Logistic Regression

Statistics in Medical Research Fall Series

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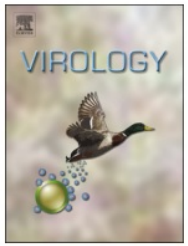
Summary

1. Introduction
2. Relative effects
3. Logistic Regression
4. Predictive Model

Contents lists available at ScienceDirect

Virology

journal homepage: www.elsevier.com/locate/yviro



Interferon lambda and hepatitis C virus core protein polymorphisms associated with liver cancer

João Paulo Moreira [a,b], Fernanda de Mello Malta [a,b,*], Márcio Augusto Diniz [b,c], Luciana Kikuchi [b], Aline Lopes Chagas [b], Livia de Souza Botelho Lima [a,b], Michele Soares Gomes-Gouvêa [a,b], Vanessa Fusco Duarte de Castro [d], Rubia Anita Ferraz Santana [d], Nairo Massakazu Sumita [e], Denise Cerqueira Paranagua Vezozzo [b], Flair José Carrilho [b], João Renato Rebello Pinho [a,b,d]

Example

- Hypothesis: Polymorphisms could be associated to liver damage in chronic hepatitis C;
- Groups: HCC (Hepatocellular Carcinoma) and Cirrhotic without HCC;
- Polymorphisms: rs12980275 (AA/ AG+GG);
- Design: Case-Control.

rs12980275	HCC	Cirrhotic without HCC	Total
AG + GG	43	29	72
AA	16	21	37
Total	59	50	109

HCC: Hepatocellular Carcinoma

Table: Distribution genotype by group

How should we compare the groups?

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- Our first attempt would be to calculate the proportions $43/72 = 0.59$ and $16/37 = 0.43$.

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- Our first attempt would be to calculate the proportions $43/72 = 0.59$ and $16/37 = 0.43$.
- However, they cannot be calculated. Why?
- The study is retrospective.

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4 Predictive Model

What type of study do you have?

Prospective

- Prospective studies are carried out from the present time into the future;

Retrospective

- Retrospective cohort studies are carried out at the present time and look to the past to examine medical events or outcomes;

Song JW, Chung KC. Observational studies: cohort and case-control studies. Plastic and reconstructive surgery. 2010 Dec;126(6):2234.

What type of study do you have?

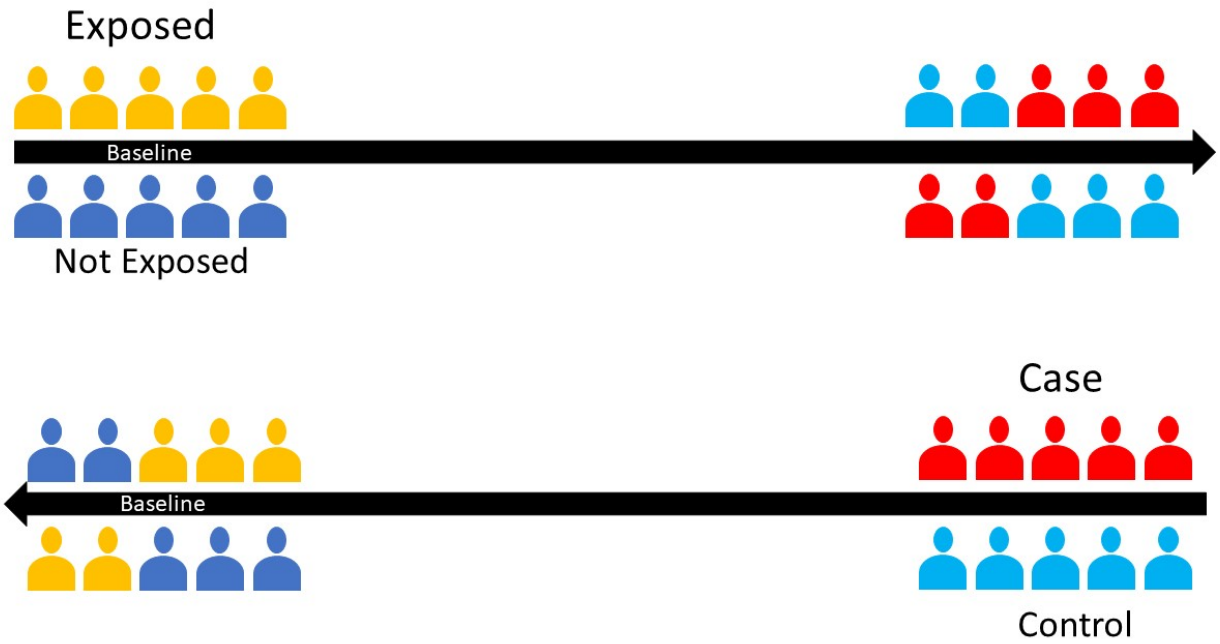

Figure: Prospective Cohort and Case-Control

Relative risk

What is relative risk?

Group	Disease	Non-Disease	Total
Exposed	a	b	E
Non-Exposed	c	d	NE
Total	D	ND	n

Table: 2×2

Prospective study

- The number of exposed (E) and non-exposed (NE) patients are defined in advance then it is possible to calculate the probabilities

$$P(disease|exposed) = \frac{a}{E}, \qquad P(disease|non-exposed) = \frac{c}{NE};$$

Relative risk

What is relative risk?

Group	Disease	Non-Disease	Total
Exposed	a	b	E
Non-Exposed	c	d	NE
Total	D	ND	n

Table: 2×2

Prospective study

- Then the effect measure relative risk (RR) is straightforward calculated by

$$RR = \frac{P(disease|exposed)}{P(disease|non-exposed)} = \frac{\frac{a}{E}}{\frac{c}{NE}} = \frac{a \times NE}{E \times c}.$$

Odds ratio

What is odds ratio?

Group	Disease	Non-Disease	Total
Exposed	a	b	E
Non-exposed	c	d	NE
Total	D	ND	n

Table: 2×2

Retrospective study

- The number exposed and non-exposed patients are not defined in advance, therefore the probabilites

$$P(disease|exposed) = \frac{a}{E}, \qquad P(disease|non-exposed) = \frac{c}{NE};$$

cannot be calculated and compared using relative risk.

Odds ratio

What is odds ratio?

Group	Disease	Non-Disease	Total
Exposed	a	b	E
Non-exposed	c	d	NE
Total	D	ND	n

Table: 2×2

Retrospective study

- We can calculate the odds for exposed patients

$$\begin{aligned} Odds(disease|exposed) &= \frac{P(disease|exposed)}{P(non-disease|exposed)}; \\ &= \frac{\frac{a}{E}}{\frac{b}{E}} = \frac{a}{b}; \end{aligned}$$

Odds ratio

What is odds ratio?

Group	Disease	Non-Disease	Total
Exposed	a	b	E
Non-exposed	c	d	NE
Total	D	ND	n

Table: 2×2

Retrospective study

- We can calculate the odds for non-exposed patients

$$\begin{aligned} Odds(disease|non-exposed) &= \frac{P(disease|non-exposed)}{P(non-disease|non-exposed)}; \\ &= \frac{\frac{c}{NE}}{\frac{d}{NE}} = \frac{c}{d}; \end{aligned}$$

Odds ratio

What is odds ratio?

Group	Disease	Non-Disease	Total
Exposed	a	b	E
Non-exposed	c	d	NE
Total	D	ND	n

Table: 2×2

Retrospective study

- Then, the effect measure odds ratio (OR) is calculated by

$$OR = \frac{Odds(disease|exposed)}{Odds(disease|non-exposed)} = \frac{\frac{a}{b}}{\frac{c}{d}} = \frac{a \times d}{b \times c}.$$

Odds ratio and Relative risk

Example

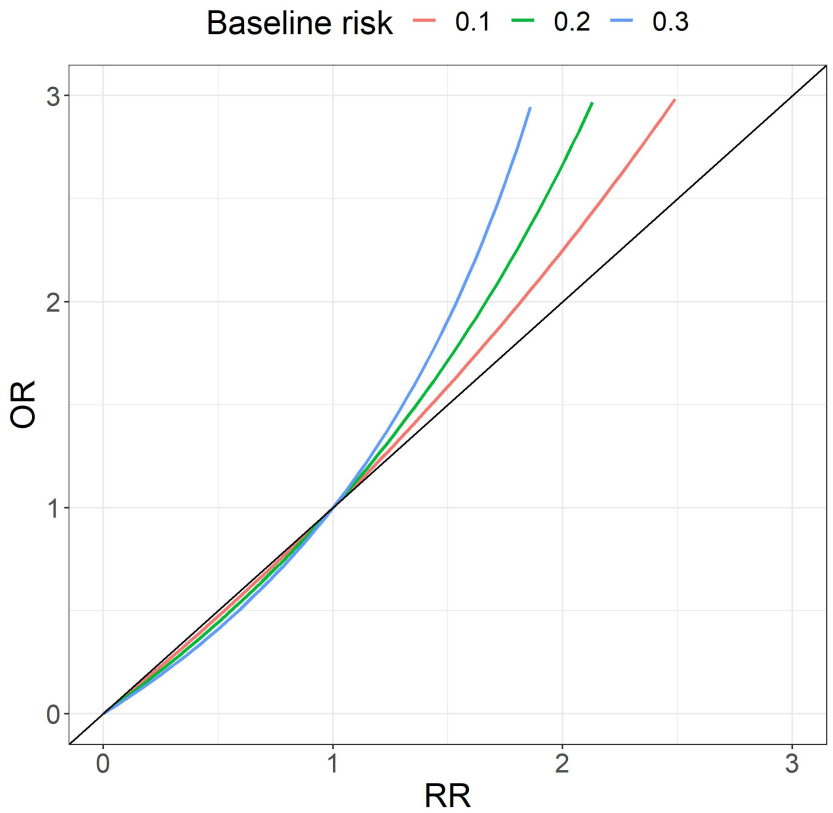

Figure: Relationship between odds ratio and relative risk for several baseline risks

Relative effects

Attention

- Relative effects are calculated based on the risk or odds of a reference group;
- If the risk/odds of a reference group is small, large values of OR and RR could not be meaningful;
- It is always possible to calculate absolute risk in a prospective study, but not in a retrospective study.

Odds ratio

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Total	59	50	109

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Table: Distribution of genotype by group

How should we compare the groups?

- Now, we can compare the groups:

$$Odds(HCC|AG + GG) = \frac{43}{29}, Odds(HCC|AA) = \frac{16}{21};$$

Odds ratio

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How should we compare the groups?

- Now, we can compare the groups:

$$OR(HCC|AG + GG : AA) = \frac{43 \times 21}{29 \times 16} = 1.94;$$

Odds ratio

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Table: Distribution of genotype by group

How should we compare the groups?

- H_0: there is no association between genotype and HCC;
- H_1: there is association between genotype and HCC;

Odds ratio

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Table: Distribution of genotype by group

How should we compare the groups?

- H_0: OR $= 1$;
- H_1: OR $\neq 1$;
- Chi-square test p value $= 0.11$.

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Logistic regression

Interferon lambda and hepatitis C virus core protein polymorphisms associated with liver cancer

Regression model

- Let be Y the presence of HCC;
- Y is a categorical measure;
- $Y \sim Bernouli(p)$ where p is the probability of the patient having HCC;
- p is a function of the SNP rs12980275:

$$log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 SNP : AG + GG.$$

Logistic regression

Interferon lambda and hepatitis C virus core protein polymorphisms associated with liver cancer

Coefficients	Estimate	Std. Error	t value	p value
(Intercept) β_0	-0.27	0.33	-0.819	0.413
(rs12980275) β_1	0.66	0.41	1.625	0.104

Table: Fitted Simple Logistic model

What do these p values mean?

- $H_0 : \beta_0 = 0 \qquad H_1 : \beta_0 \neq 0,$
- $H_0 : \beta_1 = 0 \qquad H_1 : \beta_1 \neq 0.$

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How to interpret the coefficients?

- We calculate the odds ratio,

$$OR(HCC|AG + GG : AA) = \exp\{\beta_1\} = 1.94.$$

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How to interpret the coefficients?

- The group with genotype AG+GG is 1.94 times (95% CI: 0.87 ; 4.39) more likely to be associated with HCC than the genotype AA.

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What are the advantages of a logistic regression from the Table 2×2?

- Odds ratios adjusted by confounding variables can be calculated and continuous covariables can be incorporated without cut-offs.

Logistic regression

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Regression model

- Let be Y the presence of HCC;
- Y is a categorical measure;
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- p is a function of the SNP rs12980275:

$$log\left(\frac{p}{1-p}\right) = \beta_0 + \beta_1 age + \beta_2 gender + \beta_3 SNP : AG + GG.$$

Logistic regression

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Coefficients	Estimate	Std. Error	t value	p value
(Intercept) β_0	-0.27	0.33	-0.819	0.413
(Age) β_1	0.07	0.02	2.684	0.007
(Gender) β_2	0.78	0.43	1.802	0.071
(SNP:AG+GG) β_3	0.66	0.44	2.019	0.043

Table: Fitted Multivariable Logistic model

Logistic regression

Interferon lambda and hepatitis C virus core protein polymorphisms associated with liver cancer

How to interpret the coefficients?

- We calculated the odds ratio followed by its confidence interval,

$$OR(HCC|AG + GG : AA) = exp(0.66) = 2.41,$$
$$95\% CI[1.04; 5.82].$$

- The group with genotype AG+GG is 2.41 times (95% CI: 1.04 ; 5.82) more likely to be associated with HCC than the genotype AA.

Logistic regression

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Logistic regression

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How to interpret the coefficients?

- We calculated the odds ratio followed by its confidence interval,

$$OR(HCC|(x+1):x) = exp(0.07) = 1.07, 95\%CI[1.02; 5.12].$$

- A patient of age **x+1** has odds 1.07 (95% CI: 1.02 ; 5.12) of having HCC times higher than a patient of age **x**.

Logistic regression

Interferon lambda and hepatitis C virus core protein polymorphisms associated with liver cancer

How to interpret the coefficients?

- We calculated the odds ratio followed by its confidence interval,

$$OR(HCC|(x+5):x) = exp(5 \times 0.07) = 1.07^5,$$
$$95\% CI[1.02^5; 5.12^5].$$

How to interpret the coefficients?

- We calculated the odds ratio followed by its confidence interval,

$$OR(HCC|(x+5):x) = 1.40, 95\%CI[1.10; 3518.437].$$

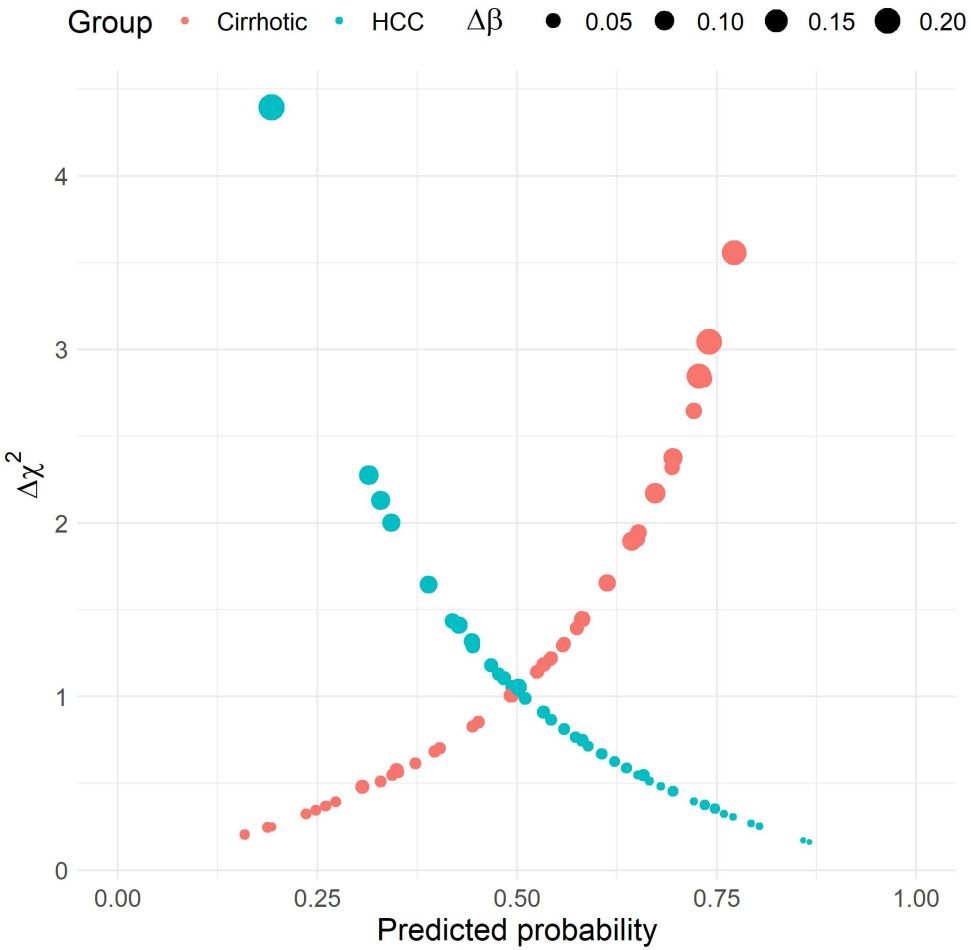
- A patient of age **x+5** has odds 1.40 (95% CI: 1.10 ; 3518.437) of having HCC times higher than a patient of age **x**.

Diagnostics

- Similarly to linear regression, logistic regression also requires diagnostic methods;
- Typical measures are $\Delta\beta$ and $\Delta\chi^2$ that measures the change in the regression coefficients and Chi-square statistic when an observation is removed;
- If the a fitted model suffers drastic changes on the estimates, then the observation is influential and results should be interpreted carefully.

Logistic regression

Diagnostics



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Logistic regression

Stroke Trajectory Project

- Objective: To develop prediction models to advice patients on quality of life (QOL) and caregiving needs.
- Study population: 1495 stroke patients discharged from acute care hospital are available in the database.
- Joint work with Sungjin Kim, Pamela Roberts and Harriet Aronow.

Outcomes

- Functional Independence Measure (< 80 vs. $>= 80$);
- Eating (All Others vs. 6/7);
- Dressing Upper (All Others vs. 6/7);
- Dressing Lower (All Others vs. 6/7);
- Toileting (All Others vs. 6/7);
- Walking (All Others vs. 6/7).

Covariates

- Gender;
- Age at admission;
- Marital status;
- Race (White, Black/AA, or Other);
- Modified Rankin at DC;
- NIHSS;
- Impairment Group Code;
- Diagnosis;
- DC Destination (Home vs. Institution);
- Length of Stay.

Prediction vs Inference

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Prediction vs Inference

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  - Discrimination and calibration are important;
  - p-values could be a possible guide to select predictors. They are not essential.

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- van Diepen, M., et al. (2017). Prediction versus aetiology: common pitfalls and how to avoid them. Nephrology Dialysis Transplantation, 32(suppl2), ii1-ii5

Discrimination

- It is also known as predictive performance;
- It measures the ability to separate different responses;
- Statistical tools: Area Under the Curve (AUC), Net Reclassification Index (NRI).

Calibration

- It is also known as goodness-of-fit;
- It measures the ability to make unbiased estimates for the probability of the event of interest;
- Statistical tools: Calibration plot, calibration-in-large and calibration slope.

References

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