**Supplemental methods:**

Using $\pi_{si}$ and $\pi_{di}$ to denote the underlying risks of stroke and DWI+ in the *i*th treatment group and $N_i$, $S_i$ and $D_i$ to denote the observed numbers of patients, patients suffering a stroke and patients classified as DWI+ in that group respectively, the model is specified by the following three equations.

$$S_i \sim Binomial(N_i, \pi_{si}) \quad (1)$$

$$D_i - S_i \sim Binomial\left(N_i - S_i, ((\pi_{di} - \pi_{si})/(1 - \pi_{si}))\right) \quad (2)$$

$$\begin{pmatrix} \log(\pi_{di}/(1-\pi_{di})) \\ \log(\pi_{si}/(1-\pi_{si})) \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_d \\ \mu_s \end{pmatrix}, \begin{pmatrix} \sigma_d^2 & r\sigma_d\sigma_s \\ r\sigma_d\sigma_s & \sigma_s^2 \end{pmatrix}\right) \quad (3)$$

Equation (1) states that the number of strokes in the *i*th treatment group follows a binomial distribution. Equation (2) states that the number of DWI+ cases among those not suffering a stroke also follows a binomial distribution whose mean is chosen such that the overall risk of being DWI+ in that treatment group is $\pi_{di}$ ($\pi_{di} = \pi_{si} + (1 - \pi_{si}) \times (\pi_{di} - \pi_{si})/(1 - \pi_{si})$). Equation (3) states that the underlying log odds of the two types of event follow a bivariate normal distribution. This model was fitted using PROC NLMIXED in SAS software, version 9.2 (copyright, SAS Institute Inc., Cary, NC, USA), with 95% confidence intervals for *r* (the correlation coefficient for the association between the two log odds) constructed using the profile likelihood, and the p-value from a likelihood ratio test. Secondary analyses restricted to treatment groups of patients receiving CEA or CAS respectively were also attempted.

To illustrate the effect of imprecision in the two observed risks (DWI+ and stroke) on the association between them we performed a simulation (figure 2). Data from 30 treatment groups with sample sizes typical of those in our data were simulated using the model defined above with

parameters taken to be similar to the parameter estimates from the model using all included studies.

To estimate the change in sample size requirements for a future clinical trial that can be achieved by switching the primary outcome from stroke risk to DWI+ risk it is necessary to convert a postulated effect on stroke risk to one on DWI+ risk. For example, if it is anticipated that a new drug or interventional technique will reduce the risk of procedural stroke from 6% to 3% it is necessary to convert each of these anticipated underlying stroke risks to anticipated underlying DWI+ risks. The sample size of a phase II trial investigating proof of concept of such an intervention could then be calculated to demonstrate the anticipated reduction in DWI+ risk. Estimation of the parameters in the bivariate random effects logistic regression model allows such conversions to be made because equation (3) implies that there is a linear relationship between the underlying log odds of a stroke and the underlying log odds of being DWI+. Specifically, with the underlying log odds of being DWI+ as the dependent variable and the underlying log odds of a stroke the predictor the line passes through the point $\binom{\mu_d}{\mu_s}$ and its slope is $r\sigma_d/\sigma_s$.

**Supplementary Table 1:**
List of all included studies investigating carotid artery stenting (CAS) for carotid stenosis. CAS treatment groups of comparative studies (CEA vs. CAS) are also included (see supplementary table 2 for CEA treatment groups from the same study). The total number of treatment groups in each study is provided (i.e. n=2 if CAS subgroup is part of a comparative study (CAS vs. CEA or CAS vs. CAS); N/A: information not available. Outcome data are provided per study including all CAS treatment groups.

| Author | Year of first publication | Number of treatment groups included in Study, N | Number of CAS treatment groups included | Number of CEA treatment groups included | CAS Procedures included in study, N | Symptomatic carotid stenoses, N | Number of reported ischaemic strokes, N (%) | Relative Risk of Ischaemic Stroke (%) | Number of reported DWI +, N (%) | Relative Risk of DWI+ (%) | Use of any Protection Device (Yes / No / both) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Loevblad*** [116] | 2000 | 1 | 1 | 0 | 19 | N/A | 2 | 10.5 | 4 | 21.1 | No |
| ***Jaeger*** [120] | 2001 | 1 | 1 | 0 | 20 | 13 | 0 | 0.0 | 5 | 25.0 | Yes |
| ***Jaeger*** [117] | 2002 | 1 | 1 | 0 | 70 | 52 | 1 | 1.4 | 22 | 31.4 | No |
| ***Kopp*** [164] | 2003 | 3 | 3 | 0 | 80 | 13 | 3 | 3.8 | 23 | 28.8 | Both |
| ***Schlueter*** [121] | 2003 | 1 | 1 | 0 | 44 | 13 | 1 | 2.3 | 10 | 22.7 | Yes |
| ***Flach*** [166] | 2004 | 2 | 1 | 1 | 21 | 21 | 1 | 4.8 | 9 | 42.9 | Yes |
| ***Garcia-Sanchez*** [167] | 2004 | 2 | 1 | 1 | 10 | 10 | 0 | 0.0 | 4 | 40.0 | No |
| ***Gauvrit*** [158] | 2004 | 2 | 2 | 0 | 23 | 12 | 1 | 4.3 | 2 | 8.7 | Both |
| ***Cosottini*** [159] | 2005 | 2 | 2 | 0 | 52 | 23 | 1 | 1.9 | 16 | 30.8 | Both |
| ***Roh*** [168] | 2005 | 2 | 1 | 1 | 22 | 18 | 2 | 9.1 | 8 | 36.4 | No |
| ***du Mesnil de Rochemont*** [122] | 2006 | 1 | 1 | 0 | 50 | 50 | 0 | 0.0 | 19 | 38.0 | Yes |
| ***Iihara*** [169] | 2006 | 2 | 1 | 1 | 92 | 33 | 7 | 7.6 | 32 | 34.8 | Yes |
| ***Maleux*** [123] | 2006 | 1 | 1 | 0 | 53 | 17 | 0 | 0.0 | 22 | 41.5 | Yes |
| ***McDonnell*** [124] | 2006 | 1 | 1 | 0 | 110 | 81 | 8 | 7.3 | 23 | 20.9 | Both |
| ***Pinero*** [125] | 2006 | 1 | 1 | 0 | 162 | 122 | 1 | 0.6 | 28 | 17.3 | Yes |
| ***Poppert*** [170] | 2006 | 2 | 1 | 1 | 41 | 18 | 1 | 2.4 | 22 | 53.7 | No |
| ***Rosenkranz*** [118] | 2006 | 1 | 1 | 0 | 27 | 27 | 0 | 0.0 | 8 | 29.6 | No |
| ***Grunwald*** [128] | 2006 | 1 | 1 | 0 | 10 | N/A | 0 | 0.0 | 4 | 40.0 | Yes |
| ***Schillinger*** [129] | 2006 | 1 | 1 | 0 | 14 | 0 | 0 | 0.0 | 1 | 7.1 | Yes |
| ***Asakura*** [126] | 2006 | 1 | 1 | 0 | 45 | 21 | 0 | 0.0 | 20 | 44.4 | Both |
| ***Asakura*** [127] | 2006 | 1 | 1 | 0 | 11 | 7 | 0 | 0.0 | 2 | 18.2 | Yes |
| ***El-Koussy*** [161] | 2007 | 2 | 2 | 0 | 44 | 25 | 2 | 4.5 | 13 | 29.5 | Yes |
| ***Faraglia*** [172] | 2007 | 2 | 1 | 1 | 35 | 11 | 2 | 5.7 | 12 | 34.3 | Yes |
| ***Kim*** [162] | 2007 | 2 | 2 | 0 | 71 | 47 | 3 | 4.2 | 28 | 39.4 | Yes |
| ***Lacroix*** [171] | 2007 | 2 | 1 | 1 | 61 | 21 | 2 | 3.3 | 26 | 42.6 | Yes |
| ***Peynircioglu*** [119] | 2007 | 1 | 1 | 0 | 13 | 13 | 0 | 0.0 | 1 | 7.7 | No |
| ***Rapp*** [130] | 2007 | 1 | 1 | 0 | 54 | 29 | 2 | 3.7 | 36 | 66.7 | Yes |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Tedesco*** [173] | 2007 | 2 | 1 | 1 | 34 | 18 | 3 | 8.8 | 24 | 70.6 | Yes |
| ***Kastrup*** [160] | 2008 | 2 | 2 | 0 | 243 | 134 | 14 | 5.8 | 144 | 59.3 | Both |
| ***Palombo*** [132] | 2008 | 1 | 1 | 0 | 98 | 30 | 3 | 3.1 | 20 | 20.4 | Yes |
| ***Faggioli*** [134] | 2008 | 1 | 1 | 0 | 59 | 0 | 0 | 0.0 | 34 | 57.6 | Yes |
| ***Schofer*** [133] | 2008 | 1 | 1 | 0 | 59 | 8 | 0 | 0.0 | 19 | 32.2 | Yes |
| ***Faraglia*** [137] | 2008 | 1 | 1 | 0 | 43 | N/A | 1 | 2.3 | 6 | 14.0 | Yes |
| ***Ghorab*** [131] | 2008 | 1 | 1 | 0 | 50 | 31 | 2 | 4.0 | 6 | 12.0 | Yes |
| ***Skjelland*** [174] | 2009 | 2 | 1 | 1 | 28 | N/A | 2 | 7.1 | 6 | 21.4 | Yes |
| ***Tedesco*** [135] | 2009 | 1 | 1 | 0 | 20 | 9 | 0 | 0.0 | 7 | 35.0 | Yes |
| ***Zhou*** [175] | 2009 | 2 | 1 | 1 | 68 | N/A | 2 | 2.9 | 31 | 45.6 | Yes |
| ***Taha*** [136] | 2009 | 1 | 1 | 0 | 98 | 51 | 3 | 3.1 | 42 | 42.9 | Yes |
| ***Bonati*** [176] | 2010 | 2 | 1 | 1 | 124 | 124 | 9 | 7.3 | 62 | 50.0 | Both |
| ***Kim*** [165] | 2010 | 1 | 1 | 0 | 32 | 32 | 0 | 0.0 | 17 | 53.1 | Both |
| ***Palombo*** [138] | 2010 | 1 | 1 | 0 | 111 | N/A | 4 | 3.6 | 33 | 29.7 | Yes |
| ***Rosenkranz*** [115] | 2010 | 1 | 1 | 0 | 147 | 147 | 6 | 4.1 | 43 | 29.3 | No |
| ***Wasser*** [177] | 2010 | 2 | 1 | 1 | 21 | N/A | 2 | 9.5 | 15 | 71.4 | Both |
| ***Yamada*** [178] | 2011 | 2 | 1 | 1 | 56 | 34 | 2 | 3.6 | 23 | 41.1 | Yes |
| ***Grunwald*** [114] | 2011 | 1 | 1 | 0 | 194 | 133 | 2 | 1.0 | 67 | 34.5 | No |
| ***Mitsuoka*** [183] | 2011 | 2 | 1 | 1 | 20 | 17 | 0 | 0 | 10 | 50 | Yes |
| ***Uchiyama*** [140] | 2011 | 1 | 1 | 0 | 19 | 19 | 1 | 5.3 | 15 | 78.9 | Yes |
| ***Pinter*** [139] | 2011 | 1 | 1 | 0 | 31 | N/A | 1 | 3.2 | 5 | 16.1 | Yes |
| ***Tulip*** [141] | 2012 | 1 | 1 | 0 | 34 | 17 | 1 | 2.9 | 17 | 50.0 | Yes |
| ***Felli*** [179] | 2012 | 2 | 1 | 1 | 150 | 12 | 3 | 2.0 | 51 | 34.0 | Yes |
| ***Leal*** [142] | 2012 | 2 | 2 | 0 | 64 | 44 | 0 | 0.0 | 15 | 23.4 | Yes |
| ***Capoccia*** [180] | 2012 | 2 | 1 | 1 | 28 | 0 | 1 | 3.6 | 6 | 21.4 | Yes |
| ***Palombo*** [143] | 2012 | 1 | 1 | 0 | 34 | 9 | 0 | 0.0 | 8 | 23.5 | Yes |
| ***Akutsu*** [182] | 2012 | 2 | 1 | 1 | 41 | 19 | 1 | 2.4 | 14 | 34.1 | Yes |
| ***Bijuklic*** [163] | 2012 | 2 | 2 | 0 | 62 | 25 | 1 | 1.6 | 41 | 66.1 | Yes |
| ***Zhou*** [181] | 2012 | 2 | 1 | 1 | 16 | 8 | 0 | 0.0 | 8 | 50.0 | Yes |
| ***Takayama*** [144] | 2013 | 2 | 2 | 0 | 61 | 28 | 2 | 3.3 | 25 | 41.0 | Yes |
| ***Tanemura***[151] | 2013 | 1 | 1 | 0 | 47 | 23 | 1 | 2.1 | 26 | 55.3 | Yes |
| ***Castro-Afonso***[150] | 2013 | 2 | 2 | 0 | 40 | 33 | 0 | 0 | 13 | 32.5 | Yes |
| ***Cano*** [145] | 2013 | 2 | 2 | 0 | 60 | 15 | 1 | 1.7 | 39 | 65.0 | Yes |
| ***Pini*** [146] | 2013 | 1 | 1 | 0 | 20 | 13 | 0 | 0.0 | 18 | 90.0 | Yes |
| ***Park*** [147] | 2013 | 2 | 2 | 0 | 91 | 76 | 1 | 1.1 | 36 | 39.6 | Both |
| ***Patti*** [148] | 2013 | 4 (2x2 design) | 2 | 0 | 156 | 22 | 5 | 6.4 | 40 | 33.3 | Yes |
| ***Bijuklic*** [149] | 2013 | 1 | 1 | 0 | 728 | N/A | 8 | 1.1 | 241 | 33.1 | Yes |
| ***Gunduz***[152] | 2014 | 1 | 1 | 0 | 52 | 39 | 2 | 3.8 | 33 | 63.5 | Yes |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Huang*[153]** | 2014 | 1 | 1 | 0 | 126 | 47 | 4 | 3.2 | 33 | 26.2 | Yes |
| ***Kuliha*[184]** | 2015 | 2 | 1 | 1 | 77 | 39 | 1 | 1.3 | 38 | 49.4 | Yes |
| ***Matsukawa*[154]** | 2015 | 1 | 1 | 0 | 36 | 24 | 0 | 0 | 11 | 30.6 | Yes |
| ***Adhikari*[155]** | 2016 | 1 | 1 | 0 | 35 | N/A | 2 | 5.7 | 10 | 28.6 | Yes |
| ***Kuliha*[156]** | 2016 | 1 | 1 | 0 | 81 | 32 | 0 | 0 | 46 | 56.8 | Yes |
| ***Ruffino*[157]** | 2016 | 1 | 1 | 0 | 23 | 14 | 0 | 0 | 7 | 30.4 | Yes |

**Supplementary Table 2:**
List of all included studies investigating CEA for carotid stenosis. CEA subgroups of comparative studies (CEA vs. CAS) are included (see supplementary table 1 for corresponding CAS subgroups). Number of treatment groups displays the total number of subgroups in each study, i.e. n=2 if CEA subgroup is part of a comparative study (CAS vs. CEA or CEA vs. CEA); N/A: information not given

| Author | Year of fist publication | Number of treatment groups included in study, N | Number of CEA treatment groups included, N | Number of CAS treatment groups included, N | CEA Procedures included in study, N | Symptomatic carotid stenoses, N | Number of reported ischaemic strokes, N (%) | Relative Risk of Ischaemic Stroke (%) | Number of reported DWI +, N (%) | Relative Risk of DWI + (%) | Type of Anaesthesia (Local or General or Both) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Feiwell*[100]** | 2001 | 1 | 1 | 0 | 25 | N/A | 0 | 0 | 1 | 4 | Local |
| ***Tomczak*[101]** | 2001 | 1 | 1 | 0 | 51 | 33 | 2 | 3.9 | 6 | 11.8 | N/A |
| ***Mueller*[102]** | 2003 | 1 | 1 | 0 | 33 | 22 | 1 | 3.0 | 9 | 27.3 | General |
| ***Flach*[166]** | 2004 | 2 | 1 | 1 | 23 | 23 | 1 | 4.3 | 2 | 8.7 | General |
| ***Garcia-Sanchez*[167]** | 2004 | 2 | 1 | 1 | 10 | 10 | 1 | 10.0 | 1 | 10.0 | General |
| ***Roh*[168]** | 2005 | 2 | 1 | 1 | 26 | 19 | 0 | 0.0 | 1 | 3.8 | General |
| ***Iihara*[169]** | 2006 | 2 | 1 | 1 | 139 | 92 | 3 | 2.2 | 13 | 9.4 | General |
| ***Inoue*[103]** | 2006 | 1 | 1 | 0 | 72 | 32 | 1 | 1.4 | 3 | 4.2 | General |
| ***Poppert*[170]** | 2006 | 2 | 1 | 1 | 93 | 44 | 2 | 2.2 | 16 | 17.2 | General |
| ***Faraglia*[172]** | 2007 | 2 | 1 | 1 | 40 | 8 | 0 | 0.0 | 3 | 7.5 | Both |
| ***Lacroix*[171]** | 2007 | 2 | 1 | 1 | 60 | 41 | 2 | 3.3 | 7 | 11.7 | General |
| ***Tedesco*[173]** | 2007 | 2 | 1 | 1 | 30 | 22 | 0 | 0.0 | 1 | 3.3 | General |
| ***Ogasawara*[104]** | 2008 | 1 | 1 | 0 | 163 | 118 | 2 | 1.2 | 28 | 17.2 | General |
| ***Soinne*[105]** | 2008 | 1 | 1 | 0 | 44 | 21 | 0 | 0.0 | 2 | 4.5 | General |
| ***Skjelland*[174]** | 2009 | 2 | 1 | 1 | 30 | N/A | 1 | 3.3 | 2 | 6.7 | General |
| ***Zhou*[175]** | 2009 | 2 | 1 | 1 | 100 | N/A | 2 | 2.0 | 12 | 12.0 | General |
| ***Bonati*[176]** | 2010 | 2 | 1 | 1 | 107 | 107 | 3 | 2.8 | 18 | 16.8 | Both |
| ***Hebb*[106]** | 2010 | 1 | 1 | 0 | 50 | 18 | 0 | 0.0 | 0 | 0.0 | General |
| ***Wasser*[177]** | 2010 | 2 | 1 | 1 | 28 | N/A | 0 | 0.0 | 1 | 3.6 | General |
| ***Mitsuoka*[183]** | 2011 | 2 | 1 | 1 | 25 | 22 | 0 | 0 | 0 | 0 | N/A |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Yamada*** [178] | 2011 | 2 | 1 | 1 | 25 | 16 | 0 | 0.0 | 2 | 8.0 | General |
| ***Felli*** [179] | 2012 | 2 | 1 | 1 | 150 | 138 | 2 | 1.3 | 6 | 4.0 | Local |
| ***Capoccia*** [180] | 2012 | 2 | 1 | 1 | 32 | 0 | 0 | 0.0 | 1 | 3.1 | Local |
| ***Akutsu*** [182] | 2012 | 2 | 1 | 1 | 63 | 34 | 0 | 0.0 | 11 | 17.5 | General |
| ***Zhou*** [181] | 2012 | 2 | 1 | 1 | 35 | 19 | 0 | 0.0 | 3 | 8.6 | General |
| ***Oikawa*** [107] | 2013 | 1 | 1 | 0 | 101 | 101 | 2 | 2.0 | 9 | 8.9 | General |
| ***Yoshida*** [108] | 2013 | 2 | 1 | 0 | 67 | 36 | 0 | 0.0 | 7 | 10.4 | General |
| ***Cho*** [109] | 2013 | 1 | 1 | 0 | 45 | 31 | 0 | 0.0 | 4 | 8.9 | Local |
| ***Sfyroeras*** [110] | 2013 | 1 | 1 | 0 | 66 | 17 | 0 | 0.0 | 5 | 7.6 | General |
| ***Akpinar***[111] | 2015 | 1 | 1 | 0 | 51 | 28 | 0 | 0 | 8 | 15.7 | General |
| ***Kuliha***[184] | 2015 | 2 | 1 | 1 | 73 | 48 | 1 | 1.4 | 18 | 24.7 | General |
| ***Bourke***[112] | 2016 | 1 | 1 | 0 | 206 | 149 | 4 | 1.9 | 27 | 13.1 | Local |
| ***Zhang***[113] | 2016 | 1 | 1 | 0 | 36 | 25 | 0 | 0.0 | 0 | 0 | General |