REDUCING DIAGNOSTIC ERROR IN MEDICINE

THROUGH AN UNDERSTANDING OF THE LOGICAL BASIS UNDERLYING THE CONCEPT OF A DIAGNOSIS

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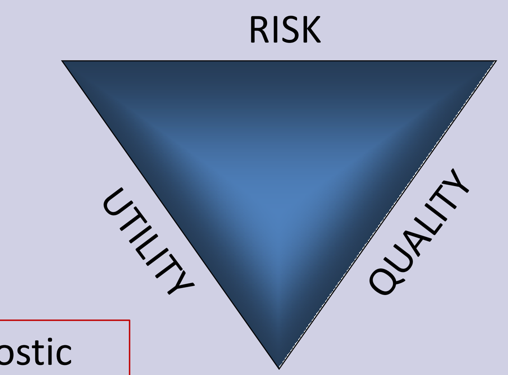


1. Explain how the logical basis of medicine combined with statistical inference is the foundation of the diagnostic process. 2. Describe how Venn diagrams can assist in determine what epidemiologic data is needed to assure reliable diagnostic criteria. 3. Explain why it will require computer assistance to implement this endeavor.

SITUATION

The concept of a diagnosis is very complex and involves correlating clinical observations with one or more potential diseases using a combination of statistical inference and one or more logical approaches.

However, data regarding frequency of multiple clinical findings, their relation to each other within any one disease, as well as between more than one disease, are not generally available in the literature.

This prevents us from assessing the reliability of clinical findings singly and as coincident sets in establishing the correct diagnosis with the highest degree of certainty.

PROBLEM

How can we

RISK	*Maximize patient safety* by establishing the true prior probabilities for clinical sets
QUALITY	*Minimize* discomfort and the pain *suffered* due to misdiagnosis caused by absence of these clinical sets
UTILITY	*Minimize expenditure* of scarce resources by relating clinical data to disease using prior probabilities

SOLUTION

It is proposed that data be gathered regarding the frequency with which multiple clinical findings coincide within and across all diseases.

From this, diseases most associated with any clinical set can be identified as well as how the relationship of clinical findings within diagnostic sets affect the probability of a disease being present or absent.

It is further proposed that set theory applied through differential diagnosis engines will allow for the very complex Bayes Probabilities to be calculated allowing prioritized differential diagnoses that direct clinical investigation resulting in a high probability of a correct diagnosis.

IMPLEMENTATION

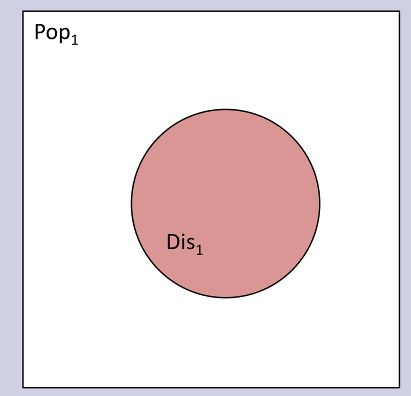
A review of the literature regarding the logic of diagnostic medicine, set theory, and statistical analysis was carried out.

Several prior theoretical models proposed for establishing reliable clinical diagnostic criteria were evaluated.

A set of Venn diagrams is presented to illustrate the problem we face regarding potential complexity of the diagnostic process and to show how truly reliable diagnostic criteria can only be established through a higher level of stratification and collation of epidemiologic data.

EXAMPLE VENN DIAGRAMS FOR ESTABLISHING BAYES THEOREM

SIMPLIFIED EXAMPLE OF HOW EPIDEMIOLOGY CAN INCREASE THE CERTAINTY OF A CORRECT DIAGNOSIS BY PRIOR PROBABILITY



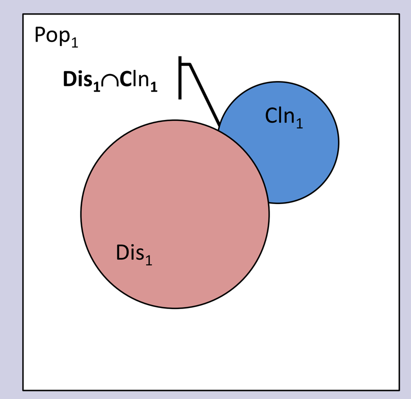
Pop_1 = A specified **Patient Population**
Pop_1 is an ordinal set where the elements of the set are people

Dis_1 = A specified subset of Pop_1 that has a specific **Disease**
Dis_1 is an ordinal set where the elements are a set of people with Disease Dis_1

The probability of having **Disease Dis_1** given **Population Pop_1** is:

$$P(Dis_1|Pop_1) = Count(Dis_1)/Count(Pop_1)^*$$

*** Below $Count(Dis_1)$ and $Count(Cln_1)$ are represented by set symbols Dis_1 and Cln_1**



Cln_1 = A specified subset of **Pop_1** that has a specific **Clinical finding**
Cln_1 is an ordinal set where the elements are a set of people with the specified **Clinical finding**

Now the probability of **Disease Dis_1** given **Clinical finding Cln_1** is increased to:

$$P(Dis_1|Cln_1) = (Dis_1 \cap Cln_1)/Cln_1$$

And the probability of **Clinical finding Cln_1** given **Disease Dis_1** is increased to:

$$P(Cln_1|Dis_1) = (Dis_1 \cap Cln_1)/Dis_1$$

Where **$Dis_1 \cap Cln_1$** is the intersection of **Dis_1** and **Cln_1**

- By knowing the patient has **Clinical Finding Cln_1** we reduce the probability denominator from **Pop_1** to **Cln_1**
- This increases the ratio and so the probability the patient has **Disease Dis_1** given **Clinical Finding Cln1**
- Conversely, by knowing the patient has **Disease Dis_1** we reduce the probability denominator from **Pop_1** to **Dis_1**
- This increases the ratio and so the probability the patient has **Clinical Finding Cln_1** given **Disease Dis_1**
- The probability the patient has both **Disease Dis1** and **Clinical Finding Cln1** equals **$Dis_1 \cap Cln_1 / Pop_1$**

This is the concept of Bayes' prior probability.

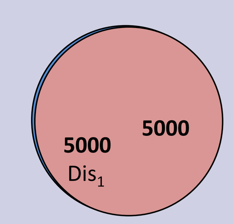
HOWEVER, WE FACE A PROBLEM. WITH JUST ONE DISEASE AND ONE CLINICAL FINDING THERE ARE FIVE POSSIBLE VENN DIAGRAMS. ADD ANOTHER CLINICAL FINDING OR DISEASE AND THE NUMBER RISES TO $5^2 = 25$. ADD ANOTHER AND IT'S $5^3 = 125$!

SIMPLEST CASE: GIVEN ONE DIAGNOSIS DIS_1 AND ONE CLINICAL FINDING CLN_1 IN POPULATION POP_1 OF 100,000 THERE ARE FIVE POSSIBILITIES:

IDENTITY: Cln_1 IS PATHOGNOMONIC OF Dis_1

1:1 and On to
Clinical Finding Cln_1 is present if and only if Disease Dis_1 is present
[Disease Dis_1 is present if and only if Clinical Finding Cln_1 is present]

5%



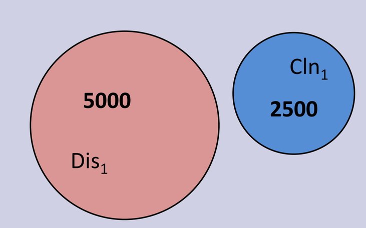
IDENTITY: Cln_1 IS PATHOGNOMONIC OF Dis_1

$P(Cln_1|Dis_1) = P(Dis_1|Cln_1) = Cln_1/Pop_1 = Dis_1/Pop_1$
$P(Cln_1|NOT\ Dis_1) = P(Dis_1|NOT\ Cln_1) = 0$

EXCLUSION: Cln_1 IS PATHOGNOMONIC OF NOT Dis_1

If Clinical Finding Cln_1 is present, then Disease Dis_1 is not present
If Disease Dis_1 is present, then Clinical Finding Cln_1 is not present

0%



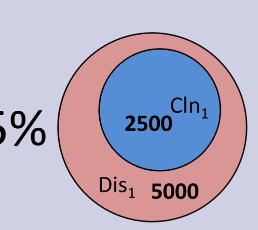
EXCLUSION: Cln_1 IS PATHOGNOMONIC OF NOT Dis_1

$P(Cln_1|Dis_1) = P(Dis_1|Cln_1) = 0.0$
$P(Cln_1|NOT\ Dis_1) = Cln_1/(Pop_1 - Dis_1)$
$P(Dis_1|NOT\ Cln_1) = Dis_1/(Pop_1 - Cln_1)$

Cln_1 IS A SUBSET OF Dis_1

Clinical Finding Cln_1 is present if and only if Disease Dis_1 is present

1.25%



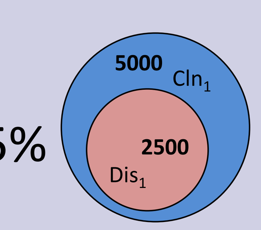
Cln_1 IS A SUBSET OF Dis_1

$P(Cln_1|Dis_1) = Cln_1/Dis_1$
$P(Cln_1|NOT\ Dis_1) = 0$

Dis_1 IS A SUBSET OF Cln_1 [1.25%]

Disease Dis_1 is present if and only if Clinical Finding Cln_1 is present

1.25%



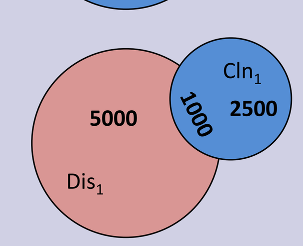
Dis_1 IS A SUBSET OF THE Cln_1

$P(Dis_1|Cln_1) = Dis_1/Clin_1$
$P(Dis_1|NOT\ Cln_1) = 0$

INTERSECTION OF Dis_1 AND Cln_1 < UNION OF Dis_1 AND Cln_1

Disease Dis_1 is present where Dis_1 and Cln_1 intersect
Clinical Finding Cln_1 is present where Dis_1 and Cln_1 intersect

1%



INTERSECTION OF Dis_1 AND Cln_1 < UNION OF Dis_1 AND Cln_1

$P(Cln_1|Dis_1) = Cln_1 \cap Dis_1/Dis_1$
$P(Dis_1|Cln_1) = Cln_1 \cap Dis_1/Cln_1$
$P(Cln_1|NOT\ Dis_1) = (Cln_1 - Cln_1 \cap Dis_1)/Pop_1$
$P(D_1|NOT\ Cln_1) = (Dis_1 - Cln_1 \cap Dis_1)/Pop_1$

THIS MEANS THAT, IF WE WISH TO SOLVE THE PROBLEM OF DIAGNOSTIC ERROR IN MEDICINE, IT WILL REQUIRE DEVELOPING EPIDEMIOLOGIC DATA THAT ALLOWS FOR CALCULATING PROBABILITIES FOR ALL POSSIBLE COMBINATIONS OF CLINICAL CRITERIA

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COST BENEFIT ANALYSIS

It can be shown mathematically that calculation of prior probabilities related to sets of clinical findings greatly increases the probability of making a correct diagnosis, and/or, excluding an incorrect diagnosis.

The result would be a dramatic improvement of:

- Patient Safety due to improved diagnostic accuracy
- Quality of Patient Care due to more timely and appropriate therapy
- Value of Resources Spent in the diagnostic and therapeutic process

EXAMPLE

For a relatively simple diagnosis of acute appendicitis, sources in the literature list varying frequencies for some of the most common findings:

- Fever
- Leukocytosis
- Abdominal Pain
- Nausea and Vomiting

However, only a small number of prior probabilities for simultaneously occurring clinical findings can be found. [For example: **Fever $\cap$ Leuko-cytosis $\cap$ Abdominal Pain**]. Rarely does the literature routinely include sets of clinical findings that would reliably rule out acute appendicitis. Lack of this epidemiologic data limits the capacity to avoid a misdiagnosis.

The Venn diagrams show that, to assure the highest certainty in making or ruling out a diagnosis, many critical elements of set theory and Bayesian statistics must be understood by both researchers and clinicians.

Therefore, to establish a foundation for significantly **Reducing Diagnostic Error in Medicine** it will be necessary to create:

- Clinical data sets based on accurate and precise epidemiologic data
- Application of set theory to determine prior probabilities
- Differential diagnosis engines to carry out the complex calculations
- **eHR**'s that produce accurate clinical data to feed into these engines

CONCLUSION

The present state of diagnostic "science" is not well developed regarding the underlying logic that drives it.

This is largely due to the absence of reliable epidemiologic data upon which to assemble diagnostic criteria sets that include the probability relationship between the elements of these sets.

Until this issue is fully addressed, all other efforts to:

REDUCE DIAGNOSTIC ERROR IN MEDICINE

are destined to fail.