01 PROJECT DESCRIPTION

INITIAL GOAL
To study the incidence rate of misdiagnosis in rare diseases.

PROBLEM EXPLANATION
"If there was a medical test with 98% reliability to detect if a person suffers a certain illness (such as cancer) and that 1 in 200 suffer that illness and we are tested positive one day, to what extent should we worry about it? How likely is it that we have that illness?"

Source: Paul Bozick ("We teach the mathematics to hunt dragons, what maths and what are they are not?"

02 DATA and GRAPHS

ABOUT RARE DISEASES (R.D.)
What is considered a rare disease?
A disease that affects 1 out of 2000 people.

Medical and social consequences
Most of them cannot be cured, which makes the patients vulnerable.

How many rare diseases are there?
Up to now 6038 rare diseases are known.

Treatment and diagnosis
There has been progress but these are orphan diseases, only 20% of them are studied.

RARE DISEASES DAY
It is the last day of February since 2008.

Origin and characteristics
Most of them are genetic, but not all of them. They are chronic and progressive.

MEDICAL ATTENTION IN R.D.
As we can observe:
Only 35% get the treatment that they need.
Almost 20% of the patients have had to wait 10 or more years for their diagnosis.

DISABILITY AND DEPENDENCY WITH R.D.
Almost a 25% of the patients have a disability bigger than 75%
More than a 40% of the patients have a severe level of dependency.

DISCRIMINATION
One of the pieces of information that stands out is that in the educational field the discrimination exceeds the 40%.

But what is most impressive is the fact that, since 2006, discrimination has risen in every field.

BAYES’ THEOREM
Thomas Bayes (s XVIII): If \( A_1, A_2, ..., A_n \) is a system of events, where \( S \) is an event of anytype for which we know the \( P(S|A_i) \), then:

\[
P(A_i|S) = \frac{P(A_i) \cdot P(S|A_i)}{ \sum P(A_i) \cdot P(S|A_i)}
\]

\( P(A_i) \) are called “Prior probability” because they are known.
\( P(S|A_i) \) are called “Likelihood” as they are easily understood.
\( P(A_i|S) \) are called “Posterior probability”, they must be calculated.

Application: medical diagnosis; establish the diagnosis of a patient from a series of symptoms; the symptoms and the disease don’t have a binomial correspondence.

03 STUDIED DISEASES

ULLRICH CONGENITAL DYSTROPHY (UCMD)
Early appearances, muscle weakness, slow progression, multiple contractures, marked hypermobility and normal intelligence.
There are only 30 confirmed cases in the world.

Let’s see the different way to teach in the explained test.
As Prevalence: 9:100000 and Test Reliability of 95%, then:

\( P(E) = \frac{\text{Total healthy}}{\text{Total people}} = \frac{9999}{10000} = 0,9999 \)

\( P(T^+) = \frac{\text{Positive test}}{\text{Total people}} = \frac{9751}{10000} = 0,9751 \)

\( P(T^-) = \frac{\text{Negative test}}{\text{Total people}} = \frac{249}{10000} = 0,00249 \)

\( P(T^+|E) = \frac{\text{Positive test}}{\text{Total healthy}} = \frac{9751}{9999} = 0,97972 \)

\( P(T^-|E) = \frac{\text{Negative test}}{\text{Total healthy}} = \frac{249}{9999} = 0,00249 \)

\( P(T^+|\neg E) = \frac{\text{Positive test}}{\text{Total sick}} = \frac{74}{199} = 0,3719 \)

\( P(T^-|\neg E) = \frac{\text{Negative test}}{\text{Total sick}} = \frac{19}{199} = 0,09547 \)

Where: \( E \) is the event of people suffering from the disease, \( T^+ \) is a positive test and \( T^- \) is a negative test.

BETHLEHEM MYOPATHY
Rare autosomal dominant form of slowly progressive muscular dystrophy. Less than 100 cases throughout history.

Prevalence: 1:100000; Test Reliability of 95%, then:

\( P(T^+) = \frac{\text{Positive test}}{\text{Total people}} = \frac{9751}{10000} = 0,9751 \)

\( P(T^-) = \frac{\text{Negative test}}{\text{Total people}} = \frac{249}{10000} = 0,00249 \)

\( P(T^+|E) = \frac{\text{Positive test}}{\text{Total healthy}} = \frac{9751}{9999} = 0,97972 \)

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CUSHING’S SYNDROME (CS)
Hormonal disorders due to high and prolonged levels of exposure to glucocorticoids, can be of both endogenous and exogenous origin.

Prevalence: 9:100000; Sensitivity test 100% and Specificity 93%, then:

\( P(T^+) = \frac{\text{Positive test}}{\text{Total people}} = \frac{9751}{10000} = 0,9751 \)

\( P(T^-) = \frac{\text{Negative test}}{\text{Total people}} = \frac{249}{10000} = 0,00249 \)

\( P(T^+|E) = \frac{\text{Positive test}}{\text{Total healthy}} = \frac{9751}{9999} = 0,97972 \)

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04 ANALYSIS OF THE RESULTS.

In cases like those studied, there is only a 5-7% chance of suffering from the disease having tested positive.

Many shocking results stem from “the false positive paradox” with low prevalences, false positive tests are much more likely than true positives.

These results are with tests whose reliability is at least 95%.

Probability combined with Statistics is a diagnostic tool to decide if a person is sick (using Bayes’ Theorem).

Rare diseases, despite their numbers, are still truly unknown.

People who get sick will always be a small percentage compared to what would seem to us due to the reliability of the test (95%).

It’s always better to keep calm, be patient and optimistic.