## SUPPLEMENTARY MATERIAL

**Suppl. Table 1.** Baseline characteristics of ESCAPE LATE patients, late window ESCAPE EVT arm patients and late window ESCAPE control arm patients (see also Zerna et al [under review])

| Variable | ESCAPE-LATE (n = 200) | ESCAPE EVT arm (n = 29) | ESCAPE control arm (n = 20) | P-value |
|---|---|---|---|---|
| Age – median (IQR) | 72 (62 – 81), n = 197 | 66 (54 – 79), n = 29 | 69 (60 - 74), n = 20 | 0.188 |
| Female sex – n (%) | 85/200 (42.5) | 18/29 (62.1) | 8/20 (40.0) | 0.122 |
| Baseline NIHSS | 15 (10 – 20), n = 192 | 14 (13 - 16), n = 28 | 20 (15 – 26), n = 20 | 0.040 |
| Pre-stroke mRS >2 | 15/108 (13.9%) | 0/28 (0) | 0/20 (0) | 0.568 |
| Medical history – n (%) | | | | |
| Atrial fibrillation | 65/192 (33.9) | 13/29 (44.8) | 8/20 (40.0) | 0.436 |
| Coronary artery disease | 29/200 (14.5) | 8/29 (27.6) | 3/20 (15.0) | 0.201 |
| Congestive heart failure | 19/200 (9.5) | 6/29 (20.7) | 3/20 (15.0) | 0.139 |
| Past stroke or TIA | 22/200 (11.0) | 4/29 (13.8) | 1/20 (5.0) | 0.690 |
| Peripheral venous disease | 2/200 (1.0) | 1/29 (3.5) | 1/20 (5.0) | 0.175 |
| Dyslipidemia | 61/200 (30.5) | 11/29 (37.9) | 8/20 (40.0) | 0.515 |
| Hypertension | 130/200 (65.0) | 18/29 (62.1) | 15/20 (75.0) | 0.619 |
| Diabetes | 32/200 (16.0) | 5/29 (17.2) | 4/20 (20.0) | 0.856 |
| Current smoker | 25/200 (12.5) | 7/29 (24.1) | 2/20 (10.0) | 0.235 |
| ASPECTS – median (IQR) | 8 (7 – 10), n = 186 | 9 (7 – 9), n = 28 | 9 (8 – 10), n = 20 | 0.567 |
| Collateral score – n (%) | | | | <0.001 |
| Poor | 15/150 (10.0) | 0/27 (0) | 1/20 (5.0) | |
| Intermediate | 44/150 (29.3) | 0/27 (0) | 2/20 (10.0) | |
| Good | 91/150 (60.7) | 27/27 (100) | 17/20 (85.0) | |
| Cervical ICA occlusion (%) | 13/200 (6.5) | 3/29 (12.6) | 0/1 (0) | 0.474 |
| Occlusion site – n (%)* | | | | 0.140 |
| Intracranial ICA | 39/190 (20.5) | 8/29 (27.6) | 7/20 (35.0) | |
| M1 segment | 125/190 (65.8) | 20/29 (69.0) | 13/20 (65.0) | |
| M2 segment | 26/190 (13.7) | 1/29 (3.5) | 0 (0) | |
| Anesthesia type – n (%) | | | | <0.001 |

| | | | | |
|---|---|---|---|---|
| General anesthesia | 40/176 (22.7) | 3/29 (10.3) | - | |
| Conscious sedation | 134/176 (76.1) | 17/29 (58.6) | - | |
| None | 2/176 (1.1) | 9/29 (31.0) | - | |
| Intravenous alteplase – n (%) | 30/199 (15.1) | 7/29 (24.1) | 11/20 (55.0) | <0.001 |
| Workflow times (min) – median (IQR) | | | | |
| Last known well to CT/MR | 621(469 – 798), n = 193 | 479 (377 – 560), n = 29 | 376 (362 - 495), n = 19 | <0.001 |
| Last known well to CSC arrival | 615 (458 – 778), n = 193 | 430 (337 - 531), n = 29 | 374 (328 - 448), n = 20 | <0.001 |
| CT/MR to puncture | 68 (39 – 121), n = 189 | 43 (31 – 65), n = 28 | - | 0.003 |
| Puncture to reperfusion | 30 (18 – 50), n = 168 | 34 (18 – 49), n = 26 | - | 0.734 |

*Occlusion determined by the proximal clot interface.
Note: EVT = endovascular treatment, IQR = interquartile range, mRS = modfied Rankin Score, NIHSS = National Institutes of Health Stroke Scale, ASPECTS = Alberta Stroke Program Early CT Score, CSC = comprehensive stroke center, TIA = transient ischemic attack, ICA = internal carotid artery

**Suppl. Table 2:** Base-case values and Model Input Parameters

| **Parameter** | **Expected value** | **Distribution** | **Reference** |
|---|---|---|---|
| ***Initial probabilities for achieving mRS 0/ 1/ 2/ 3/ 4/ 5/ 6 – unadjusted analysis*** | | | |
| ESCAPE trial EVT arm | 4/ 6/ 3/ 5/ 3/ 3/ 5 | Dirichlet | Zerna et al (under review) |
| ESCAPE-LATE study EVT patients | 19/ 23/ 24/ 25/ 13/ 8/ 29 | | |
| ESCAPE trial control arm | 2/ 2/ 1/ 0/ 6/ 5/ 3 | | |
| ***Initial probabilities for achieving mRS 0/ 1/ 2/ 3/ 4/ 5/ 6 – adjusted analysis**** | | | |
| ESCAPE trial EVT arm | 4/ 6/ 5/ 5/ 4/ 2/ 4 | Dirichlet | Zerna et al (under review) |
| ESCAPE-LATE study EVT patients | 17/ 23/ 21/ 23/ 19/ 12/ 25 | | |
| ESCAPE trial control arm | 3/ 2/ 3/ 2/ 2/ 2/ 4 | | |
| ***Initial probabilities for receiving intravenous alteplase*** | | | |
| ESCAPE trial EVT arm | 24.1% | Beta | Zerna et al (under review) |
| ESCAPE-LATE study EVT patients | 15.1% | | |
| ESCAPE trial control arm | 55.0% | | |
| ***Transition probabilities*** | | | |
| Recurrent stroke rate | 0.059 (for first year) | Beta | Pennlert et al[12] |
| Annual death rate | 0.022 (for 72 years) | Beta | Arias et al[13] |

| | | | |
|---|---|---|---|
| Annual death hazard rate ratios for mRS 0/ 1/ 2/ 3/ 4/ 5 | 1.53/ 1.52/ 2.17/ 3.18/ 4.55/ 6.55 | Log-normal | Hong et al[11] |
| After recurrent stroke | HERMES meta-analysis control arm | Dirichlet | Goyal et al[25] |
| ***Healthcare costs*** | | | |
| Costs within first 90 days after stroke for mRS 0/ 1/ 2/ 3/ 4/ 5/ 6 | $27,543/ $24,467 /$13,029/ $69,344/ $41,783/ $85,198/ $14,447 | Gamma | Sevick et al[26] |
| Additional cost of EVT | $17,834 | Gamma | Shireman et al[18] |
| Long-term annual costs after stroke for mRS 0/ 1/ 2/ 3/ 4/ 5 | $12,458/ $12,828/ $14,840/ $525,482/ $51,575/ $75,825 | Gamma | Shireman et al[18] |
| Costs for hospitalization due to recurrent stroke | $26,972 | Gamma | Gloede et al[27] |
| ***Societal costs*** | | | |
| Median annual salary of employed population | $45,000 (for 72 years) | Gamma | US Census Bureau 2022 |
| Population employment rate | 0.258 (for 65-74 years) | Beta | US Bureau of Labor Statistics 2022 |
| Relative earnings of stroke survivors | 0.825 | Beta | Vyas et al[28] |
| Return to work probability after stroke for mRS 0/ 1/ 2/ 3/ 4/ 5 | 0.63/ 0.72/ 0.49/ 0.19/ 0.14/ 0.00 | Beta | Tanaka et al[29] |
| Informal annual caregiving costs | mRS 0–2: $5,261, mRS 3–5: $28,778 | Gamma | Barral et al[30] |
| ***Utilities mRS 0/ 1/ 2/ 3/ 4/ 5/ 6*** | 1.00/ 0.91/ 0.76/ 0.65/ 0.33/ 0.00/ 0.00 | Beta | Chaisinanunkul et al[16] |

* adjusted for patient age, sex, baseline NIHSS, baseline ASPECTS and occlusion location.
Note: EVT = endovascular treatment, mRS = modified Rankin Score, ASPECTS = Alberta Stroke Program Early CT Score, NIHSS = National Institutes of Health Stroke Scale.

**Suppl. Table 3.** Costs, QALYs gained and incremental cost-effectiveness ratios (ICER) with late time-window EVT in addition to best medical care vs. best medical care only in a real-world setting in the unadjusted and adjusted analysis in patients presenting between 6-12 hours.

| | **EVT with best medical care** | **Best medical care only** | **Difference** |
|---|---|---|---|
| Unadjusted real-world setting (ESCAPE-LATE EVT group vs. ESCAPE trial control group) | | | |
| Cumulative lifetime QALYs gained | 3.51 | 1.93 | 1.58 |

| | | | |
|---|---|---|---|
| Cumulative lifetime costs (healthcare perspective) - $ | 126,831 | 150,509 | 23,677 |
| ICER (healthcare perspective) - $ | EVT dominant | | |
| Cumulative lifetime costs (societal perspective) - $ | 149,210 | 174,213 | 25,004 |
| ICER (societal perspective) - $ | EVT dominant | | |
| Adjusted real-world setting (ESCAPE-LATE EVT group vs. ESCAPE trial control group) | | | |
| Cumulative lifetime QALYs gained | 3.41 | 3.09 | 0.32 |
| Cumulative lifetime costs (healthcare perspective) - $ | 137,207 | 123,609 | 13,598 |
| ICER (healthcare perspective) - $ | 42,700 | | |
| Cumulative lifetime costs (societal perspective) - $ | 160,100 | 47,512 | 12,588 |
| ICER (societal perspective) - $ | 39,529 | | |

Note: adjusted mRS probabilities were derived from multivariable ordinal logistic regression models (adjusted for patient age, sex, baseline NIHSS, baseline ASPECTS and occlusion location). EVT = endovascular treatment, QALY = quality adjusted life year, ICER = incremental cost-effectiveness ratio.

**Suppl. Table 4.** Mean net monetary benefits with respective 95% prediction intervals and acceptability for late time-window EVT in addition to best medical care vs. best medical care only a) in a trial setting, and b) in a real-world setting in the unadjusted analysis.

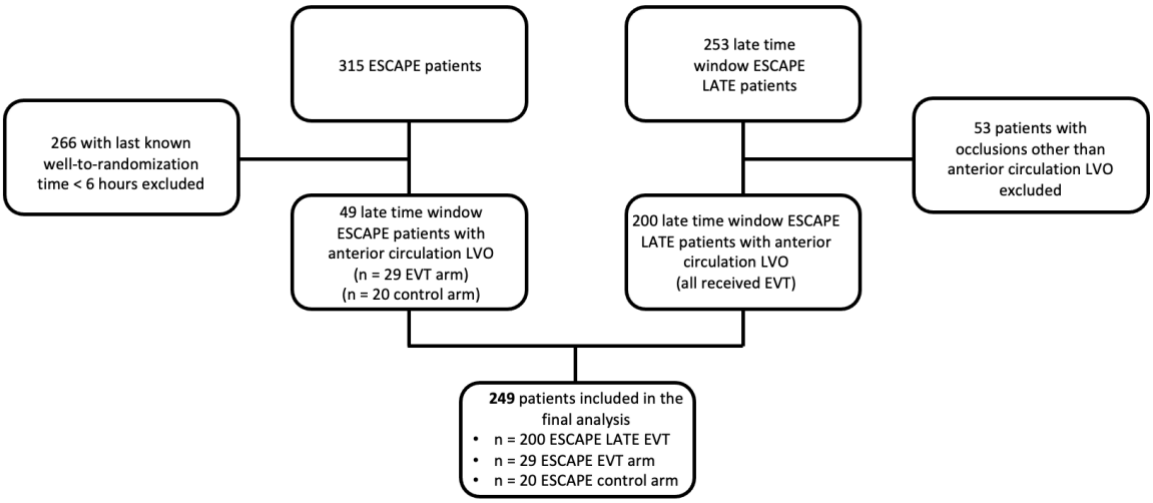
| | **EVT with best medical care** | **Best medical care only** |
|---|---|---|
| Trial setting (ESCAPE trial EVT group vs. ESCAPE trial control group) | | |
| Mean NMB (95%PI) at the upper/ lower WTP in $ - healthcare perspective | 189,083 (188,087 – 190,080) / 28,502 (27,958 – 29,046) | 41,4229 (40,202 – 42,655) / -56,653 (-57,376 – [-55,930]) |
| Acceptability of EVT at the upper/lower WTP - healthcare perspective | 96.6% / 96.8% | |
| Mean NMB (95%PI) at the upper/ lower WTP in $ - societal perspective | 166,306 (165,298 – 167,315) / 5,196 (4,646 – 5,746) | 16,510 (15,285 – 17,735) / -79,710 (-80,441 – [-78,978]) |
| Acceptability of EVT at the upper/lower WTP - societal perspective | 96.6% / 96.5% | |
| Real-world setting (ESCAPE-LATE EVT group vs. ESCAPE trial control group) | | |
| Mean NMB (95%PI) at the upper/ lower WTP in $ - healthcare perspective | 200,033 (199,523 – 200,543) / 38,670 (38,404 – 38,935) | 40,927 (39,709 – 42,144) / -56,635 (-57,358 – [-55,912]) |
| Acceptability of EVT at the upper/lower WTP - healthcare perspective | 99.0% / 99.0% | |
| Mean NMB (95%PI) at the upper/ lower WTP in $ - societal perspective | 177,762 (177,243 – 178,281) / 15,774 (15,502 – 16,046) | 17,935 (16,693 – 19,178) / -79,376 (-80,115 – [-78,637]) |
| Acceptability of EVT at the upper/lower WTP - societal perspective | 98.7% / 99.0% | |

Note: The upper and lower willingness-to-pay thresholds were set at $100,000 and $50,000 respectively. NMB = net monetary benefit, WTP = willingness-to-pay threshold, 95% PI = 95% prediction interval.

**Suppl. Table 5.** Mean net monetary benefits with respective 95% prediction intervals and acceptability for late time-window EVT in addition to best medical care vs. best medical care only a) in a trial setting, and b) in a real-world setting in the adjusted analysis.

| | **EVT with best medical care** | **Best medical care only** |
|---|---|---|
| Trial setting (ESCAPE trial EVT group vs. ESCAPE trial control group) | | |
| Mean NMB (95%PI) at the upper/ lower WTP in $ - healthcare perspective | 209,830 (208,893 – 210,767) / 36,941 (36,426 – 37,456) | 187,784 (186,591 – 188,977) / 36,062 (35,407 – 36,716) |
| Acceptability of EVT at the upper/lower WTP - healthcare perspective | 61.6% / 50.9% | |
| Mean NMB (95%PI) at the upper/ lower WTP in $ - societal perspective | 186,148 (185,180 – 187,115) / 13,177 (12,653 – 13,701) | 164,580 (163,390 – 165,770) / 12,956 (12,302 – 13,610) |
| Acceptability of EVT at the upper/lower WTP - societal perspective | 61.5% / 49.9% | |
| Real-world setting (ESCAPE-LATE EVT group vs. ESCAPE trial control group) | | |
| Mean NMB (95%PI) at the upper/ lower WTP in $ - healthcare perspective | 175,653 (175,137 – 176,169) / 21,596 (21,312 – 21,880) | 187,850 (186,673 – 189,028) / 35,797 (35,156 – 36,438) |
| Acceptability of EVT at the upper/lower WTP - healthcare perspective | 42.6% / 33.3% | |
| Mean NMB (95%PI) at the upper/ lower WTP in $ - societal perspective | 152,221 (151,701 – 152,740) / -1,907 (-2,199 – [-1,616]) | 165,671 (164,460 – 166,883) / 12,966 (12,308 – 13,625) |
| Acceptability of EVT at the upper/lower WTP - societal perspective | 42.2% / 32.9% | |

Note: adjusted mRS probabilities were derived from multivariable ordinal logistic regression models (adjusted for patient age, sex, baseline NIHSS, baseline ASPECTS and occlusion location). The upper and lower willingness-to-pay thresholds were set at $100,000 and $50,000 respectively. NMB = net monetary benefit, WTP = willingness-to-pay threshold, 95% PI = 95% prediction interval.




**Suppl. Figure 1**. Pooled patient sample with included and excluded patients. A total of 249 late time window anterior circulation LVO patients were included in the final, pooled patient sample. Patients belonged to one of the following three groups: 1) ESCAPE trial EVT group (n=29), 2) ESCAPE trial control group (n=20), 3) ESCAPE-LATE EVT group (n=200). The 90-day modified Rankin Score distribution in these three groups served as input probabilities for the 90-day modified Rankin Score in the short-run component of the cost-effectiveness model (see also Table 1). Note: EVT = endovascular treatment, LVO = large vessel occlusion.