

A) To investigate whether severity of injury and age may be confounding variables, 4 key criteria below are concerned:

1. Risk factor of the outcome, independent of exposure
2. Associated with exposure (imbalance across exposure groups)
3. Not affected by the exposure or outcome (although it may affect the exposure)
4. Not in the causal pathway between the exposure and outcome

Start with the binary variable, severity of injury:

The three tabulations below are shown to assess the association between severity of injury and in-hospital death in a general, low-severity and high-severity case separately:

<b><i>General Case</i></b>	<b>Ground Ambulance (GA)</b>	<b>Helicopter (H)</b>	<b>Total</b>
<b>Alive</b>	359	102	461
<b>Dead</b>	773	191	964
<b>Total</b>	1132	293	1425

Crude OR =  $(191/102) / (773/359) = 0.87$  (2 d.f.)     $SE(\log(OR)) = \sqrt{1/191 + 1/102 + 1/773 + 1/359} = 0.14$  (2 d.f.) and

Crude 95% CI =  $\exp[\log_e(OR) \pm 1.96 \times SE(\log_e(OR))] = \exp [\log_e(0.87) \pm 1.96 \times 0.14]$

Thus, Crude 95% CI = (0.66, 1.15) (2 d.f.)

<i>Low-severity</i>	<b>GA</b>	<b>H</b>	<b>Total</b>
<b>Alive</b>	327	35	362
<b>Dead</b>	592	25	617
<b>Total</b>	919	60	979

<i>High-severity</i>	<b>GA</b>	<b>H</b>	<b>Total</b>
<b>Alive</b>	32	67	99
<b>Dead</b>	181	166	347
<b>Total</b>	213	233	446

Apply the same formula above, we can achieve the severity-specific odds ratios as follows:

Low-severity OR=0.39 (95% CI: 0.22 to 0.69) High-severity OR=0.44 (95% CI: 0.26 to 0.72)

The severity-specific ORs are highly like each other in terms of both value and CI but differ from the crude OR suggesting a confounder (instead of effect modifier).

Criterion 1: Overall, 63% (617/979) of low-severity patients and 78% (347/446) of high-severity patients finally died. In a similar computation, among helicopter service, 42% of low-severity patients and 71% of high-severity patients died, and for ground ambulance service, it's 64% versus 85%. Thus, low-severity patients held a smaller chance of in-hospital death, irrespective of taken transportation. Criterion 1 fulfilled.

Criterion 2: See the table below:

	<b>Ground Ambulance (GA)</b>	<b>Helicopter (H)</b>	<b>Total</b>
<b>Low-severity</b>	919	60	979
<b>High-severity</b>	213	233	446
<b>Total</b>	1132	293	1425

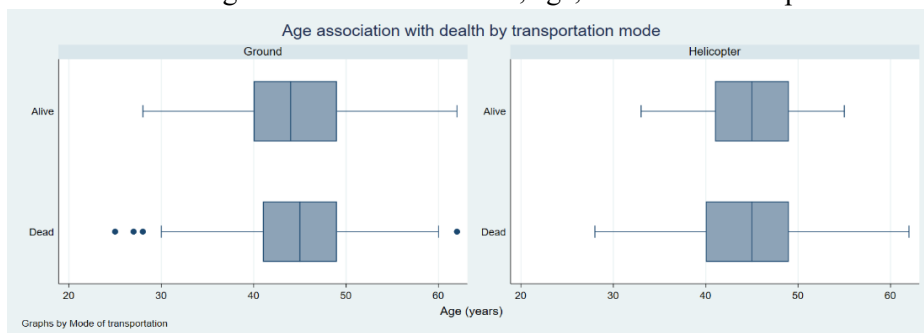
6% (60/979) of low-severity patients and 52% (233/446) of high-severity patients use helicopter, suggesting an association between severity of injury and mode of transportation. Plus, 19% (213/1132) of people using ground ambulance are high-severity, which largely differs from 80%(233/293) for helicopter users. Thus, severity of injury seems associated with transportation mode, and it appears imbalance across exposure groups. Criterion 2 fulfilled.

Criterion 3: severity of injury is not affected by either the transportation mode or the in-hospital death.

Criterion 4: severity of injury is not on the causal pathway between transportation mode and the in-hospital death. Both are clearly due to chronological order.

Therefore, the four criteria are met and together based on the evident difference between crude OR and severity-specific ORs, we conclude that severity of injury confounds association between mode of transportation and in-hospital death.

Further considering the continuous variable, age, the relevant box plots are introduced below:



Although some little difference noted, we see the boxplots generally share nearly same distribution with range from around 25 to 65 and a median about 45. Thus, we would argue that age has no evident association with in-hospital death, thus criterion 1 not fulfilled. Also, we cannot see clear relationship between age and severity of injury due to similar

boxplot distribution, which not met criterion 2. (Though criterion 3 and 4 are met: age does not be affected by the exposure and outcome, and it's not in the causal pathway between the exposure and the outcome since age is an objective property noted at injury regardless other factors like transportation mode or in-hospital death) Consequently, the conclusion that there's no strong evidence suggesting age is a confounder can be made.

B)

$$\text{Model: } \log\left(\frac{\pi}{1-\pi}\right) = \beta_1 + \beta_2 \times \text{mode} + \beta_3 \times \text{severity} + \beta_4 \times \text{age}$$

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$$\text{Model: } \log\left(\frac{\pi}{1-\pi}\right) = \beta_1 + \beta_2 \times \text{mode} \quad [\text{Unadjusted Model}]$$

Odds Ratio	95% Confidence Interval	P-value
0.87	0.66-1.14	0.31

$$\text{Model: } \log\left(\frac{\pi}{1-\pi}\right) = \beta_1 + \beta_2 \times \text{mode} + \beta_3 \times \text{severity} \quad [\text{Final Chosen: Adjusted Model}]$$

Odds Ratio	95% Confidence Interval	P-value
0.42	0.29-0.60	<0.001

The first model that I tried is the full model, which contains all the variables. The P-values for age (continuous) are at least or greater than 0.218 ( $> 0.05$ ). Therefore, the result we get is the same as our findings in the exploratory investigation, suggesting that there is not enough evidence of an association between in-hospital death and age.

We suspect the effect of severity may differ by mode. However, we find that the interaction term (severity##mode) is not statistically significant (p-value = 0.773). There is little evidence that the effect of severity depends on modes; therefore, the model without the interaction term is probably adequate.

According to our exploratory investigation findings, severity might be a possible confounder, and the degree of confounding can be assessed by comparing the adjusted and unadjusted estimates of the model with confounders and one without.

Consider the unadjusted effect: the odds ratio is 0.87 (95% CI: 0.66-1.14, P-value = 0.31), and the odds ratio for the adjusted effect is 0.42 (95% CI: 0.29-0.60, P-value < 0.001). When we compare the two estimates, we see that the association and precision improve after adjusting for severity, as evidenced by a 58% decrease in the odds ratio after adjusting for severity. Therefore, an adjusted model would be appropriate to test the effectiveness of the helicopter.

Considering estimates from the adjusted model, the odds ratio is 0.42. We may notice that the odds of in-hospital death are 58% lower if using a helicopter as the transportation compared with a ground ambulance. The 95% confidence interval of the odds ratio is 0.29-0.60, which suggests the "true" reduction is between 71% and 40%. The P-value is < 0.001, and since the CI excludes 1, there is enough evidence that helicopter transportation improved in-hospital survival.

C) We noticed that severity of injury could said to be a strong confounder and age presents little relationship with the exposure and outcome. Therefore, we decide to select severity of injury as matching factor to maximize efficiency. The data had about 461 patients alive, and 964 patients died. Thus, for individually matching, we decided to match a patient died for each patient alive according to same level of severity. Practically, it would be difficult to select a single matching as severity of injury is binary, but as the dataset noted: low severity (score 0-49), high severity (score 50-100). We would

suggest one-to-one matching based on original score to boost accuracy.

Then, 461 pairs should be produced and summarized:

	Died in pair – use helicopter?	
Alive in pair – use helicopter?	Yes	No
Yes	a	b
No	c	d

Matched Odds Ratio is computed by discordant pairs = b/c

and CI =  $\exp[\log_e(OR) \pm 1.96 \times SE(\log_e(OR))]$  where  $SE(\log_e(OR)) = (1/b + 1/c)^{1/2}$

Confounding is not singly resolved by matching. Proper methods are needed to analyze the matched data. One way is *McNemar's test* to test  $H_0$ : *No association between mode of transportation and in-hospital death.*

The test statistic =  $(b-c)^2 / (b+c)$  would be evaluated under  $\chi^2_1$  and p-value achieved should statistically suggest whether the association exists. Another way is conditional logistic regression considering a suitable

model:  $\log\left(\frac{\pi}{1-\pi}\right) = \beta_1 + \sum_{i=2}^{461} \beta_i \text{ matched\_pair}_i + \beta_h \text{ helicopter}$ ,  $\beta_h$  can be estimated through maximizing the conditional likelihood. Odds Ratio achieved can be used to show whether helicopter improves patient outcome.