Lecture 21 Normal Approximation To Binomial Distribution & Sampling Distribution of The Sample Proportion

BIO210 Biostatistics

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LIFE SCIENCES

Clinical Infectious Diseases

BRIEF REPORT

Relationship Between the ABO Blood Group and the Coronavirus Disease 2019 (COVID-19) Susceptibility

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ABO Blood Types And The COVID-19

- The results showed that blood group A was associated with a higher risk for acquiring COVID-19 compared with non-A blood groups, whereas blood group O was associated with a lower risk for the infection compared with non-O blood groups.
- The ABO blood group in $3,694$ normal people in Wuhan:

Total	A	B	AB	O
$3,694$	$1,188$	920	336	$1,250$

Data from: Xu P, Xiong Y, Cao K. Distribution of ABO and RhD blood group among Healthy Han population in Wuhan. J Clin Hematol (China). 2015(28):837.

ABO Blood Types

Allele	Frequency
I^A	p
I^B	q
i	r

$$p + q + r = 1$$

Allele frequency:

$$\mathbb{P}(G) = \frac{0.64N \times 2N + 0.32N}{2N} = 0.8$$

$$\mathbb{P}(g) = \frac{0.32N + 0.04 \times 2N}{2N} = 0.2$$

Genotype	Phenotype	Probability
$I^A I^A$	A	p^2
$I^A i$	A	$2pr$
$I^B I^B$	B	q^2
$I^B i$	B	$2qr$
$I^A I^B$	AB	$2pq$
ii	O	r^2

Estimation of ABO Blood Type Proportions In Wuhan

The ABO blood types in 3,694 normal people in Wuhan:

Total		A	B	AB	O
Number	3694	1,188	920	336	1,250
Proprotion	1	0.32	0.25	0.09	0.34

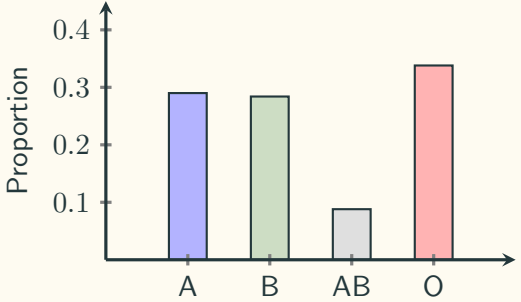
Calculation of allele freqquencies (p, q, r) of (I^A, I^B, i) using the Hardy-Weinberg model:

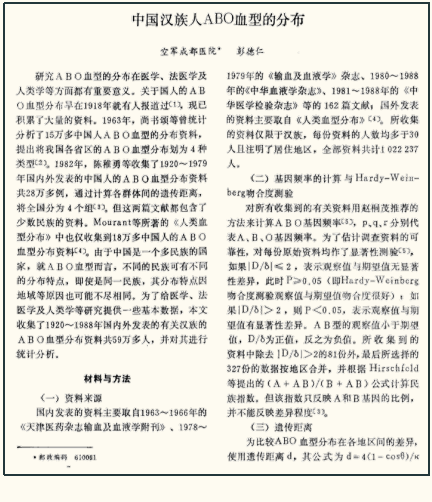
$$\begin{cases} p^2 + 2pr & = 0.32 \\ q^2 + 2qr & = 0.25 \\ 2pq & = 0.09 \\ r^2 & = 0.34 \end{cases} \Rightarrow \begin{cases} p & = 0.23 \\ q & = 0.19 \\ r & = 0.58 \end{cases}$$

ABO Blood Types Proportions In Han Chinese

Population distribution of ABO blood types in Han Chinese.

Total	A	B	AB	O
592,243	171,473	168,040	52,088	200,642
1	0.290	0.284	0.088	0.338





中国汉族人ABO血型的分布

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研究ABO血型的分布在医学、法医学及人类学等方面都有重要意义。关于国人的ABO血型分布早在1918年就有人报道过[1]，现已积累了大量的资料。1963年，简书颌等曾统计分析了15万多中国人ABO血型的分布资料，提出将我国各省区的ABO血型分布划为4种类型[2]。1982年，陈雅勇等收集了1920～1979年国内外发表的中国人的ABO血型分布资料共28万多例，通过计算各群体间的遗传距离，将全国分为4个组[3]。但这两篇文献都包含了少数民族的资料。Mourant等所著的《人类血型分布》中也仅收集到18万多中国人的ABO血型分布资料[4]。由于中国是一个多民族的国家，就ABO血型而言，不同的民族可有不同的分布特点，即使是同一民族，其分布特点因地域等原因也可能不尽相同。为了给医学、法医学及人类学等研究提供一些基本数据，本文收集了1920～1988年国内外发表的有关汉族的ABO血型分布资料共59万多人，并对其进行统计分析。

材料与方法

（一）资料来源

国内发表的资料主要取自1963～1966年的《天津医药杂志输血及血液学附刊》、1978～1979年的《输血及血液学》杂志、1980～1988年的《中华血液学杂志》、1981～1988年的《中华医学检验杂志》等的162篇文献，国外发表的资料主要取自《人类血型分布》[4]。所收集的资料仅限于汉族，每份资料的人数均多于30人且注明了居住地区。全部资料共计1 022 237人。

（二）基因频率的计算与Hardy-Weinberg吻合度测验

对所有收集到的有关资料用赵桐茂推荐的方法来计算ABO基因频率[3]，p、q、r分别代表A、B、O基因频率。为了估计调查资料的可靠性，对每份原始资料均作了显著性测验[5]。如果$|D/\delta|\leqslant 2$，表示观察值与期望值无显著性差异，此时$P\geqslant 0.05$（即Hardy-Weinberg吻合度测验观察值与期望值吻合度很好）；如果$|D/\delta|>2$，则$P<0.05$，表示观察值与期望值有显著性差异。AB型的观察值小于期望值，D/δ为正值，反之为负值。所收集到的资料中除去$|D/\delta|>2$的81份外，最后所选择的327份的数据按地区合并，并根据Hirschfeld等提出的$(A+AB)/(B+AB)$公式计算民族指数，但该指数只反映A和B基因的比例，并不能反映差异程度[3]。

（三）遗传距离

为比较ABO血型分布在各地区间的差异，使用遗传距离d，其公式为$d=4(1-\cos\theta)/\kappa$

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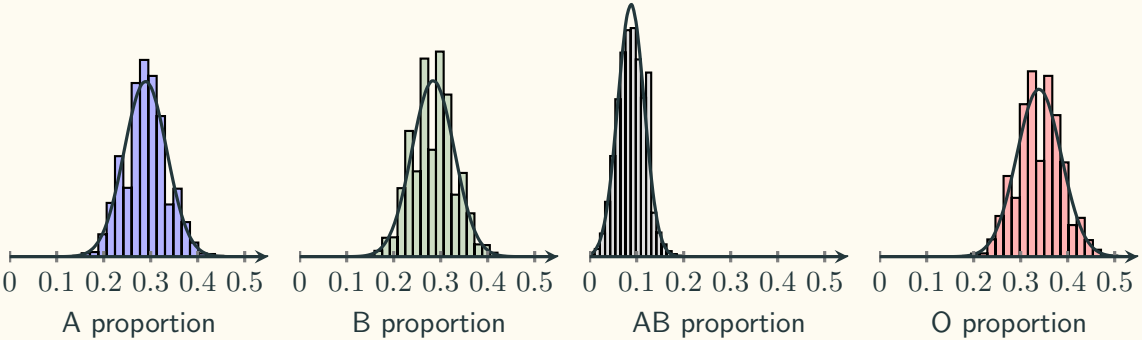
Sampling Distribution of ABO Blood Type Proportions

Population distribution of ABO blood types in Han Chinese.

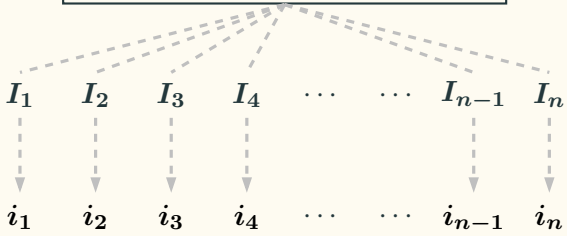
Total	A	B	AB	O
1	0.290	0.284	0.088	0.338



Sampling Distribution of The Sample Proportion

Fraction of type A blood in the population: π

A, A, B, O, O, AB, O, A, O, B, ...



I_1	I_2	I_3	I_4	$\cdots$	$\cdots$	I_{n-1}	I_n	$Y = \sum_{i=1}^{n} I_i$	$\bar{I} = \frac{1}{n}Y$	
i_1	i_2	i_3	i_4	$\cdots$	$\cdots$	i_{n-1}	i_n	y	$\bar{i}$	
1	0	1	1	$\cdots$	$\cdots$	1	0	$0.3n$	0.3	sample 1
0	1	1	0	$\cdots$	$\cdots$	1	1	$0.4n$	0.4	sample 2
0	1	0	0	$\cdots$	$\cdots$	0	1	$0.35n$	0.35	sample 3

The Sum And The Mean of Indicator Variables

$\boldsymbol{I}$: Indicator Variable

$$
\begin{aligned}
&i.i.d. \\
&\boldsymbol{I_1} \sim Ber(\pi) \\
&\boldsymbol{I_2} \sim Ber(\pi) \\
&\boldsymbol{I_3} \sim Ber(\pi) \\
&\vdots \\
&\vdots \\
&\boldsymbol{I_{n-1}} \sim Ber(\pi) \\
&\boldsymbol{I_n} \sim Ber(\pi)
\end{aligned}
$$

Meaning of $\boldsymbol{Y}$: number of people with blood type A per n people.
Meaning of $\bar{\boldsymbol{I}}$: The proportion of people with blood type A.

$$\boldsymbol{Y} = \sum_{i=1}^{n} \boldsymbol{I_i} \sim ? \qquad \bar{\boldsymbol{I}} = \frac{1}{n}\boldsymbol{Y} \sim ?$$

By definition:

$$\boldsymbol{Y} \sim B(n, \pi)$$

By The Central Limit Theorem:

$$\bar{\boldsymbol{I}} \dot{\sim} \mathcal{N}\left(\mu = \pi, \sigma^2 = \frac{\pi(1-\pi)}{n}\right)$$

$$\boldsymbol{Y} = n\bar{\boldsymbol{I}} \dot{\sim} \mathcal{N}\left(\mu = n\pi, \sigma^2 = n\pi(1-\pi)\right)$$

Normal Approximation To A Binomial Distribution

Our knowledge about Han Chinese (Peng, 1991):

Total	A	B	AB	O
1	0.290	0.284	0.088	0.338

A sample from Wuhan (Xu $et\ al.$, 2015): $1,188$ out of $3,694$ people have blood type A.

Questions:

1. When draw a random sample ($n = 3,694$), what is the probability of getting $1,100 - 1,200$ people with blood type A?
2. When draw a random sample ($n = 3,694$), what is the probability of getting $1,188$ people with blood type A?

Normal Approximation To A Binomial Distribution

Question 1:

Use the Binomial probability :

$$\sum_{k=1100}^{1200} \binom{3694}{k} 0.29^k \, 0.71^{3694-k} = 0.152949$$

Use the Normal probability :

$$\mathbb{P}\left(1100 \leqslant x \leqslant 1200\right) = \mathbb{P}\left(\frac{1100 - 1071.26}{27.58} \leqslant z \leqslant \frac{1200 - 1071.26}{27.58}\right) = 0.148681$$

Use the Normal probability with continuity correction :

$$\mathbb{P}\left(1100 - 0.5 \leqslant x \leqslant 1200 + 0.5\right) = 0.152923$$

Normal Approximation To A Binomial Distribution

Question 2:

Use the Binomial probability :

$$\binom{3694}{1188} 0.29^{1188} 0.71^{3694-1188} = 2.16 \times 10^{-6}$$

Use the Normal probability with continuity correction :

$$\mathbb{P}\left(1188 - 0.5 \leqslant x \leqslant 1188 + 0.5\right) = 1.86 \times 10^{-6}$$

Sampling Distribution of The Sample Proportion

- $\bar{I} \sim$ **Sampling Distribution of The Sample Proportion**
- Generally, we used $p = \frac{x}{n}$ to represent the sample proportion, which is an estimate for the population parameter π.
- According to the **Central Limit Theorem**, when the sample size n is large enough, we have:

$$\boldsymbol{P} \dot{\sim} \mathcal{N}(\mu_{\boldsymbol{P}}, \sigma^2_{\boldsymbol{P}}), \text{ where } \mu_{\boldsymbol{P}} = \pi, \sigma^2_{\boldsymbol{P}} = \frac{\pi(1-\pi)}{n}$$

Sampling Distribution of The Sample Proportion