital, Adelaide, South Australia, Australia

<sup>4</sup>Institute of Evolutionary Medicine, The University of Zurich, Zürich, Switzerland

## Correspondence to

Dr Arjun Burlakoti;  
[arjun.burlakoti@unisa.edu.au](mailto:arjun.burlakoti@unisa.edu.au)

## ABSTRACT

**Objective** Cerebral aneurysms (CAs) are linked to variations in the cerebral basal arterial network (CBAN). This study aimed to find the optimal age for screening to detect brain arterial variations and predict aneurysms before rupture.

**Design** An observational, quantitative and retrospective research.

**Setting** The study analysed 1127 cases of CAs published from 1761 to 1938. Additionally, CT angiography images of 173-patients at the Royal Adelaide Hospital (RAH), South Australia between 2011 and 2019 were examined for the presence and the location of aneurysms in CBAN.

**Participants** The data were collected from patients at RAH and 407 published sources, including males and females across the entire age range, up to 100 years old.

**Outcome measures and results** Data, CAs cases, from 1761 to 1938 included (526 males, 573 females and 28 unknown sexes). The age of these patients varied from 18 months to 89 years (mean age=42, SD=18). Approximately 11.5% of the CAs occurred in patients aged <20 years. Among the 1078 aneurysms whose location was reported, 76% were located in the internal carotid (IC), middle cerebral (MC) and anterior communicating artery complex (AcomAC) regions, while the remaining 24% were in the vertebrobasilar region. Among 173 patients from RAH aged between 18 and 100 years (male=83 and female=90, mean age=60, SD=16), 94% of the CAs were found in the IC, MC and AcomAC regions. The pattern of aneurysm occurrence, as indicated by values at the 25th, 50th and 75th percentiles, along with the minimum and maximum patient ages, has remained consistent from 1761 to 2019.

**Conclusion** The distribution pattern of CAs in relation to sex, age and locations in the CBAN, remained steady over the last 260 years resulting in risk of strokes early in life. Therefore, early screening for CBAN segment variations is advised for stroke prevention if possible.

## INTRODUCTION

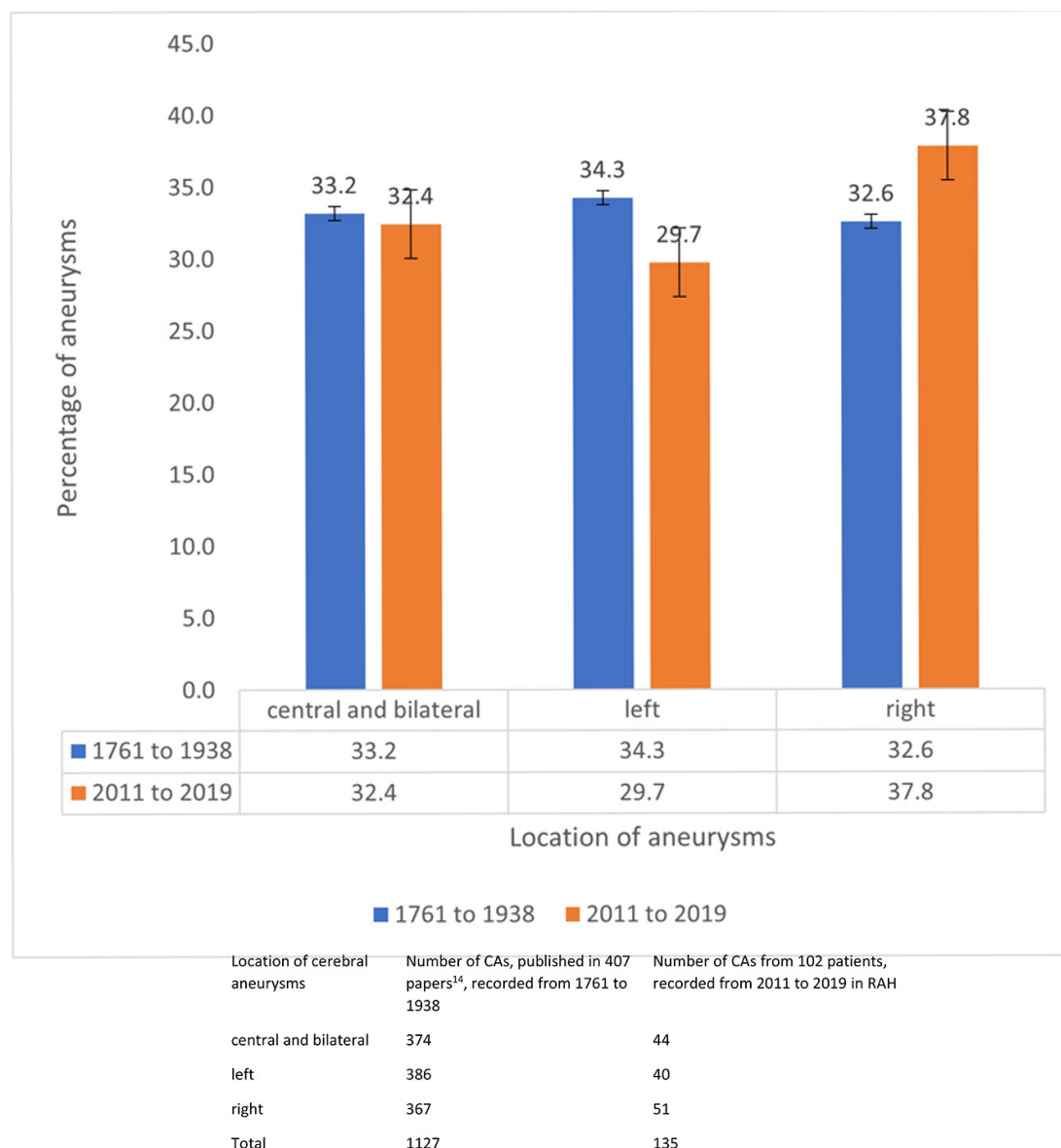
Anatomical variations among components of the cerebral basal arterial network (CBAN) in addition to the trauma, infection, spontaneous dissections and collagen disorders have been linked to the formation of cerebral aneurysms (CAs)<sup>1–3</sup> and such variations develop during the period of embryonic life.<sup>2</sup> The period taken for the development of CAs may vary among individuals and once formed they may enlarge, compress the surrounding

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ To our knowledge, the patterns of distribution and trends of occurrence of cerebral aneurysms have not been systematically studied over the past 260 years.
- ⇒ Aneurysms can develop at any age in the presence of variations in cerebral basal arterial network (CBAN).
- ⇒ Early detection of variations in CBAN in infant using non-invasive Doppler ultrasound technique is recommended and continuing screening regularly as needed.
- ⇒ Reported cases from the tertiary medical centres and 407 papers published over the past 260 years may not represent the general population precisely.
- ⇒ This investigation is not a continuous study.

tissues and rupture leading to subarachnoid haemorrhage (SAH).<sup>3</sup>

CAs of all sizes have been observed to cause SAH in adults<sup>4</sup> (incidence 6–10/100 000), however, they also occur in the age group 0–20 years (incidence rate=1.4–2 per 100 000).<sup>5–7</sup> It is not clear that the occurrence of anatomical variation-related aneurysms is limited to any specific age. The management of complicated CAs is costly and the CAs can leave permanent disabilities or even become fatal costing millions of dollars to families and governments.<sup>7–12</sup> The majority of childhood SAH (ie, incidence 1.4–2 per 100 000 children) are caused by the pre-existing CAs.<sup>13</sup> About 5% of the total cerebral aneurysmal cases diagnosed in the clinical setup were in the age group 0–19 years and the incidence of childhood SAH is significantly greater in the older age children.<sup>13</sup> The clinical manifestation of aneurysmal cases seen later in life might be the consequence of aneurysms that developed in early childhood. Therefore, this study aims to review cases of CAs using data collected from a tertiary medical centre (Royal Adelaide Hospital (RAH), South Australia) and published sources to investigate the recent pattern of CAs and how it has changed over the past 260 years. The null hypothesis is that the advancement of



**Figure 1** Comparison of the location of cerebral aneurysms (CAs) between Royal Adelaide Hospital (RAH) sample (2011–2019) (n=135 CAs from 102 patients, orange colour) with those recorded in 407 publications (1761–1938) (n=1127 CAs, blue colour).<sup>14</sup>

medical science did not lead to a reduction in the prevalence of aneurysms by age.

## MATERIALS AND METHODS

### Study design and setting

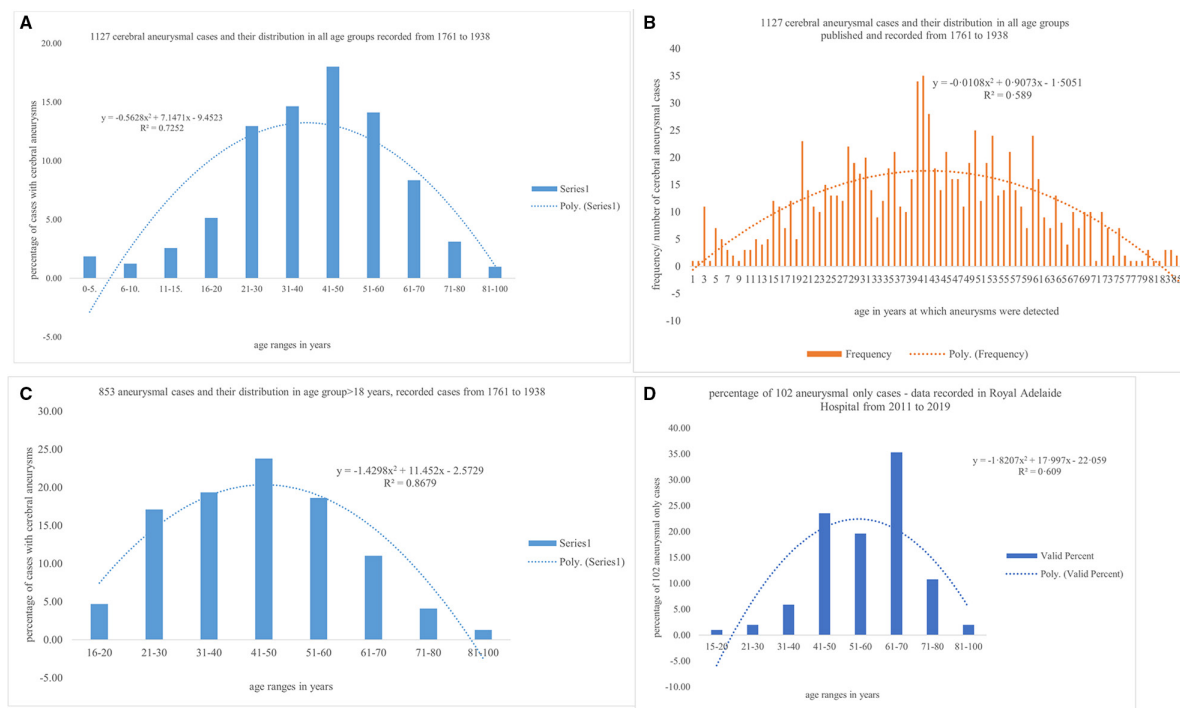
Two types of data were used in this study:

1. Type 1 data are composed of 1127 cerebral aneurysmal cases that were published in the 407 papers from 1761 to 1938, as compiled by McDonald and Korb.<sup>14</sup> These CAs were identified at autopsy and included patients of all ages (average age=41.7 years, mode age=41 years, median age=41 years, SD=17.7, age range 1.5–89 years) (online supplemental files 1 and 2).
2. Type 2 data were cerebral CT angiography (CTA) images obtained from 173 randomly selected patients, who visited RAH, South Australia, between January 2011 and December 2019 for a variety of cranial pathologies;

their age ranged from 18 to 100 years, males=83, females=90, mean age=60 years, median age=62 years, mode age=61 years, SD=15.72) with (n=102) or without (n=71) aneurysms (online supplemental files 2 and 3). These images were anonymised, stored in the Carestream data registry system. The consent documents taken from each patient were not provided to the researchers to ensure privacy. The research materials used in this study comprised 1229 observed cases of CAs that spread across all age groups, spanning a period of approximately 260 years.

### Data sources and size

Type 1 data: a range of variables (such as, the year CAs was detected, age, sex, location of the aneurysm) related to 1127 cases of CAs reported in publications from 1761 to 1938,<sup>14</sup> were transferred into an excel data file, rearranged and subjected to analysis (online supplemental



**Figure 2** Figures displaying the distribution patterns of cerebral aneurysms (CAs) in different age groups recorded from 1761 to 1938 and from 2011 to 2019. A polynomial regression lines show the number and distribution of CA cases across all age groups. (A) The distribution of cerebral aneurysmal cases (n=1127) in various age groups, recorded from 1761 to 1938.<sup>14</sup> (B) The frequency of cerebral aneurysmal cases and their distribution (n=1127) across all age groups recorded<sup>14</sup> from 1761 to 1938. (C) Age-related ( $\geq 18$  years) distribution of individuals affected with CAs over the past 260 years (1761–1938) (n=853), recorded<sup>14</sup> from 1761 to 1938, and (D) age-related (18–100 years) prevalence (%) of CAs in Royal Adelaide Hospital (RAH) sample from 2011 to 2019 (n=102). The peak prevalence occurred between 31 and 60 years (p<0.001).

file 1). Type 2 data: the cerebral CTA of 173 patients recorded from 2011 to 2019 in RAH were accessed to study the presence and absence of CAs in different locations of CBAN based on diagnoses made by clinicians. Some cases had multiple aneurysms located in the various segments of CBAN (online supplemental file 3).

The above cases of CAs were grouped into age ranges 0–5, 6–10, 11–15, 16–20, 21–30, 31–40, 41–50, 51–60, 61–70, 71–80 and >81 years and transferred into the SPSS V.25 software, for analyses (online supplemental file 1). The observation error has been tested by repeating the observation of the location of CAs in the cerebral CTA images in 20 cases, a month after the first study. There was 100% agreement of repeated observations with those of the first one. The sites of the formation of aneurysms were recorded as the left and right, internal carotid artery (ICA), middle cerebral artery (MCA), anterior cerebral artery (ACA), anterior communicating artery complex (AcomAC), posterior communicating artery, posterior cerebral artery, vertebral artery, basilar artery, posterior inferior cerebellar artery, anterior inferior cerebellar artery, superior cerebellar and pial arterial regions. In some cases, the areas of location of aneurysms seemed not to have been mentioned and those cases were tabulated under the heading of ‘aneurysms located in CBAN’. Overall, the locations of nearly 1229 aneurysmal cases from both datasets were broadly divided into four categories: central and bilateral, left

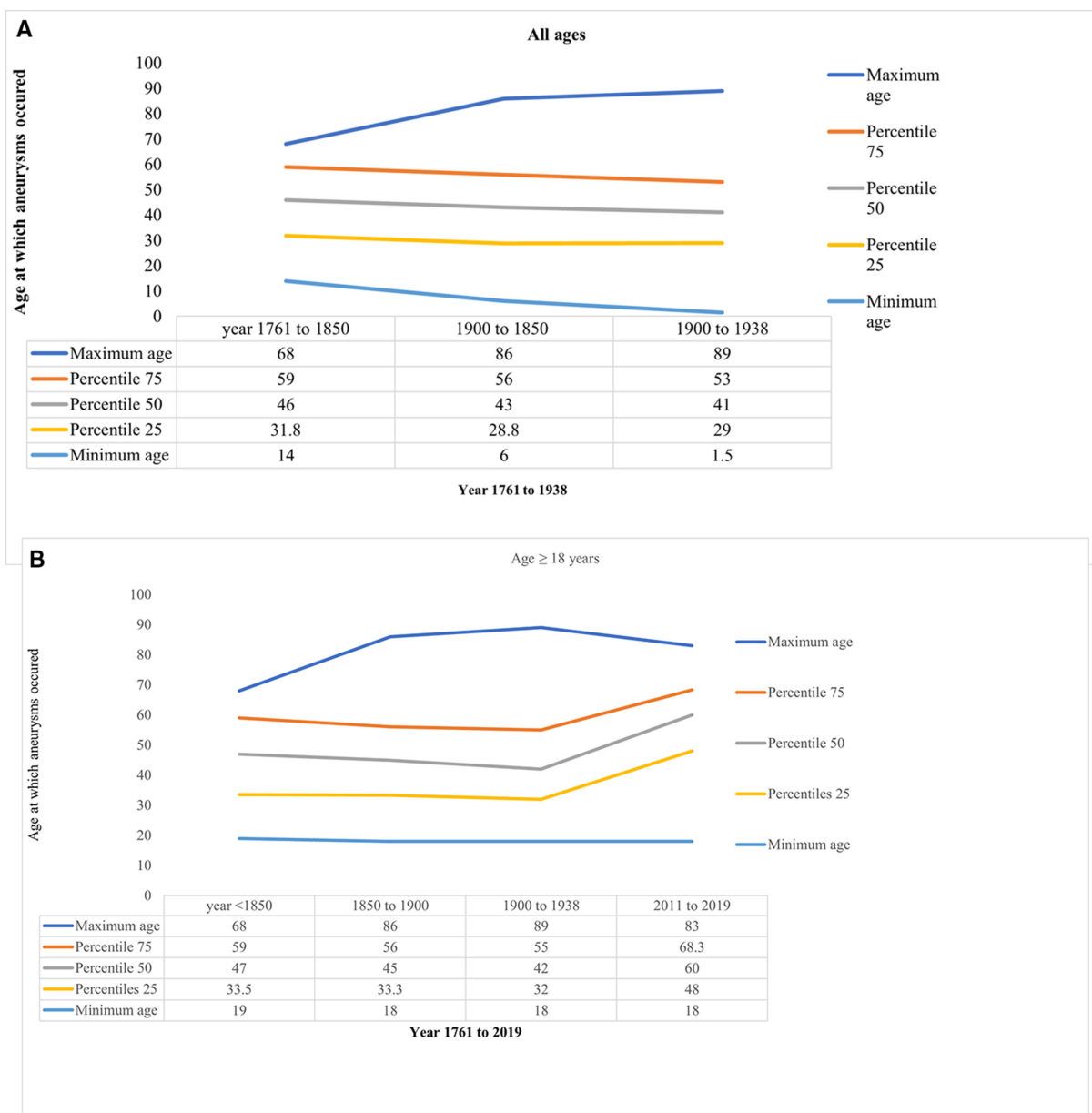
and right (figure 1) before being plotted in the bar charts to study the location and distribution trends of aneurysms in the arterial network over the past 260 years (figure 2). The aneurysms located in the AcomAC, and basilar arterial regions were classified as the central group of aneurysms. Additionally, in a few cases aneurysms were located simultaneously on left and right sides and those cases were grouped as ‘bilateral’ (online supplemental files 1 and 3 and figure 1).

### Statistical methods

Data were analysed using Excel and Statistical Package for the Social Sciences (SPSS-IBM, V.25) program (eg, descriptive and  $\chi^2$  tests). The p values <0.05 were considered as statistically significant.

### Patient and public involvement

Involving patients was challenging for conducting and planning this research, since researchers were allowed the access only to anonymised raw data recorded in the database. As per the ethics permit, we accessed retrospective anonymised data, precluding patient involvement in research planning and execution. The shared outcome of this study will be informed to the public, families and patients who attend medical centres for various clinical visits, through a series of meetings, seminars and media releases.



**Figure 3** Comparison figures showing the trend of occurrence of cerebral aneurysms at different age group (n=1127) from 1761 to 2019. (A) The values of the 25th, 50th and 75th percentiles, as well as the minimum and maximum observed all ages of patients with aneurysms, from 1761 to 1938.<sup>14</sup> (B) The values of the 25th, 50th and 75th percentiles, as well as the minimum and maximum observed patients with >18 years of age with aneurysms, recorded from 1761 to 1938<sup>14</sup> and 2011 to 2019 in Royal Adelaide Hospital.

## Findings

This study reviewed 1127 aneurysmal cases of patients of all ages from a total of 407 published articles prior to the year 1939. The ages of these patients (males=526, females=573, unknown sex=28) ranged from 18 months to 89 years of age with an average of 41.70 years, mode of 41 years and median of 41 years (SD=17.7) (online supplemental file 2, figure 2A–C and online supplemental file 1). The second group of patients with CAs (44 males and 58 females, and n=102) from RAH (2011–2019) with the age range 18–100 years showed that the most common age for diagnosis or complication of CAs ranged from 31 to 60 years with the calculated mean, median, mode

and SD of 57.60, 60.00, 48.00 and 13.12 years, respectively (figure 2D and online supplemental file 4). Analysis of both sets of data revealed that the majority of the patients who presented with complicated aneurysms were in their third to sixth decades of life (online supplemental file 2).

The most important aspect of the two sets of data was the wide age range of occurrence of CAs and the fact that some of the complicated aneurysmal cases appeared at an early age (figure 2A,B, online supplemental file 1). A separate analysis was conducted for 853 out of the 1127 cases of CAs recorded before 1938 (males=409, females=438, unknown sex=6), specifically focusing on the age range of 18–89 years to align the age groups with



**Table 1** Prevalence of cerebral aneurysms in males and females: a comparison of the recent hospital-based data recorded in RAH from 2011 to 2019 with the autopsy data published before from 1761 to 1938

Sex	N=173, cases with or without cerebral aneurysms recorded in RAH from 2011 to 2019	N=1127 aneurysm cases (from 1761 to 1938) recorded in 407 publications <sup>14</sup>
Sex not defined	0	28
Female	90	573
Male	83	526
Female-to-male sex ratio	1.08	1.09

\*This study investigated the prevalence of cerebral aneurysms in both males and females, drawing a comparison between recent hospital-based data recorded in RAH (2011–2019) and autopsy data published between 1761 and 1938.

N, Number of aneurysmal cases; RAH, Royal Adelaide Hospital; RAH, Royal Adelaide Hospital.

the RAH recorded data from 2011 to 2019 (online supplemental file 2, [figure 2C,D](#)). The similarities of SD (15.45) of those 853 cases (from 1761 to 1938) and the cases that were recorded from 2011 to 2019 in RAH (13.12 years) validated the comparability of our data and the findings (online supplemental file 2). The values of the 25th, 50th and 75th percentiles, as well as the minimum and maximum observed ages of patients with aneurysms, remained relatively stable from 1761 to 1938 ([figure 3A](#)). Some of these percentile values increased slightly as life expectancy extended from 1761 to the 21st century ([figure 3B](#)). Therefore, the SD, and age distribution of adult patients with ruptured or diagnosed CAs presented in the 2011–2019 dataset were consistent with those cases reported before 1938, indicating persistence of a pattern ([table 1](#), [figures 2 and 3](#)). Specifically, aneurysms are being frequently diagnosed in individuals aged 30–60 years, and this age range has remained relatively unchanged over the past 260 years ([table 1](#), [figures 2 and 3](#)). Forty-nine out of 1127 cases recorded across 407 publications from 1761 to 1938 seemed not to have information about the location of aneurysms in the CBAN, however, 818 out of 1078 identified aneurysms (76%) were in the ICA, MCA and AcomAC regions and rest of them were in the vertebrobasilar region (online supplemental file 1). The location and distribution pattern of aneurysms from 102 patients recorded in RAH was consistent with 1078 cases recorded from 1761 to 1938 (online supplemental files 1–3).

In the type 2 dataset, a total of 135 aneurysms were identified in 102 individuals, with ages ranging from 18 to 83 years, across various components of CBAN ([figure 2D](#) and online supplemental file 3). Among these aneurysms, 38 (28.14%) were detected in the right MCA region, while 17 (12.6%) were in the right ICA region. In comparison, the left MCA and ICA regions had 27 (20%) and 12 (8%) aneurysms, respectively, which appeared to be lower in number compared with the right MCA and ICA regions. When considering the distribution of aneurysms based on territory, 55 out of 135 aneurysms (40.74%) in 50 patients were found in the right ICA and MCA territories, whereas 39 out of 135 aneurysms (28.88%) in 37 patients were detected in the left ICA and MCA regions (online

supplemental file 3). Out of the 102 individuals with aneurysmal cases included in the study, 33 (24.44%) had aneurysms located in the AcomAC region, accounting for 33 out of the total 135 aneurysms. An additional 5.9% of the total aneurysms (8 out of 135 aneurysms) were found in the vertebral and basilar arterial regions, as indicated in the online supplemental file 3. A majority of the CAs, 127 out of the total 135 (94% of the total), were in the MCA, ICA and AcomAC regions (online supplemental file 3). Some cases had multiple aneurysms, for example, 2 cases had right ICA and MCA aneurysms, while 10 cases had left ICA and MCA aneurysms (online supplemental file 3).

There were no significant differences between male and female patients affected with CAs in all 1229 cases analysed in those two datasets ( $\chi^2$  statistic=0.83,  $p \geq 0.36$ ) ([table 1](#)). The sex, age of occurrence and location of CAs appear to have remained steady over the past 260 years across all age groups ([table 1](#) and online supplemental file 2, and [figure 3](#)). The mode, mean and median age and SD of patients with ruptured or diagnosed CAs studied from 2011 to 2019 in RAH matched well with the cerebral aneurysmal cases recorded in the past considering the difference in life expectancy between the two time periods studied (1761–1938 and 2011–2019) ([figure 3](#) and [table 1](#)).

## DISCUSSION

The age and locations at which CAs occur in the CBAN has not changed over past 260 years ([figures 1–3](#), [table 1](#)) despite the life expectancy has increased over time worldwide and the progress in medicine. In the past people had shorter life span on average, and yet the CAs occurred at the same ages as they do now.<sup>15</sup> The life expectancy recorded at below 50 years in 1940 and even below 40 years in 1850 was way lower compared with the one recorded above 80 years of age since the year 2000 in Australia.<sup>15</sup> A separate analysis was done for 853 out of the 1127 CAs recorded<sup>14</sup> before 1938 focusing on the age range of 18–89 years to align the age group with the currently RAH recorded data from 2011 to 2019, since there were no aneurysmal cases of children (age <18

years) in the RAH dataset. In Adelaide, there is a separate hospital for children where aneurysmal cases would have been treated, but the authors had no access to these data (online supplemental file 3). RAH is a general hospital, thus individuals aged 18 years and less are not admitted. Current study compared the cases of CAs diagnosed by CTA imaging technique (from 2011 to 2019) with those verified by surgery and autopsy,<sup>14</sup> since there were no cerebral angiogram facilities in early years (ie, before 1938). The cases of aneurysms are commonly diagnosed, when the patients are presented at medical centres after attacks of stroke.<sup>16</sup> CAs in the past seemed to be ruptured and complicated as early as 18 months of age and as late as 89 years of age with a wide range of age (online supplemental file 1). The findings suggested that the change in lifestyle or medical practice had no effect at the age/time of formation of CAs in general population. Clinical investigation of lipid profiles in patients commenced after 1950,<sup>17</sup> and they started attributing arterial diseases and aneurysms to the hyperlipidaemia, however, the manifestation of occurrence of aneurysms by age in the past 260 years seems not to be different from the current age of occurrence. Although the lifestyle and the external influences, including medical practice, changed over more than two centuries, aneurysms still occur at approximately the same age. Therefore, aneurysms occur and rupture on their own internal circumstances and are not related to the diet, environmental and external factors.<sup>18</sup> The most likely internal factor is the severity of the variation on the segments of CBAN that adversely affects the haemodynamics resulting in the formation of aneurysms.<sup>1 19</sup> The condition of the arterial wall should not have changed over the last 260 years and that seems to be less significant than the variation in the components of CBAN. The segmental and communicating arteries play a crucial role in dampening the systolic pressure within the CBAN and reducing the likelihood of aneurysm formation.<sup>1 19</sup> The severity of arterial variation can have negative effects on the blood flow dynamics through the variant segment of the component of the CBAN.<sup>1 19</sup> The incidence of CAs is about 3.3% in the general population and may not be diagnosed, until they get enlarged as the size of the aneurysm <3 mm in diameter can be missed.<sup>20</sup> Imaizumi *et al* found that the prevalence rate of CAs was 4.32% in Japan.<sup>12</sup> The incidence rate of CAs in childhood (age <18 years) has been reported to be 0.5%–4.6%, which is almost as common as the incidence rate observed among adults.<sup>13</sup> Treating cases of CAs with a diameter <3 mm requires careful consideration, as pre-existing small aneurysms of ≤3 mm could rupture, resulting in spontaneous SAH.<sup>21</sup> The majority of CAs are detected only when they cause a stroke or other pathological effect (eg, compression of the optic tract).<sup>4</sup> Individuals >18 years are no longer considered children.<sup>6 13</sup>

Most of the symptomatic cases of CAs in the paediatric age group were observed in older children (15+ years),<sup>13</sup> and only complicated cases of CAs were generally diagnosed and reported.<sup>22 23</sup> If the incidence

of childhood CAs described (ranges from 0.17% to 4.6%)<sup>24</sup> is corrected for number of years lived, it would be 18.4% of the total aneurysmal cases among adults. The adult patients included in CAs studies ideally have an age range of 18 years and above, which can include individuals up to the age of 100 years.<sup>12 15</sup> In contrast, the childhood group included in aneurysmal studies typically ranges from birth up to 18 years of age and a few studies have categorised patients who are 18 years or older under the adult group.<sup>6 13</sup> When the age range, 0–18 years and 19–100 years is considered, the incidence of childhood CAs, that should be multiplied by 5 times to correct for the number of years lived, can be comparable to that in adults because the childhood period of life is much shorter than the adulthood. Therefore, the age range of adult group (≥20 years up to 100 years) included in the CAs and stroke studies would be about 5 times more than the age range of children (ie, ≤18 years).<sup>22 23</sup> That means adults have 5 times more years to develop CAs compared with children. Therefore, the incidence of childhood CAs per year is almost equivalent to adult.<sup>21 25</sup> Hence, CAs could develop in early childhood in the presence of a significantly variant component of cerebral arterial anatomy,<sup>1 2</sup> and it could take years for them to balloon before becoming symptomatic and being observed in a tertiary medical centre. The overall pattern of location and distribution of childhood CAs was similar to adult as they commonly occurred in ICA, MCA and AcomAC regions.<sup>3</sup> Therefore, the development of CAs is not age related and found to be prevalent in all age ranges.<sup>10 12 13 26</sup> CAs may not always be associated with the advanced age, history of smoking, drinking alcohol but start forming as early as in the childhood in the presence of variant components of cranial blood vessels.<sup>27</sup> The mean age at which people were affected by CAs was reported to be 55–57 years of age in a study conducted using 1085 aneurysmal cases from 2008 to 2016.<sup>28</sup> There are a few reports of CAs published between 1938 and 2011 that could have been compiled for statistical analyses. However, their inclusion into this study would not have changed its basic conclusions, that is, large age range and no change through time in the occurrence of CAs.

Ultrasonographic video screening by placing the probe in the fontanelles of babies before they close has been found to be safe and effective in studying brain vessels<sup>26 29</sup> and can be incorporated as a screening tool to detect variations in intracranial vessels that could predispose to the development of CAs later in life. One illustration of such possibility is that individuals with the left and right ACA proximal segment diameter ratio >1.4 have a 27-fold increased risk of developing CAs in the AcomAC region.<sup>1</sup> Parents of children found to have variations in CBAN could be advised to schedule follow-up screening periodically, especially if a more affordable and convenient technology

for detecting brain aneurysms becomes available. The current screening recommendation is based on the congenital variations of segments of CBAN, but such variations could occur later on life in cases of pathology like atherosclerosis and could cause aneurysms. Future studies to test the association of presence of anatomical variations in CBAN in infancy and future risk of both unruptured and ruptured intracranial aneurysms in adulthood are recommended.

The estimated cost of a single stroke is approximately \$A300 000 in Australia.<sup>9</sup> With a haemorrhagic stroke incidence of 10 per 100 000, the total cost amounts to \$A45 million per year in a city like Adelaide,<sup>1</sup> South Australia, which has a population of 1.5 million. Regular screening for individuals with significantly variant brain arteries identified, representing 50% of the population, once every 5 years, and assuming the cost of a single CTA or magnetic resonance angiogram is about \$A100 each, the total screening cost would be \$A1.5 million per year, that means 30 times reduction in cost of strokes. Additionally, the government would receive millions of dollars in return as tax revenue from working individuals who would survive with little to no disability from potential strokes resulting from aneurysms. This study was not designed to examine the characteristics of aneurysms, but the focus was on the distribution of aneurysms in different segments of CBAN, trend of occurrence of aneurysms over the past 260 years and the comparison of CAs in all age ranges.

## Limitations

The insufficient data on the lack of personal and family history, history of smoking, lipid profile and blood pressure are limitations of this study. A larger survey and a prospective study could be conducted. A prospective study could involve using ultrasound techniques to identify variations in brain vessels among infants.

## CONCLUSION

Brain arterial aneurysms can develop early in the presence of variant arterial components. Screening children under 24 months using transcranial ultrasonography for variant cerebral arteries may be practical. Those with variations should undergo periodic tests for aneurysms, aiming to prevent some haemorrhagic strokes if an affordable and convenient technology for detecting brain aneurysms becomes available.

**Twitter** Arjun Burlakoti @draburlakoti

**Contributors** AB is responsible for the overall content as the guarantor and accepts full responsibility for the work and the conduct of the study, has access to the data and controls the decision to publish. AB conceived the idea, collected and analysed both sets of data, took pictures, recorded videos, contributed to conceptualisation, prepared and drafted the manuscript. JK conceived the idea, contributed to the concept, aided in data interpretation, editing and the revision of the manuscript and approving the article. JT conceived the idea, contributed to the concept, aided in data interpretation, editing and the revision of the manuscript and approving the article. MH conceived the idea, masterminded and helped in statistics, data analysis and interpretation, editing and approving the article.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** The Human Ethics permit (approval number: H2014176, Research Ethics Committee, Office of Research Ethics, Compliance and Integrity, Faculty of Health Sciences, University of Adelaide) granted permission to access and use the de-identified dataset from the Carestream data registry system (Vue-RIS-version-11.0.14.35) for research. The patients gave their consent to use their clinical information for research activities.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available on reasonable request. Not applicable/uploaded as supplementary information.

**Supplemental material** This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

## ORCID iDs

Arjun Burlakoti <http://orcid.org/0000-0001-9317-6352>

Maciej Henneberg <http://orcid.org/0000-0003-1941-2286>

## REFERENCES

- Burlakoti A, Kumaratilake J, Taylor J, *et al*. Relationship between cerebral aneurysms and variations in cerebral basal arterial network: a morphometric cross-sectional study in computed tomography angiograms from a neurointerventional unit. *BMJ Open* 2021;11:e051028.
- Menshawi K, Mohr JP, Gutierrez J. A functional perspective on the embryology and anatomy of the cerebral blood supply. *J Stroke* 2015;17:144–58.
- Mehrotra A, Nair AP, Das KK, *et al*. Clinical and radiological profiles and outcomes in pediatric patients with intracranial aneurysms. *J Neurosurg Pediatr* 2012;10:340–6.
- Roessler K, Cejna M, Zachenhofer I. Aneurysmatic subarachnoidal haemorrhage: incidence and location of small ruptured cerebral aneurysms – a retrospective population-based study. *Wien Klin Wochenschr* 2011;123:444–9.
- Storrs BB, Humphreys RP, Hendrick EB, *et al*. Intracranial aneurysms in the pediatric age-group. *Pediatr Neurosurg* 1982;9:358–61.
- Proust F, Toussaint P, Garnié J, *et al*. Pediatric cerebral aneurysms. *J Neurosurg* 2001;94:733–9.
- Horikoshi T, Akiyama I, Yamagata Z, *et al*. Retrospective analysis of the prevalence of asymptomatic cerebral aneurysm in 4518 patients undergoing magnetic resonance angiography—when does cerebral aneurysm develop? *Neurol Med Chir (Tokyo)* 2002;42:105–12.
- Froelich JJ, Neilson S, Peters-Wilke J, *et al*. Size and location of ruptured intracranial aneurysms: a 5-year clinical survey. *World Neurosurg* 2016;91:260–5.
- Cadilhac DA, Carter R, Thrift AG, *et al*. Estimating the long-term costs of ischemic and hemorrhagic stroke for Australia: new evidence derived from the North East Melbourne stroke incidence study (NEMESIS). *Stroke* 2009;40:915–21.
- Jeong Y-G, Jung Y-T, Kim M-S, *et al*. Size and location of ruptured intracranial aneurysms. *J Korean Neurosurg Soc* 2009;45:11–5.
- Korja M, Kivisaari R, Rezaei Jahromi B, *et al*. Size and location of ruptured intracranial aneurysms: consecutive series of 1993 hospital-admitted patients. *J Neurosurg* 2017;127:748–53.

- 12 Imaizumi Y, Mizutani T, Shimizu K, *et al.* Detection rates and sites of unruptured intracranial aneurysms according to sex and age: an analysis of MR angiography-based brain examinations of 4070 healthy Japanese adults. *J Neurosurg* 2018;130:573–8.
- 13 Jordan LC, Johnston SC, Wu YW, *et al.* The importance of cerebral aneurysms in childhood hemorrhagic stroke: a population-based study. *Stroke* 2009;40:400–5.
- 14 McDonald CA, Korb B. Intracranial aneurysms. *Arch Neuropsych* 1939;42:298.
- 15 Moore S, Simon JL. The greatest century that ever was. New York Times; 1999.
- 16 McGuinness B, Chieng N, Skipworth C, *et al.* Small ruptured cerebral aneurysms—do they rupture on formation or not? *Neuroradiology* 2022;64:597–602.
- 17 Long MT, Fox CS. The framingham heart study--67 years of discovery in metabolic disease. *Nat Rev Endocrinol* 2016;12:177–83.
- 18 McCorry S, Literature MJ. Literature and meat since 1900. 1st edn. Cham: Springer International Publishing, 2019.
- 19 Alastruey J, Parker KH, Peiró J, *et al.* Modelling the circle of Willis to assess the effects of anatomical variations and occlusions on cerebral flows. *J Biomech* 2007;40:1794–805.
- 20 Yoon NK, McNally S, Taussky P, *et al.* Imaging of cerebral aneurysms: a clinical perspective. *Neurovasc Imaging* 2016;2:1–7.
- 21 McGuinness B, Chieng N, Skipworth C, *et al.* Small ruptured cerebral aneurysms—do they rupture on formation or not? *Neuroradiology* 2022;64:597–602.
- 22 Brown RD, Broderick JP. Unruptured intracranial aneurysms: epidemiology, natural history, management options, and familial screening. *Lancet Neurol* 2014;13:393–404.
- 23 Walendy V, Strauss C, Rachinger J, *et al.* Treatment of aneurysmal subarachnoid haemorrhage in Germany: a nationwide analysis of the years 2005–2009. *Neuroepidemiology* 2014;42:90–7.
- 24 Pasqualin A, Mazza C, Cavazzani P, *et al.* Intracranial aneurysms and subarachnoid hemorrhage in children and adolescents. *Childs Nerv Syst* 1986;2:185–90.
- 25 Matson DD. Intracranial arterial aneurysms in childhood. *J Neurosurg* 1965;23:578–83.
- 26 Huisman TA, Poretti A. Pediatric neurovascular imaging (CT/MRI/ultrasound). In: *Pediatric vascular neurosurgery*. Springer, 2016: 77–109.
- 27 Krings T, Geibprasert S, terBrugge KG. Pathomechanisms and treatment of pediatric aneurysms. *Childs Nerv Syst* 2010;26:1309–18.
- 28 Fung C, Mavrakis E, Filis A, *et al.* Anatomical evaluation of intracranial aneurysm rupture risk in patients with multiple aneurysms. *Neurosurg Rev* 2019;42:539–47.
- 29 Verlhac S. Transcranial doppler in children. *Pediatr Radiol* 2011;41:S153–65.



[illegible]

27 11-30	27	aniline	BA	a	lysine	1880			
28 12-20	28	aniline	MA	a	lysine	1881			
29 12-30	29	aniline	MA	a	lysine	1882			
30 12-30	30	aniline	MA	a	lysine	1883			
31 12-30	31	aniline	MA	a	lysine	1884			
32 12-30	32	aniline	MA	a	lysine	1885			
33 12-30	33	aniline	MA	a	lysine	1886			
34 12-30	34	aniline	MA	a	lysine	1887			
35 12-30	35	aniline	MA	a	lysine	1888			
36 12-30	36	aniline	MA	a	lysine	1889			
37 12-30	37	aniline	MA	a	lysine	1890			
38 12-30	38	aniline	MA	a	lysine	1891			
39 12-30	39	aniline	MA	a	lysine	1892			
40 12-30	40	aniline	MA	a	lysine	1893			
41 12-30	41	aniline	MA	a	lysine	1894			
42 12-30	42	aniline	MA	a	lysine	1895			
43 12-30	43	aniline	MA	a	lysine	1896			
44 12-30	44	aniline	MA	a	lysine	1897			
45 12-30	45	aniline	MA	a	lysine	1898			
46 12-30	46	aniline	MA	a	lysine	1899			
47 12-30	47	aniline	MA	a	lysine	1900			
48 12-30	48	aniline	MA	a	lysine	1901			
49 12-30	49	aniline	MA	a	lysine	1902			
50 12-30	50	aniline	MA	a	lysine	1903			
51 12-30	51	aniline	MA	a	lysine	1904			
52 12-30	52	aniline	MA	a	lysine	1905			
53 12-30	53	aniline	MA	a	lysine	1906			
54 12-30	54	aniline	MA	a	lysine	1907			
55 12-30	55	aniline	MA	a	lysine	1908			
56 12-30	56	aniline	MA	a	lysine	1909			
57 12-30	57	aniline	MA	a	lysine	1910			
58 12-30	58	aniline	MA	a	lysine	1911			
59 12-30	59	aniline	MA	a	lysine	1912			
60 12-30	60	aniline	MA	a	lysine	1913			
61 12-30	61	aniline	MA	a	lysine	1914			
62 12-30	62	aniline	MA	a	lysine	1915			
63 12-30	63	aniline	MA	a	lysine	1916			
64 12-30	64	aniline	MA	a	lysine	1917			
65 12-30	65	aniline	MA	a	lysine	1918			
66 12-30	66	aniline	MA	a	lysine	1919			
67 12-30	67	aniline	MA	a	lysine	1920			
68 12-30	68	aniline	MA	a	lysine	1921			
69 12-30	69	aniline	MA	a	lysine	1922			
70 12-30	70	aniline	MA	a	lysine	1923			
71 12-30	71	aniline	MA	a	lysine	1924			
72 12-30	72	aniline	MA	a	lysine	1925			
73 12-30	73	aniline	MA	a	lysine	1926			
74 12-30	74	aniline	MA	a	lysine	1927			
75 12-30	75	aniline	MA	a	lysine	1928			
76 12-30	76	aniline	MA	a	lysine	1929			
77 12-30	77	aniline	MA	a	lysine	1930			
78 12-30	78	aniline	MA	a	lysine	1931			
79 12-30	79	aniline	MA	a	lysine	1932			
80 12-30	80	aniline	MA	a	lysine	1933			
81 12-30	81	aniline	MA	a	lysine	1934			
82 12-30	82	aniline	MA	a	lysine	1935			
83 12-30	83	aniline	MA	a	lysine	1936			
84 12-30	84	aniline	MA	a	lysine	1937			
85 12-30	85	aniline	MA	a	lysine	1938			
86 12-30	86	aniline	MA	a	lysine	1939			
87 12-30	87	aniline	MA	a	lysine	1940			
88 12-30	88	aniline	MA	a	lysine	1941			
89 12-30	89	aniline	MA	a	lysine	1942			
90 12-30	90	aniline	MA	a	lysine	1943			
91 12-30	91	aniline	MA	a	lysine	1944			
92 12-30	92	aniline	MA	a	lysine	1945			
93 12-30	93	aniline	MA	a	lysine	1946			
94 12-30	94	aniline	MA	a	lysine	1947			
95 12-30	95	aniline	MA	a	lysine	1948			
96 12-30	96	aniline	MA	a	lysine	1949			
97 12-30	97	aniline	MA	a	lysine	1950			
98 12-30	98	aniline	MA	a	lysine	1951			
99 12-30	99	aniline	MA	a	lysine	1952			
100 12-30	100	aniline	MA	a	lysine	1953			
101 12-30	101	aniline	MA	a	lysine	1954			
102 12-30	102	aniline	MA	a	lysine	1955			
103 12-30	103	aniline	MA	a	lysine	1956			
104 12-30	104	aniline	MA	a	lysine	1957			
105 12-30	105	aniline	MA	a	lysine	1958			
106 12-30	106	aniline	MA	a	lysine	1959			
107 12-30	107	aniline	MA	a	lysine	1960			
108 12-30	108	aniline	MA	a	lysine	1961			
109 12-30	109	aniline	MA	a	lysine	1962			
110 12-30	110	aniline	MA	a	lysine	1963			
111 12-30	111	aniline	MA	a	lysine	1964			
112 12-30	112	aniline	MA	a	lysine	1965			
113 12-30	113	aniline	MA	a	lysine	1966			
114 12-30	114	aniline	MA	a	lysine	1967			
115 12-30	115	aniline	MA	a	lysine	1968			
116 12-30	116	aniline	MA	a	lysine	1969			
117 12-30	117	aniline	MA	a	lysine	1970			
118 12-30	118	aniline	MA	a	lysine	1971			
119 12-30	119	aniline	MA	a	lysine	1972			
120 12-30	120	aniline	MA	a	lysine	1973			
121 12-30	121	aniline	MA	a	lysine	1974			
122 12-30	122	aniline	MA	a	lysine	1975			
123 12-30	123	aniline	MA	a	lysine	1976			
124 12-30	124	aniline	MA	a	lysine	1977			
125 12-30	125	aniline	MA	a	lysine	1978			
126 12-30	126	aniline	MA	a	lysine	1979			
127 12-30	127	aniline	MA	a	lysine	1980			
128 12-30	128	aniline	MA	a	lysine	1981			
129 12-30	129	aniline	MA	a	lysine	1982			
130 12-30	130	aniline	MA	a	lysine	1983			
131 12-30	131	aniline	MA	a	lysine	1984			
132 12-30	132	aniline	MA	a	lysine	1985			
133 12-30	133	aniline	MA	a	lysine	1986			
134 12-30	134	aniline	MA	a	lysine	1987			
135 12-30	135	aniline	MA	a	lysine	1988			
136 12-30	136	aniline	MA	a	lysine	1989			
137 12-30	137	aniline	MA	a	lysine	1990			
138 12-30	138	aniline	MA	a	lysine	1991			
139 12-30	139	aniline	MA	a	lysine	1992			
140 12-30	140	aniline	MA	a	lysine	1993			
141 12-30	141	aniline	MA	a	lysine	1994			
142 12-30	142	aniline	MA	a	lysine	1995			
143 12-30	143	aniline	MA	a	lysine	1996			
144 12-30	144	aniline	MA	a	lysine	1997			
145 12-30	145	aniline	MA	a	lysine	1998			
146 12-30	146	aniline	MA	a	lysine	1999			
147 12-30	147	aniline	MA	a	lysine	2000			
148 12-30	148	aniline	MA	a	lysine	2001			
149 12-30	149	aniline	MA	a	lysine	2002			
150 12-30	150	aniline	MA	a	lysine	2003			
151 12-30	151	aniline	MA	a	lysine	2004			
152 12-30	152	aniline	MA	a	lysine	2005			
153 12-30	153	aniline	MA	a	lysine	2006			
154 12-30	154	aniline	MA	a	lysine	2007			
155 12-30	155	aniline	MA	a	lysine	2008			
156 12-30	156	aniline	MA	a	lysine	2009			
157 12-30	157	aniline	MA	a	lysine	2010			
158 12-30	158	aniline	MA	a	lysine	2011			
159 12-30	159	aniline	MA	a	lysine	2012			
160 12-30	160	aniline	MA	a	lysine	2013			
161 12-30	161	aniline	MA	a	lysine	2014			
162 12-30	162	aniline	MA	a	lysine	2015			
163 12-30	163	aniline	MA	a	lysine	2016			
164 12-30	164	aniline	MA	a	lysine	2017			
165 12-30	165	aniline	MA	a	lysine	2018			
166 12-30	166	aniline	MA	a	lysine	2019			
167 12-30	167	aniline	MA	a	lysine	2020			
168 12-30	168	aniline	MA	a	lysine	2021			
169 12-30	169	aniline	MA	a	lysine	2022			
170 12-30	170	aniline	MA	a	lysine	2023			
171 12-30	171	aniline	MA	a	lysine	2024			
172 12-30	172	aniline	MA	a	lysine	2025			
173 12-30	173	aniline	MA	a	lysine	2026			
174 12-30	174	aniline	MA	a	lysine	2027			
175 12-30	175	aniline	MA	a	lysine	2028			
176 12-30	176	aniline	MA	a	lysine	2029			
177 12-30	177	aniline	MA	a	lysine	2030			
178 12-30	178	aniline	MA	a	lysine	2031			
179 12-30	179	aniline	MA	a	lysine	2032			
180 12-30	180	aniline	MA	a	lysine	2033			
181 12-30	181	aniline	MA	a	lysine	2034			
182 12-30	182	aniline	MA	a	lysine	2035			
183 12-30	183	aniline	MA	a	lysine	2036			
184 12-30	184	aniline	MA	a	lysine	2037			
185 12-30	185	aniline	MA	a	lysine	2038			
186 12-30	186	aniline	MA	a	lysine	2039			
187 12-30	187	aniline	MA	a	lysine	2040			
188 12-30	188	aniline	MA	a	lysine	2041			
189 12-30	189	aniline	MA	a	lysine	2042			
190 12-30	190	aniline	MA	a	lysine	2043			
191 12-30	191	aniline	MA	a	lysine	2044			
192 12-30	192	aniline	MA	a	lysine	2045			
193 12-30	193	aniline	MA	a	lysine	2046			
194 12-30	194	aniline	MA	a	lysine	2047			
195 12-30	195	aniline	MA	a	lysine	2048			
196 12-30	196	aniline	MA	a	lysine	2049			
197 12-30	197	aniline	MA	a	lysine	2050			
198 12-30	198	aniline	MA	a	lysine	2051			
199 12-30	199	aniline	MA						

32	11-10	m	unl	BA	1	Synthetic, synthetic children of, synthetic youth	1911
33	11-10	m	unl	BA	1	no information available	1912
34	11-10	m	unl	BA	1	no information available	1913
35	11-10	m	unl	BA	1	no information available	1914
36	11-10	m	unl	BA	1	no information available	1915
37	11-10	m	unl	BA	1	no information available	1916
38	11-10	m	unl	BA	1	no information available	1917
39	11-10	m	unl	BA	1	no information available	1918
40	11-10	m	unl	BA	1	no information available	1919
41	11-10	m	unl	BA	1	no information available	1920
42	11-10	m	unl	BA	1	no information available	1921
43	11-10	m	unl	BA	1	no information available	1922
44	11-10	m	unl	BA	1	no information available	1923
45	11-10	m	unl	BA	1	no information available	1924
46	11-10	m	unl	BA	1	no information available	1925
47	11-10	m	unl	BA	1	no information available	1926
48	11-10	m	unl	BA	1	no information available	1927
49	11-10	m	unl	BA	1	no information available	1928
50	11-10	m	unl	BA	1	no information available	1929
51	11-10	m	unl	BA	1	no information available	1930
52	11-10	m	unl	BA	1	no information available	1931
53	11-10	m	unl	BA	1	no information available	1932
54	11-10	m	unl	BA	1	no information available	1933
55	11-10	m	unl	BA	1	no information available	1934
56	11-10	m	unl	BA	1	no information available	1935
57	11-10	m	unl	BA	1	no information available	1936
58	11-10	m	unl	BA	1	no information available	1937
59	11-10	m	unl	BA	1	no information available	1938
60	11-10	m	unl	BA	1	no information available	1939
61	11-10	m	unl	BA	1	no information available	1940
62	11-10	m	unl	BA	1	no information available	1941
63	11-10	m	unl	BA	1	no information available	1942
64	11-10	m	unl	BA	1	no information available	1943
65	11-10	m	unl	BA	1	no information available	1944
66	11-10	m	unl	BA	1	no information available	1945
67	11-10	m	unl	BA	1	no information available	1946
68	11-10	m	unl	BA	1	no information available	1947
69	11-10	m	unl	BA	1	no information available	1948
70	11-10	m	unl	BA	1	no information available	1949
71	11-10	m	unl	BA	1	no information available	1950
72	11-10	m	unl	BA	1	no information available	1951
73	11-10	m	unl	BA	1	no information available	1952
74	11-10	m	unl	BA	1	no information available	1953
75	11-10	m	unl	BA	1	no information available	1954
76	11-10	m	unl	BA	1	no information available	1955
77	11-10	m	unl	BA	1	no information available	1956
78	11-10	m	unl	BA	1	no information available	1957
79	11-10	m	unl	BA	1	no information available	1958
80	11-10	m	unl	BA	1	no information available	1959
81	11-10	m	unl	BA	1	no information available	1960
82	11-10	m	unl	BA	1	no information available	1961
83	11-10	m	unl	BA	1	no information available	1962
84	11-10	m	unl	BA	1	no information available	1963
85	11-10	m	unl	BA	1	no information available	1964
86	11-10	m	unl	BA	1	no information available	1965
87	11-10	m	unl	BA	1	no information available	1966
88	11-10	m	unl	BA	1	no information available	1967
89	11-10	m	unl	BA	1	no information available	1968
90	11-10	m	unl	BA	1	no information available	1969
91	11-10	m	unl	BA	1	no information available	1970
92	11-10	m	unl	BA	1	no information available	1971
93	11-10	m	unl	BA	1	no information available	1972
94	11-10	m	unl	BA	1	no information available	1973
95	11-10	m	unl	BA	1	no information available	1974
96	11-10	m	unl	BA	1	no information available	1975
97	11-10	m	unl	BA	1	no information available	1976
98	11-10	m	unl	BA	1	no information available	1977
99	11-10	m	unl	BA	1	no information available	1978
100	11-10	m	unl	BA	1	no information available	1979
101	11-10	m	unl	BA	1	no information available	1980
102	11-10	m	unl	BA	1	no information available	1981
103	11-10	m	unl	BA	1	no information available	1982
104	11-10	m	unl	BA	1	no information available	1983
105	11-10	m	unl	BA	1	no information available	1984
106	11-10	m	unl	BA	1	no information available	1985
107	11-10	m	unl	BA	1	no information available	1986
108	11-10	m	unl	BA	1	no information available	1987
109	11-10	m	unl	BA	1	no information available	1988
110	11-10	m	unl	BA	1	no information available	1989
111	11-10	m	unl	BA	1	no information available	1990
112	11-10	m	unl	BA	1	no information available	1991
113	11-10	m	unl	BA	1	no information available	1992
114	11-10	m	unl	BA	1	no information available	1993
115	11-10	m	unl	BA	1	no information available	1994
116	11-10	m	unl	BA	1	no information available	1995
117	11-10	m	unl	BA	1	no information available	1996
118	11-10	m	unl	BA	1	no information available	1997
119	11-10	m	unl	BA	1	no information available	1998
120	11-10	m	unl	BA	1	no information available	1999
121	11-10	m	unl	BA	1	no information available	2000
122	11-10	m	unl	BA	1	no information available	2001
123	11-10	m	unl	BA	1	no information available	2002
124	11-10	m	unl	BA	1	no information available	2003
125	11-10	m	unl	BA	1	no information available	2004
126	11-10	m	unl	BA	1	no information available	2005
127	11-10	m	unl	BA	1	no information available	2006
128	11-10	m	unl	BA	1	no information available	2007
129	11-10	m	unl	BA	1	no information available	2008
130	11-10	m	unl	BA	1	no information available	2009
131	11-10	m	unl	BA	1	no information available	2010
132	11-10	m	unl	BA	1	no information available	2011
133	11-10	m	unl	BA	1	no information available	2012
134	11-10	m	unl	BA	1	no information available	2013
135	11-10	m	unl	BA	1	no information available	2014
136	11-10	m	unl	BA	1	no information available	2015
137	11-10	m	unl	BA	1	no information available	2016
138	11-10	m	unl	BA	1	no information available	2017
139	11-10	m	unl	BA	1	no information available	2018
140	11-10	m	unl	BA	1	no information available	2019
141	11-10	m	unl	BA	1	no information available	2020
142	11-10	m	unl	BA	1	no information available	2021
143	11-10	m	unl	BA	1	no information available	2022
144	11-10	m	unl	BA	1	no information available	2023
145	11-10	m	unl	BA	1	no information available	2024
146	11-10	m	unl	BA	1	no information available	2025
147	11-10	m	unl	BA	1	no information available	2026
148	11-10	m	unl	BA	1	no information available	2027
149	11-10	m	unl	BA	1	no information available	2028
150	11-10	m	unl	BA	1	no information available	2029
151	11-10	m	unl	BA	1	no information available	2030
152	11-10	m	unl	BA	1	no information available	2031
153	11-10	m	unl	BA	1	no information available	2032
154	11-10	m	unl	BA	1	no information available	2033
155	11-10	m	unl	BA	1	no information available	2034
156	11-10	m	unl	BA	1	no information available	2035
157	11-10	m	unl	BA	1	no information available	2036
158	11-10	m	unl	BA	1	no information available	2037
159	11-10	m	unl	BA	1	no information available	2038
160	11-10	m	unl	BA	1	no information available	2039
161	11-10	m	unl	BA	1	no information available	2040
162	11-10	m	unl	BA	1	no information available	2041
163	11-10	m	unl	BA	1	no information available	2042
164	11-10	m	unl	BA	1	no information available	2043
165	11-10	m	unl	BA	1	no information available	2044
166	11-10	m	unl	BA	1	no information available	2045
167	11-10	m	unl	BA	1	no information available	2046
168	11-10	m	unl	BA	1	no information available	2047
169	11-10	m	unl	BA	1	no information available	2048
170	11-10	m	unl	BA	1	no information available	2049
171	11-10	m	unl	BA	1	no information available	2050
172	11-10	m	unl	BA	1	no information available	2051
173	11-10	m	unl	BA	1	no information available	2052
174	11-10	m	unl	BA	1	no information available	2053
175	11-10	m	unl	BA	1	no information available	2054
176	11-10	m	unl	BA	1	no information available	2055
177	11-10	m	unl	BA	1	no information available	2056
178	11-10	m	unl	BA	1	no information available	2057
179	11-10	m	unl	BA	1	no information available	2058
180	11-10	m	unl	BA	1	no information available	2059
181	11-10	m	unl	BA	1	no information available	2060
182	11-10	m	unl	BA	1	no information available	2061
183	11-10	m	unl	BA	1	no information available	2062
184	11-10	m	unl	BA	1	no information available	2063
185	11-10	m	unl	BA	1	no information available	2064
186	11-10	m	unl	BA	1	no information available	2065
187	11-10	m	unl	BA	1	no information available	2066
188	11-10	m	unl	BA	1	no information available	2067
189	11-10	m	unl	BA	1	no information available	2068
190	11-10	m	unl	BA	1	no information available	2069
191	11-10	m	unl	BA	1	no information available	2070
192	11-10	m	unl	BA	1	no information available	2071
193	11-10	m	unl	BA	1	no information available	2072
194	11-10	m	unl	BA	1	no information available	2073
195	11-10	m	unl	BA	1	no information available	2074
196	11-10	m	unl	BA	1	no information available	2075
197	11-10	m	unl	BA	1	no information available	2076
198	11-10	m	unl	BA	1	no information available	2077
199	11-10	m	unl	BA	1	no information available	2078
200	11-10	m	unl	BA	1	no information available	2079
201	11-10	m	unl	BA	1	no information available	2080
202	11-10	m	unl	BA	1	no information available	2081
203	11-10	m	unl	BA	1	no information available	2082
204	11-10	m	unl	BA	1	no information available	2083
205	11-10	m	unl	BA	1	no information available	2084
206	11-10	m	unl	BA	1	no information available	2085
207	11-10	m	unl	BA	1	no information available	2086
208	11-10	m	unl	BA	1	no information available	2087
209	11-10	m	unl	BA	1	no information available	2088
210	11-10	m	unl	BA	1	no information available	2089
211	11-10	m	unl	BA	1	no information available	2090
212	11-10	m	unl	BA	1	no information available	2091
213	11-10	m	unl	BA	1	no information available	2092
214	11-10	m	unl	BA	1	no information available	2093
215	11-10	m	unl	BA	1	no information available	2094
216	11-10	m	unl	BA	1	no information available	2095
217	11-10	m	unl	BA	1	no information available	2096
218	11-10	m	unl	BA	1	no information available	2097
219	11-10	m	unl	BA	1	no information available	2098
220	11-10	m	unl	BA	1	no information available	2099
221	11-10	m	unl	BA	1	no information available	2100
222	11-10	m	unl	BA	1	no information available	2101
223	11-10	m	unl	BA	1	no information available	2102
224	11-10	m	unl	BA	1	no information available	2103
225	11-10	m	unl	BA	1	no information available	2104
226	11-10	m	unl	BA	1	no information available	2105
227	11-10	m	unl	BA	1	no information available	2106
228	11-10	m	unl	BA	1	no information available	2107
229	11-10	m	unl				

[illegible]



[illegible]

1127 verified meningococcal cases and their distributions in all age groups recorded from 1961 to 1958

percentage of cases with verified age

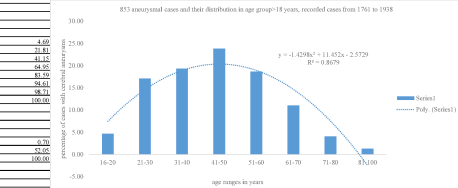
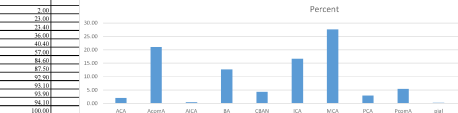
$y = -0.0426x^3 + 7.1477x^2 - 9.4323x + 0.7252$

age ranges in years

Series

Polynomial (Statistics)

age ranges in years	percentage of cases with verified age
0-5	~4.0
6-10	~2.0
11-15	~4.0
16-20	~6.0
21-25	~12.0
26-30	~14.0
31-35	~16.0
36-40	~18.0
41-45	~14.0
46-50	~12.0
51-55	~8.0
56-60	~4.0
61-65	~2.0
66-70	~1.0
71-75	~0.5
76-80	~0.5
81-100	~0.5

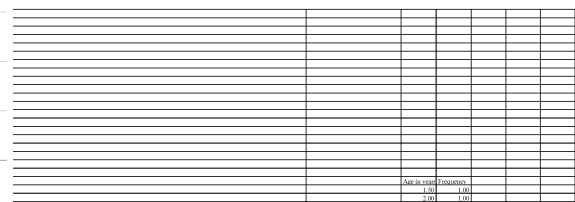












1127 confirmed meningococcal cases and their distribution in all age groups published and recorded from 1961 to 1988

$y = 4.0109E-14x^5 + 1.1241E-12x^4 - 6.78E-11x^3$

Frequency

Poly. (Frequency)



Supplementary File 2: Statistical parameters of distributions of aneurysmal cases reported from 1761-1938,<sup>14</sup> and recorded in RAH from 2011 to 2019.

		102 patients with cerebral aneurysmal aneurysms recorded in RAH from 2011 to 2019	1127 patients with cerebral aneurysms recorded in 407 publications - published from 1761 to 1938							
Statistics - all cases with cerebral aneurysms		age>18, 2011 to 2019	age>18 years, 1761 to 1938	age >= 18 & year < 1850	age >= 18 & year >= 1850 & year < 1900	age >= 18 & year >= 1900	all age, year < 1850	all age, year < 1900 & year >= 1850	all ages, year >= 1900	all age group, all years, >400 publications
Age in years										
N	Valid	102	851	41	252	560	42	278	613	935
	Missing	0	0	0	0	0	7	14	171	192
Mean age		57.6	44.7	44.3	45.6	44.3	43.6	42.6	41.2	41.7
Median age		60.0	43.0	47.0	45.0	42.0	46.0	43.0	41.0	41.0
Mode age		48.0	41.0	20.0	40.0	41.0	20.0	40.0	41.0	41.0
Std. Deviation		13.1	15.5	15.6	15.6	15.4	16.1	17.5	17.9	17.7
Minimum age		18.0	18.0	19.0	18.0	18.0	14.0	6.0	1.5	1.5
Maximum age		83.0	89.0	68.0	86.0	89.0	68.0	86.0	89.0	89.0
Percentiles	25	48.0	32.0	33.5	33.3	32.0	31.8	28.8	29.0	29.0
	50	60.0	43.0	47.0	45.0	42.0	46.0	43.0	41.0	41.0
	75	68.3	56.0	59.0	56.0	55.0	59.0	56.0	53.0	54.0

Legend: 14 = McDonald, CA & Korb, M 1939, Intracranial aneurysms, Archives of neurology and psychiatry (Chicago), vol. 42, no. 2, pp. 298-328.

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)



percentage of HSC aneuploidy only cases - data recorded at Royal Adelaide Hospital from 2011 to 2019

Y-axis: percentage of HSC aneuploidy cases (ranging from -0.005 to 0.005)

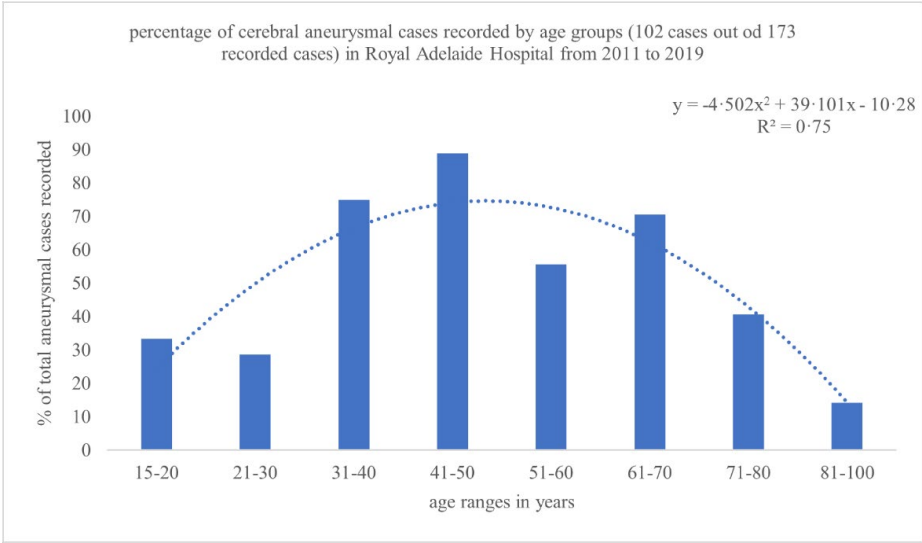
X-axis: age ranges (15-20, 21-30, 31-40, 41-50, 51-60, 61-70, 71-80, 81-100)

Legend: Valid Percent (solid blue line), Prob. Valid Percent (dashed blue line)

Equation:  $y = 4.4329e^{-0.0005x} + 0.0005$

R-squared:  $R^2 = 0.6497$

Burlakoti A, et al. *BMJ Open* 2024; 14:e081290. doi: 10.1136/bmjopen-2023-081290



Supplementary File 4: The prevalence (%) of cerebral aneurysms observed over a broad age range (18-100 years, n=173, cases with aneurysms=102, cases without aneurysm=71), with a median of 62 years, a mean of 60 years, and a standard deviation of 15.75, is shown in the chart. The peak prevalence occurs between 31-60 years (p<0.001).