Supplementary Materials — Missed Stroke in Specialty Care vs. General Practice

Enclosed below are Supplementary Materials to the peer-reviewed, scientific journal publication entitled ***Stroke Hospitalization after Misdiagnosis of "Benign Dizziness" is Lower in Specialty Care than General Practice: A Population-Based Cohort Analysis of Missed Stroke Using SPADE Methods*** *(Chang et al., Diagnosis (Berl.) 2021).*

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Appendix A. Additional Methodological Details

A1. Pathways to inclusion or exclusion in the primary analysis

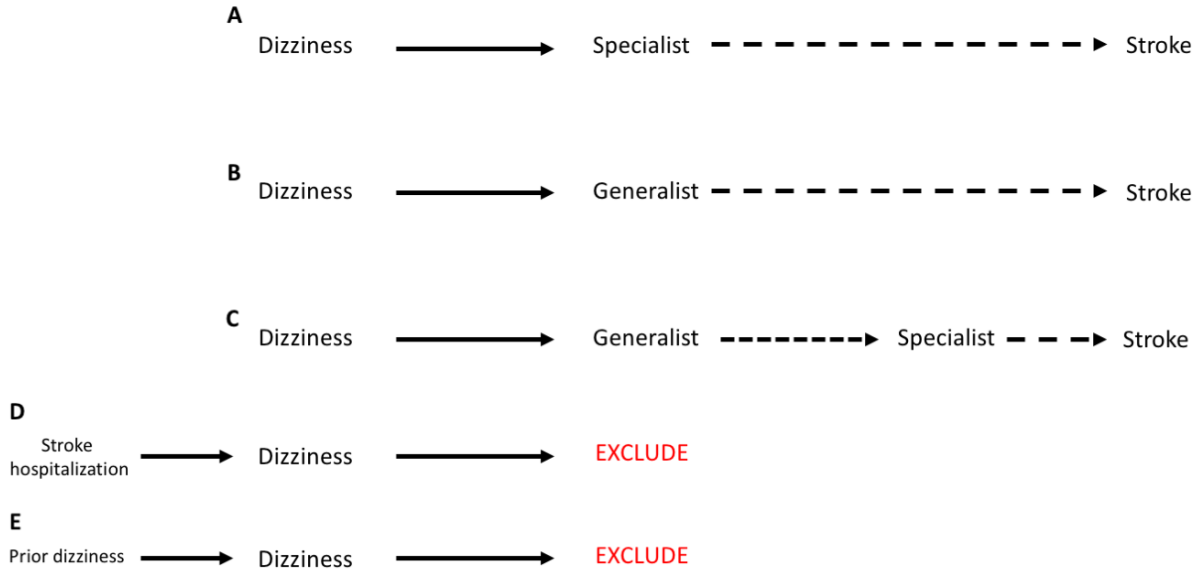

Figure A1.1 Pathways to inclusion or exclusion in the primary analysis (provided to illustrate the inclusion process). In scenario A, the patient was classified into the specialty care group in our study, while in scenarios B and C the patient was classified into the general care group. In scenario C, although the patient was referred to a specialist by a generalist, this patient was still classified into general care group in our study because the grouping was done according to the index provider. The time windows from symptom onset to clinic visit (the length of the solid arrows) are believed to be similar among groups in these examples based on our experience with the Taiwanese healthcare system. Thus, the architecture of our included population is structured to minimize immortal time bias.

A2. Distribution of ICD-9-CM codes for stroke hospitalizations.

These tables show the ICD-9-CM codes assigned at stroke hospitalization (the outcome measure in this study). The distributions are similar in both groups (specialty care and general practice).

Table A2.1 The distribution of ICD-9-CM codes for stroke hospitalization in all "benign dizziness" patients after propensity score matching.

ICD-9-CM	Frequency	Percentage (%)
434.91	116	40.0
434.9	23	7.9
435.3	22	7.6
435.9	22	7.6
436	20	6.9
431	18	6.2
433.10	9	3.1
430	7	2.4
435	6	2.1
435.1	6	2.1
437.3	5	1.7
432.1	4	1.4
434	4	1.4
437.2	4	1.4
434.90	3	1.0
437	3	1.0
437.9	3	1.0
433.11	2	0.7
433.2	2	0.7
433.31	2	0.7
434.11	2	0.7
437.1	2	0.7
437.7	2	0.7
433.1	1	0.3
433.3	1	0.3
435.2	1	0.3
Total	290	100.0

Table A2.2 The leading diagnostic codes for stroke hospitalizations in the 30 days following specialty vs. general care diagnosis

ICD-9-CM	Diagnosis	Specialty care, n (%)	General care, n (%)	Total, n (%)
434.91	Cerebral artery occlusion, unspecified with cerebral infarction	41 (36.0)	75 (42.6)	116 (40.0)
434.9	Cerebral artery occlusion unspecified	11 (9.6)	12 (6.8)	23 (7.9)
435.3	Vertebrobasilar artery syndrome	7 (6.1)	15 (8.5)	22 (7.6)
435.9	Unspecified transient cerebral ischemia	11 (9.6)	11 (6.3)	22 (7.6)
436	Acute, but ill-defined, cerebrovascular disease	6 (5.3)	14 (8.0)	20 (6.9)
431	Intracerebral hemorrhage	7 (6.1)	11 (6.3)	18 (6.2)

A3. Histograms comparing propensity scores across comparator populations

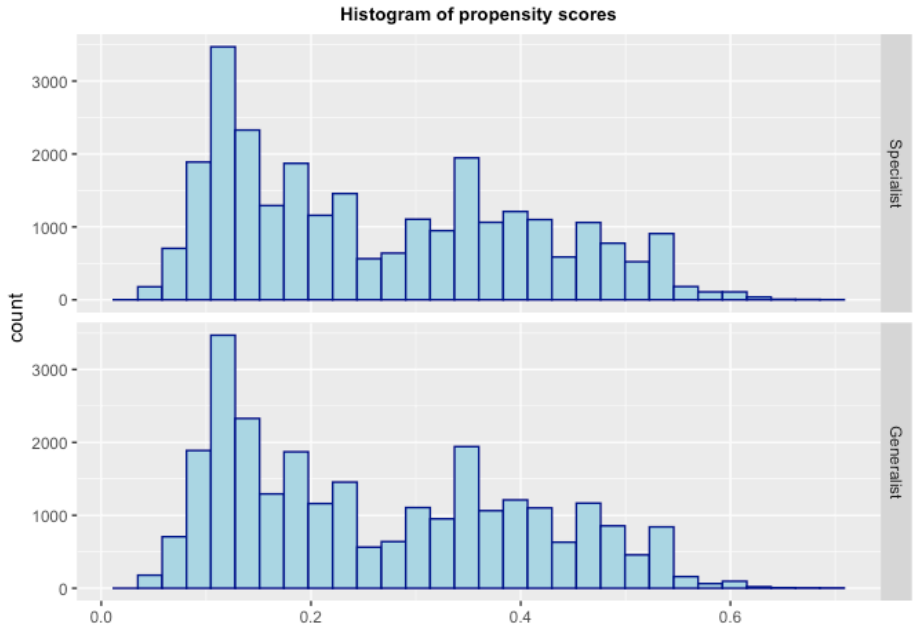

Figure A.3.1. Histogram comparing the distribution of propensity scores across specialist (top) vs generalist (bottom) care. The similar distributions corroborate good matching.

Appendix B. Internal Consistency Checks & Sensitivity Analyses

B1. Confirmatory analysis using alternative time windows for stroke hospitalizations

We checked internal consistency of our results by assessing the relative risks (RR) for three time windows – 7 days, 30 days, and 360 days. The results fit the risk model, reflecting a rapidly progressive decay in RR over time. This fits the known, characteristic risk pattern of major stroke after minor stroke or TIA (i.e. initial peak — with highest risk in the first 7 days, but remaining high for several weeks—followed by an asymptotic return to a stable, long-term base rate by about 90 days).

Table B1.1 Outcome at 7 days, 30 days, and 360 days, in specialty-care group and general-care group before and after propensity score matching.

	Before propensity score matching			After propensity score matching		
From "benign dizziness" to stroke	General care, n (%)	Specialty care, n (%)	Relative risk (95% CI)	General care, n (%)	Specialty care, n (%)	Relative risk (95% CI)
7 days	231 (0.20)	19 (0.07)	2.83 (1.77-4.51)	66 (0.24)	19 (0.07)	3.47 (2.09-5.78)
30 days	305 (0.26)	35 (0.13)	2.03 (1.43-2.87)	76 (0.28)	35 (0.13)	2.17 (1.46-3.24)
360 days	850 (0.73)	114 (0.42)	1.73 (1.43-2.11)	176 (0.65)	114 (0.42)	1.54 (1.22-1.95)

B2. Sensitivity analysis using alternative ICD codes for defining stroke hospitalizations

In this section, we compare the main study outcome according to different definitions of stroke hospitalization:

- stroke broadly-defined (ICD-9-CM 430-437), which was used in the main manuscript
- stroke broadly-defined EXCLUDING non-ruptured aneurysm (ICD-9-CM 437.3)
- narrowly-defined ischemic stroke (ICD-9-CM 433.x1, 434.x1, 436)

As the figure and table shown below, the study results hold—i.e., the short-term stroke risk is lower in specialty than general care—in all the three definitions of stroke.

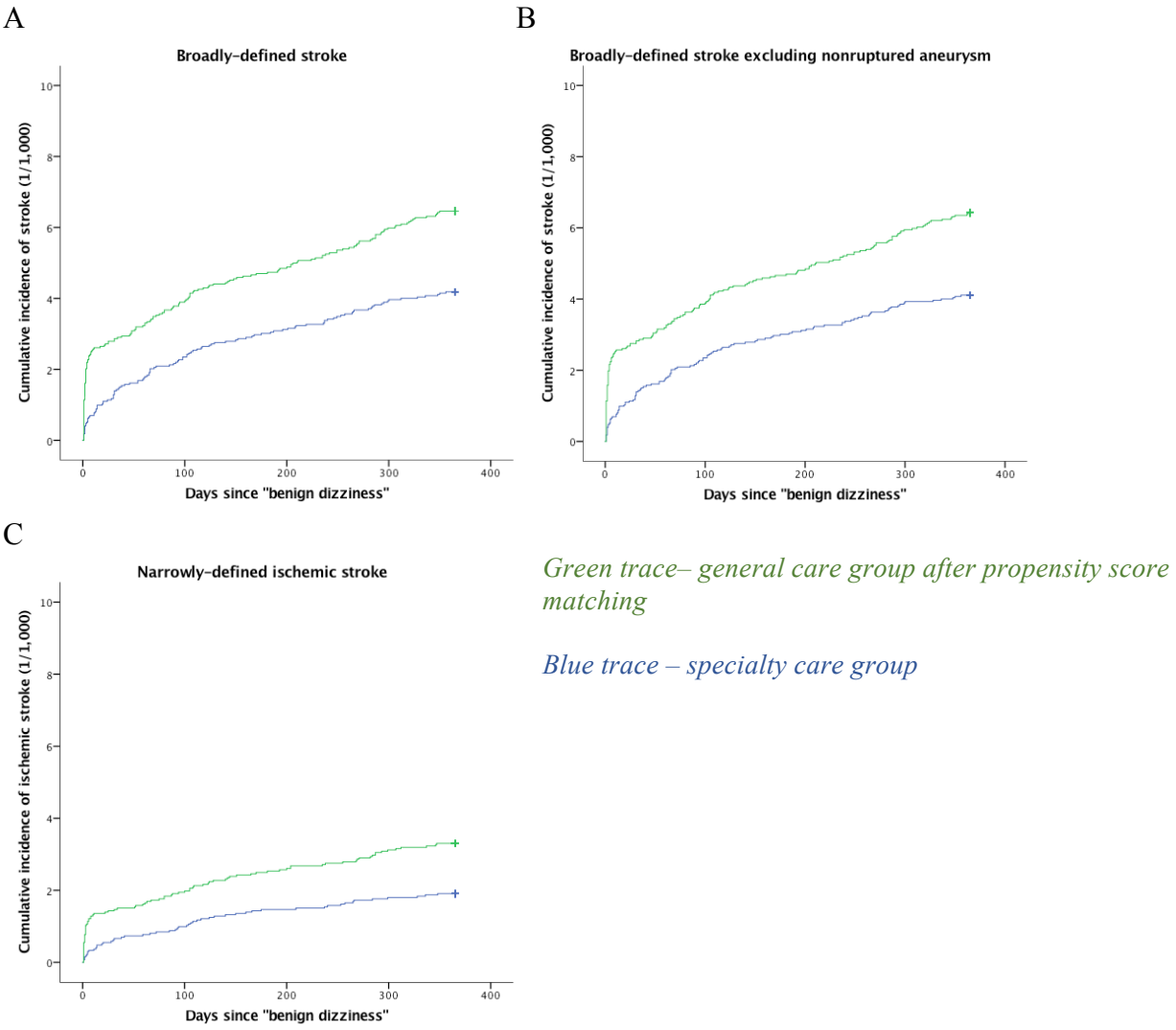

Figure B2.1 Cumulative incidence of stroke for general vs. specialty care groups by different definitions of stroke hospitalization including broadly-defined stroke (A), stroke with non-ruptured aneurysm excluded (B), and narrowly-defined ischemic stroke (C).

Table B2.1 Short- and long-term relative risk of stroke in general (matched) vs specialty care according to different definitions of stroke

General care (matched) vs. Specialty care	Short-term RR (1-30 days)	95% CI	Long-term RR (91-360 days)	95% CI
Analysis using broadly-defined stroke (ICD-9-CM 430-437)	2.17	1.46-3.24	1.33	0.94-1.89
Analysis using broadly-defined stroke but excluding non-ruptured aneurysm (ICD-9-CM 437.3)	2.14	1.44-3.20	1.34	0.94-1.91
Analysis using narrowly-defined ischemic stroke (ICD-9-CM 433.x1, 434.x1, 436)	2.29	1.30-4.05	1.36	0.83-2.21

B3. Secondary analysis with more stringent exclusion criteria for "benign dizziness"

This secondary analysis was to assess whether more stringent exclusion criteria for the retrospectively defined "benign dizziness" cohort would meaningfully impact the results. We re-ran the analysis excluding patients who, despite not being referred to emergency care, might have been recognized by providers to be at higher stroke risk and investigated in an urgent manner—patients who either (a) underwent brain imaging (CT scan or MRI) at the index clinic visit, or (b) were referred to a neurologist within 3 days of the index visit (Figure B3.1).

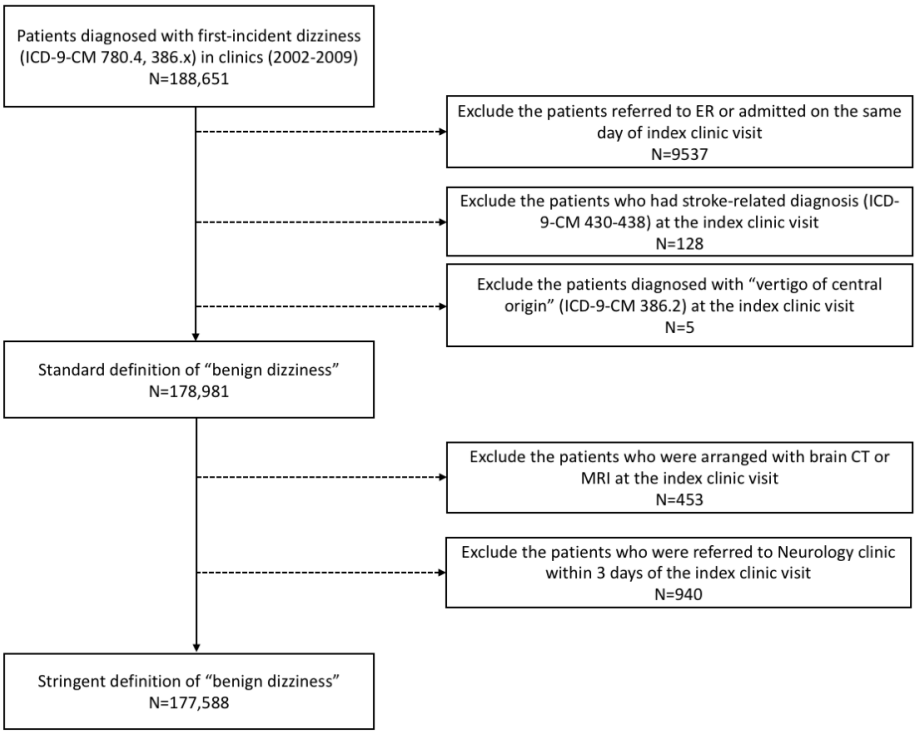

Figure B3.1 The stringent definition of "benign dizziness".

Under this stringent definition of "benign dizziness", the short- and long-term relative risk of stroke between groups was similar to that under standard definition (Table B3.1).

Table B3.1 Short- and long-term relative risk of stroke in general (propensity score-matched group) vs. specialty care under stringent definition of "benign dizziness".

Population Comparison	Short-term RR (1-30 days)	95% CI	Long-term RR (91-360 days)	95% CI
General Care VS Specialty Care	2.43	1.59-3.72	1.91	1.26-2.89

Appendix C. Population-Based Extrapolations of Potential Harms from Missed Stroke

C1. Applying the stroke misdiagnosis rate to estimate the total annual population estimate of harms from missed stroke after "benign dizziness" in Taiwan

This analysis provides the derivation of a simple weighted average extrapolation from our sample to the overall population of treat-and-release visits for dizziness in Taiwan (to yield an estimate of annual harms from missed stroke in Taiwan among those presenting dizziness).

$$Calculation:$$

$$178{,}981 \text{ benign dizziness } visits\ in\ 8\ year\ study\ period\ for\ sample \times \frac{1}{8\ years}$$

$$= 22{,}373\ yearly\ visits\ for\ dizziness\ in\ sample\ (1\ million\ patients).$$

$$\frac{22{,}373\ yearly\ visits}{1\ million\ patients} \times 23\ million$$

$$= 514{,}570\ yearly\ visits\ for\ population\ of\ Taiwan\ (23\ million\ people).$$

$$514{,}570\ population\ yearly\ visits \times \frac{\mathbf{16.93\ missed\ strokes}^{*}}{10{,}000\ visits}$$

$$= 871\ missed\ strokes\ per\ year$$

This gives an estimated 871 total patients harmed by missed strokes per year across all care settings for the population of Taiwan.

***N.B. Here, we calculated the short-term ("observed") minus long-term ("expected") stroke rate difference for treat-and-release visits across ALL care settings to achieve this population-level estimate of stroke-related harms due to diagnostic error. We included visits not included in the main analysis, such as those to pediatrics clinics and traditional Chinese medicine clinics, so that the sample would be representative of the population-level total.**

C2. Applying the stroke misdiagnosis rate to extrapolate the total annual population estimate of harms from missed stroke after "benign dizziness" in the United States

This analysis provides an estimate of annual harms from missed stroke in the United States, under the assumption that the stroke rate difference for treat-and-release visits for dizziness found in our study is similar to that found in Taiwan. We apply the Taiwanese result to data on the number of ambulatory care dizziness visits annually in the US. We do this to give readers a sense of scale with respect to the American population and prior literature.

In the US, there are an estimated 13.2M ambulatory care dizziness visits annually, including an estimated 7.1M patients diagnosed with "benign dizziness." [1].

$$Calculation:$$

$$7{,}100{,}000\ population\ yearly\ visits\ with\ diagnosis\ of\ benign\ dizziness \times \frac{\mathbf{16.93\ missed\ strokes}^{*}}{10{,}000\ visits} = 12{,}020\ missed\ strokes\ per\ year\ in\ the\ US$$

This gives an estimated 12,020 total patients harmed by missed strokes per year in ambulatory care in the US. This is close to prior US estimates $(15{,}000 - 25{,}000)$ [2].

References

1. Keita M, Nassery N, Wang Z, Newman-Toker DE. Diagnostic Errors, Harms, and Waste in Evaluating Dizziness and Vertigo in Ambulatory Care Settings across the United States. In: AcademyHealth Annual Research Meeting (Washington, DC), June 2-4, 2019.
2. Newman-Toker DE. Missed stroke in acute vertigo and dizziness: It is time for action, not debate. Ann Neurol 2016;79:27-31.