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Group Testing Considerations: A Useful Method For The Clinical Laboratory

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Abstract

Robert Dorfman first suggested group testing, commonly referred to as pooled sample testing, in 1943. Although sample pooling has been used extensively in blood banks, clinical laboratories have historically frowned upon it. To counteract supply shortages, clinical laboratories are becoming more interested in group testing as a result of the ongoing COVID-19 pandemic. We provide a practical method that a clinical laboratory may use to implement pooled testing for SARS-CoV-2 PCR testing, as well as five criteria to evaluate an analyte's suitability for pooled sample testing generally. The five standards that we suggest are: In order to maximize public health outcomes, it is imperative that (1) the analyte concentrations in diseased individuals be at least one order of magnitude (10 times) higher than in healthy individuals, (2) sample dilution not unduly reduce clinical sensitivity, (3) the current prevalence be low enough for the number of samples pooled for the particular protocol, (4) there is no need for a quick turnaround time, and (5) resource rationing be implemented. We recommend the following five essential steps for a successful implementation: (1) identifying the pooling window (pre-pre analytical, pre-analytical, and analytical); (2) verifying the pooling protocol; (3) making sure the archival system and infrastructure are sufficient; (4) setting up the laboratory information system; and (5) staff training During pool testing.

Keywords: Group Testing, Laboratory, Clinical laboratory.

Introduction:

On March 11, 2020, the World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19) to be a pandemic. Since then, it has caused lockdowns in numerous nations, ranging in severity. Clinical laboratories are under tremendous pressure to increase testing capacity in the midst of the pandemic, even though there is a global reagent shortage. One way to lessen supply shortages is to conduct group testing. In this paper, we summarize some of the standards by which an analyte's suitability for pooled sample testing is evaluated and we illustrate a workable strategy that a clinical laboratory can use to put pooled testing into practice

(Gilbert, 2008) .

During the height of World War II, in 1943, Professor Robert Dorfman first proposed group testing, also referred to as pooled sample testing. Syphilis was then diagnosed using the Wassermann complement fixation test and the Kahn flocculation test. In order to have enough reagents to screen every prospective American recruit, Dorfman suggested combining several samples. A pool's component samples are examined one at a time if it is positive. All constituent samples are considered negative if a pool is negative. The Dorfman pooling strategy preserves reagents in low disease prevalence situations (Bialynicki, 2008).

First criterion: The concentrations of analytes in individuals with diseases should be at least ten times greater than those in healthy individuals.

In order for group testing to be successful, the distribution of analyte concentrations in sick individuals must constantly exceed that of the analyte concentration in healthy individuals, preferably by at least one order of magnitude (10 times). Because of this, the concentration in the diluted pool can be much higher than the upper bound of the healthy reference interval.

Second criterion: Excessive clinical sensitivity reduction from sample dilution is not acceptable.

Ceteris paribus, diluting a positive serum from an infected patient with a negative serum from a healthy individual will inevitably lower the analyte concentration and, consequently, lower the detectability. Due to sensitivity issues, smaller pools of four to sixteen donors or individual donor nucleic acid amplification tests have become the norm in blood banking recently.

Every PCR CT value has an imprecision because of various factors such as temperature fluctuations, pipetting transfer volume, PCR efficiencies of the polymerase/primer/template complex, and fluorescence measurements (Gastwirth , 2000).

Criterion 3: The disease's current prevalence must be low enough for the pooling protocol to be effective.

The crux of reagent savings lies in optimising the sample pool size with respect to the prevalence. Before beginning a group testing protocol, it is crucial to comprehend the mathematics because careful monitoring of the prevalence is necessary. Thus far most pooled testing protocols implemented are based on the Dorfman protocol (Levinson , 2010).

Each group in the Dorfman protocol is tested after k samples have been pooled. Constituent samples are deemed negative if the group is negative. Every sample that makes up the component is tested separately if the group tests positive. This is the most straightforward and useful method for daily application (McCudden , 2009).

Criteria 4: Quick turnaround times are not necessary. If the pool

positive, the individual constituents are analyzed after the pooled sample, according to the Dorfman protocol. Results at the group testing stage will be withheld for negative samples combined with a positive sample. The turnaround time is further exacerbated by multistage adaptive protocol. Complex pipetting steps in one-stage non-adaptive protocols may also result in longer processing times. Generally, samples from the emergency room, inpatient wards, primary care, and the community are sent to a hospital clinical laboratory (Spencer, 1990).

Criterion 5: Resource rationing is imperative in order to maximize the outcomes for public health:

Prior to pooling, there should be a clear need for resource rationing. This may be due to a lack of testing reagents or financial or skilled labor constraints in an environment with limited resources. There was a global shortage of viral extraction kits during the early stages of the pandemic, necessitating the preservation of extraction kits. With a theoretical delay of only one CT and little sensitivity loss, even a pool size of two can save 48% of reagents at a prevalence of 1% and double the tests generated by using the Dorfman Protocol (Goede , 2016).

A Realistic Method for Clinical Laboratory Practice:

Once all five requirements have been met, laboratories can move forward with implementation. Using the Dorfman Protocol, we recommend the following five essential actions for a successful implementation of SARS-CoV-2 PCR pooled testing:

1- Choosing the stage at which pooling occurs (pre-pre analytical, pre- analytical, or analytical)
2- Verifying the pooling protocol.
3- supplying sufficient infrastructure and space for archives.
4- Laboratory information system (LIS) configuration.
5- Employee education.

Recommendations:

In order to evaluate an analyte's suitability for pooled sample testing, we suggest the following five criteria:

1- At the very least, the analyte concentrations in sick individuals should be one order of magnitude greater than those in healthy individuals.
2- The clinical sensitivity shouldn't be significantly decreased by sample dilution.
3- For the purpose of the particular protocol, the disease's

current prevalence must be low enough for the number of samples in each pool.

4- A quick turnaround time is not necessary.

5- Resource rationing is absolutely necessary in order to maximize public health outcomes.

Conclusion:

In conclusion, a lot of analytes have the potential to be used in pooled testing, particularly in the area of infectious diseases. The key to a successful and anticipated implementation of group testing in the clinical laboratory is proper analyte selection, assuring adequate sensitivity, monitoring prevalence, establishing a firm need for resource conservation, validating the assay method for pooling, configuring the LIS, and staff training. While pooling may provide greater testing accessibility at the expense of decreased sensitivity, it is not a magic bullet for the reagent shortage. The adage "no test is better than a bad test" means that while group testing can increase testing capacity, the consequences of false negatives must be carefully considered, and sensitivity reduction must be minimized. Clinical laboratories may be interested in one-stage non-adaptive methods that use compressed sensing with error correction codes in addition to the Dorfman protocol. These methods have the potential to lower the number of false positives and negatives in the designated prevalence band.

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