HW1 has been posted.

I will post solutions one week from now

Discrete Probability Distributions

Random Variables

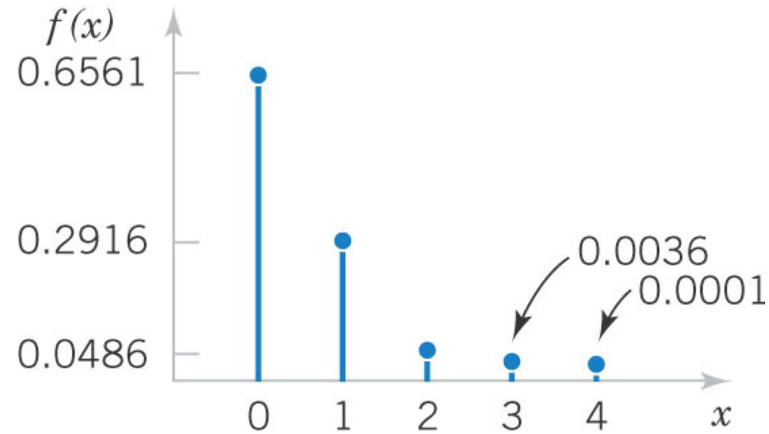
- A variable that associates a number with the outcome of a random experiment is called a random variable.
- Notation: random variable is denoted by an uppercase letter, such as X. After the experiment is conducted, the measured value is denoted by a lowercase letter, such a x. Both X and x are shown in italics, e.g., $P(X=x)$.

Continuous & Discrete Random Variables

- A discrete random variable is usually an integer number
  - N - the number of p53 proteins in a cell
  - D - the number of nucleotides different between two gene sequences of length L
- A continuous random variable is a real number
  - C=N/V – the concentration of p53 protein in a cell of volume V
  - Percentage (D/L)*100% of different nucleotides in gene sequences of different lengths L
    (depending on the set of L's it may be discrete but dense)

Probability Mass Function (PMF)

- I want to compare all <u>4-mers</u> in a pair of human genomes
- *X* – random variable: the number of nucleotide differences in a given 4-mer
- Probability Mass Function: f(x) or P(X=x) – the probability that the # of SNPs is exactly equal to x



Probability Mass Function for the # of mismatches in 4-mers

$P(X=0) =$	0.6561
$P(X=1) =$	0.2916
$P(X=2) =$	0.0486
$P(X=3) =$	0.0036
$P(X=4) =$	0.0001
$\sum_x P(X=x)=$	1.0000

Cumulative Distribution Function (CDF)

x	$P(X = x)$	CDF: $P(X \le x)$	CCDF: $P(X > x)$
-1	0.0000	0.0000	1.0000
0	0.6561	0.6561	0.3439
1	0.2916	0.9477	0.0523
2	0.0486	0.9963	0.0037
3	0.0036	0.9999	0.0001
4	0.0001	1.0000	0.0000

Cumulative Distribution Function CDF: $F(x)=P(X \le x)$

Example:

$F(3)=P(X \le 3) = P(X=0) + P(X=1) + P(X=2) + P(X=3) = 0.9999$

Complementary Cumulative Distribution Function (tail distribution) or CCDF: $F_{>}(x)=P(X>x)$

Example: $F_{>}(0)= P(X > 0) = 1 - P(X \le 0) = 1-0.6561=0.3439$

Mean or Expected Value of X

The mean or expected value of the discrete random variable X, denoted as μ or $E(X)$, is

$$\mu = E(X) = \sum_x x \cdot P(X = x) = \sum_x x \cdot f(x)$$

- The mean = the weighted average of all possible values of *X*. It represents its "center of mass"

- The mean may, or may not, be an allowed value of X

- It is also called the arithmetic mean (to distinguish from e.g. the geometric mean discussed later)

- Mean may be infinite if X any integer and tail P(X=x)>c/x^2

Outcomes of 6 random experiments

$0, 1, 0, 0, 2, 1$

$$\text{Mean} = \frac{0+1+0+0+2+1}{6} =$$

$$= \frac{3\times 0 + 2\times 1 + 1\times 2}{6} =$$

$$= 0 \times \frac{3}{6} + 1 \times \frac{2}{6} + 2 \times \frac{1}{6} = \sum_{x=0}^{2} x P(X=x)$$

- $E[X] = \sum_{x} x \cdot P(X=x)$
- $E[X^2] = \sum x^2 \cdot P(X=x)$
- $E[a \cdot X + b \cdot X^2] = \sum (ax + bx^2) \times P(X=x) = a \cdot \sum x P(X=x) + b \sum x^2 P(X=x)$
- $E[e^X] = \sum e^x P(X=x)$

Variance $V(X)$: square of a typical deviation from the mean $\mu = E(X)$

$V(X) = \sigma^2$, where σ is called standard deviation

$$\sigma^2 = V(X) = E\left((X-\mu)^2\right) =$$
$$= E(X^2 - 2\mu X + \mu^2) = E(X^2) -$$
$$- 2\mu E(X) + \mu^2 = E(X^2) - 2\mu^2 + \mu^2 =$$
$$= E(X^2) - \mu^2 = E(X^2) - \left(E(X)\right)^2$$

Variance of a Random Variable

If X is a discrete random variable with probability mass function $f(x)$,

$$E\left[h(X)\right] = \sum_x h(x) \cdot P(X = x) = \sum_x h(x) f(x) \qquad (3\text{-}4)$$

If $h(x) = (X - \mu)^2$, then its expectation, $V(x)$, is the variance of X.

$\sigma = \sqrt{V(x)}$, is called standard deviation of X

$$\sigma^2 = V(X) = \sum_x (x-\mu)^2 f(x) \text{ is the definitional formula}$$

$$= \sum_x \left(x^2 - 2\mu x + \mu^2\right) f(x)$$

$$= \sum_x x^2 f(x) - 2\mu \sum xf(x) + \mu^2 \sum_x f(x)$$

$$= \sum_x x^2 f(x) - 2\mu^2 + \mu^2$$

$$= \sum_x x^2 f(x) - \mu^2 \text{ is the computational formula}$$

Variance can be infinite

if X can be any integer

and tail of P(X=x) ≥c/x^3

Skewness of a random variable

- Want to quantify how asymmetric is the distribution around the mean?
- Need any odd moment: $E[(X-\mu)^{2n+1}]$
- Cannot do it with the first moment: $E[X-\mu]=0$
- Normalized 3-rd moment is skewness: $\gamma_1=E[(X-\mu)^3/\sigma^3]$
- Skewness can be infinite if X takes unbounded positive integer values and the tail $P(X=x) \geq c/x^4$ for large x

Geometric mean of a random variable

- Useful for very broad distributions (many orders of magnitude)?
- Mean may be dominated by very unlikely but very large events. Think of a lottery
- Exponent of the mean of *log X*: *Geometric mean=exp(E[log X])*
- Geometric mean usually is not infinite

Summary: Parameters of a Probability Distribution

- Probability Mass Function (PMF): $f(x)=\text{Prob}(X=x)$
- Cumulative Distribution Function (CDF): $F(x)=\text{Prob}(X\leq x)$
- Complementary Cumulative Distribution Function (CCDF): $F_{>}(x)=\text{Prob}(X>x)$
- The mean, $\mu=E[X]$, is a measure of the center of mass of a random variable
- The variance, $V(X)=E[(X-\mu)^2]$, is a measure of the dispersion of a random variable around its mean
- The standard deviation, $\sigma=[V(X)]^{1/2}$, is another measure of the dispersion around mean. Has the same units as X
- The skewness, $\gamma_1=E[(X-\mu)^3/\sigma^3]$, a measure of asymmetry around mean
- The geometric mean, $\exp(E[\log X])$ is useful for very broad distributions

A gallery of useful

discrete probability distributions

Discrete Uniform Distribution

- Simplest discrete distribution.
- The random variable X assumes only a finite number of values, each with equal probability.
- A random variable X has a discrete uniform distribution if each of the n values in its range, say $x_1, x_2, \ldots, x_n$, has equal probability.

$$f(x_i) = 1/n$$

Uniform Distribution of Consecutive Integers

- Let X be a discrete uniform random variable all integers from a to b (inclusive). There are $b - a + 1$ integers. Therefore each one gets:

  $$f(x) = 1/(b-a+1)$$

- Its measures are:

  $$\mu = E(x) = (b+a)/2$$

  $$\sigma^2 = V(x) = [(b-a+1)^2 - 1]/12$$

Note that the mean is the midpoint of a & b.

A random variable X has the same probability for integer numbers

x =1:10

What is the behavior of its Probability Mass Function (PMF): $P(X=x)$?

A. does not change with x=1:10
B. linearly increases with x=1:10
C. linearly decreases with x=1:10
D. is a quadratic function of x=1:10

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A random variable X has the same probability for integer numbers

$x = 1:10$

What is its mean value?

A. 0.5
B. $\boxed{5.5}$
C. 5
D. 0.1

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A random variable X has the same probability for integer numbers $x = 1:10$

What is its skewness?

A. 0.5
B. 1
C. 0
D. 0.1

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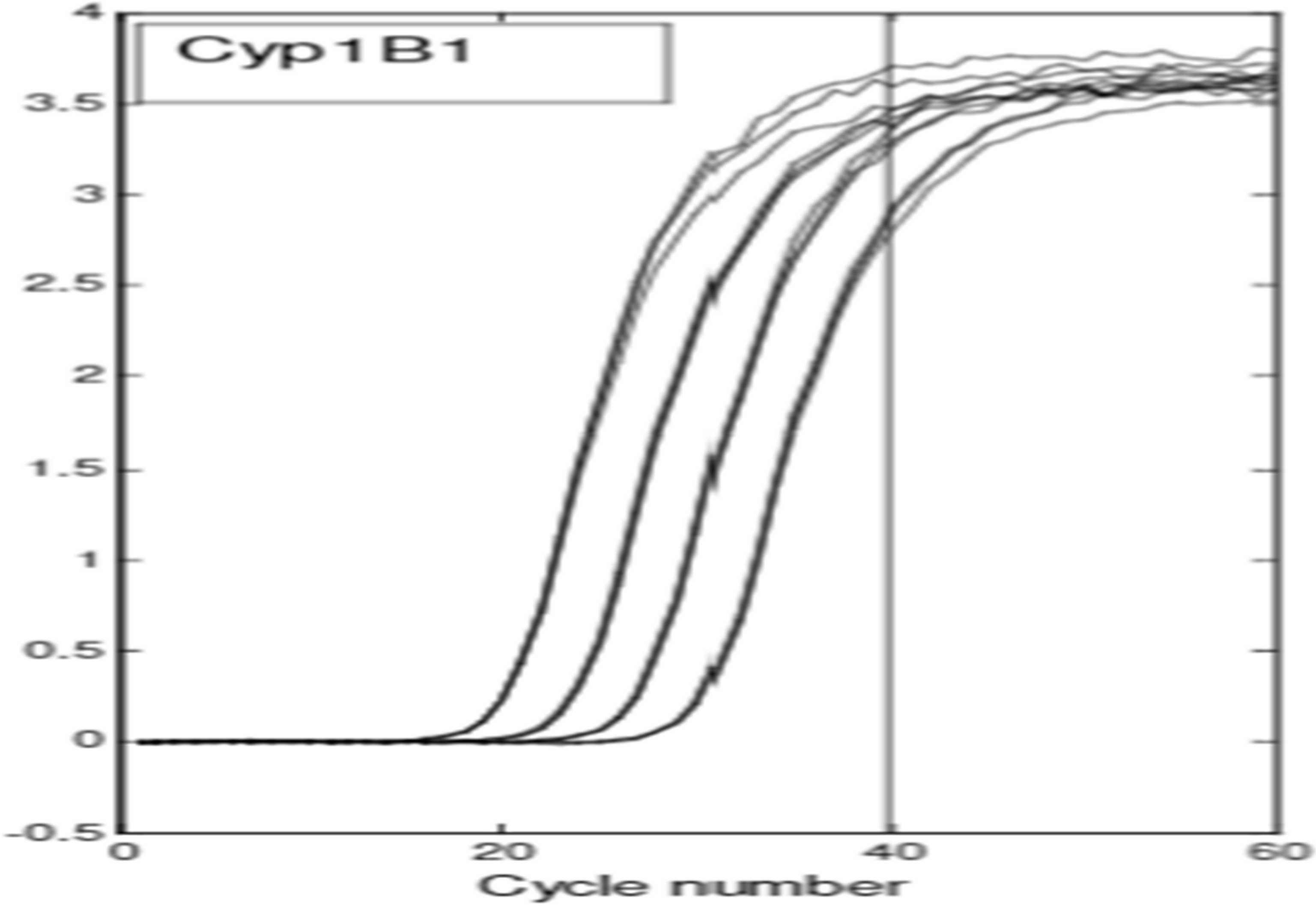
An example of the uniform distribution

Cycle threshold (Ct) value in COVID-19 infection

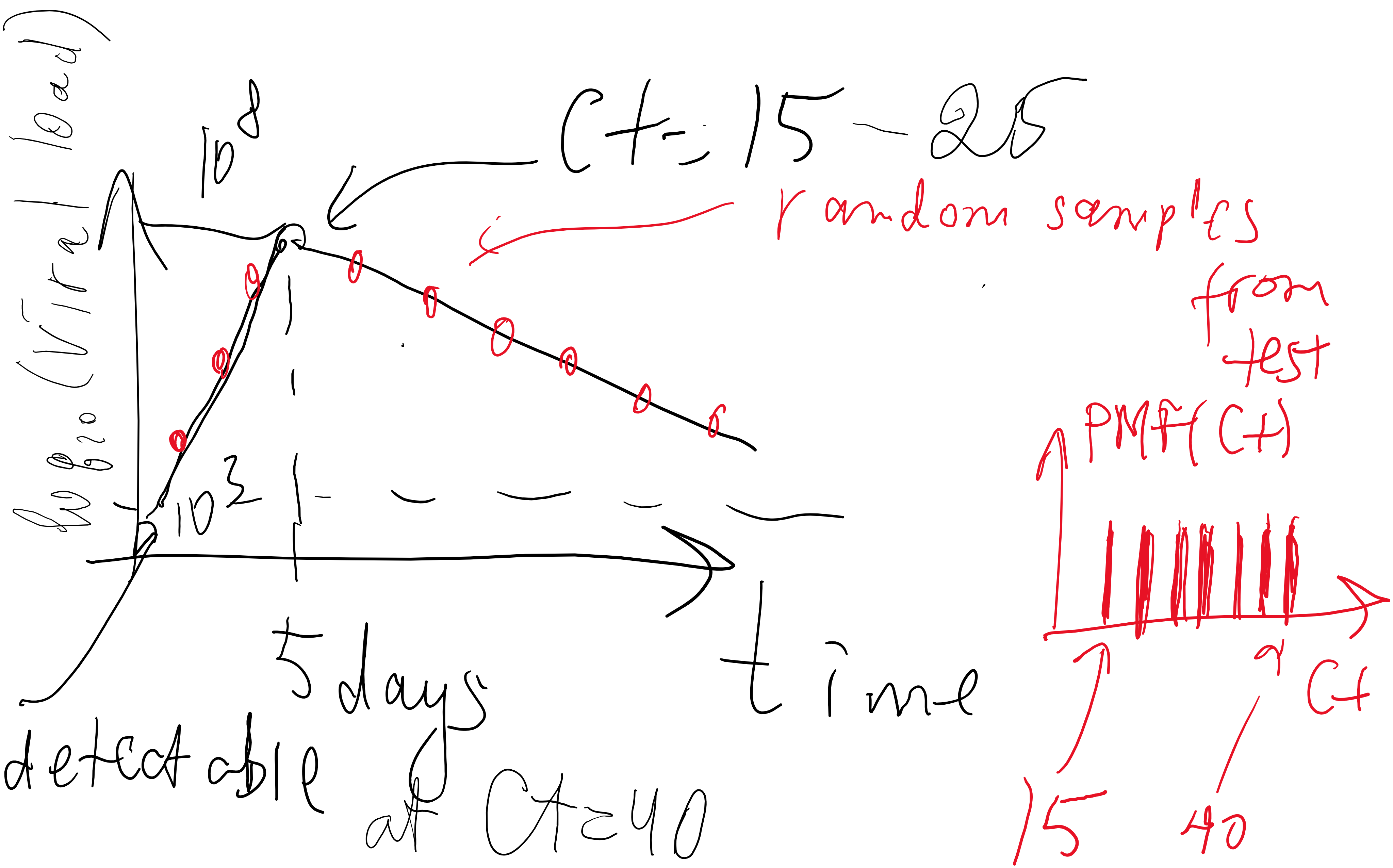
What is the Ct value of a PCR test?

Ct = const – log2(viral DNA concentration)



Why Ct distribution should be uniform?

Why Ct distribution should be uniform?



Examples of uniform distribution: Ct value of a PCR test for a virus

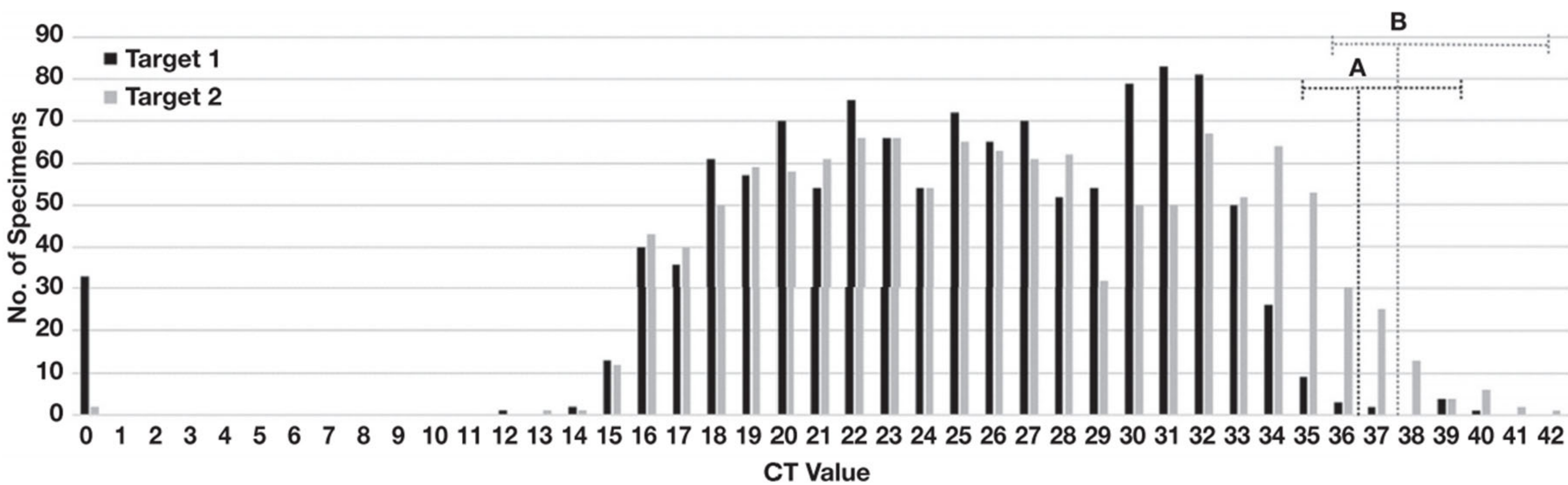


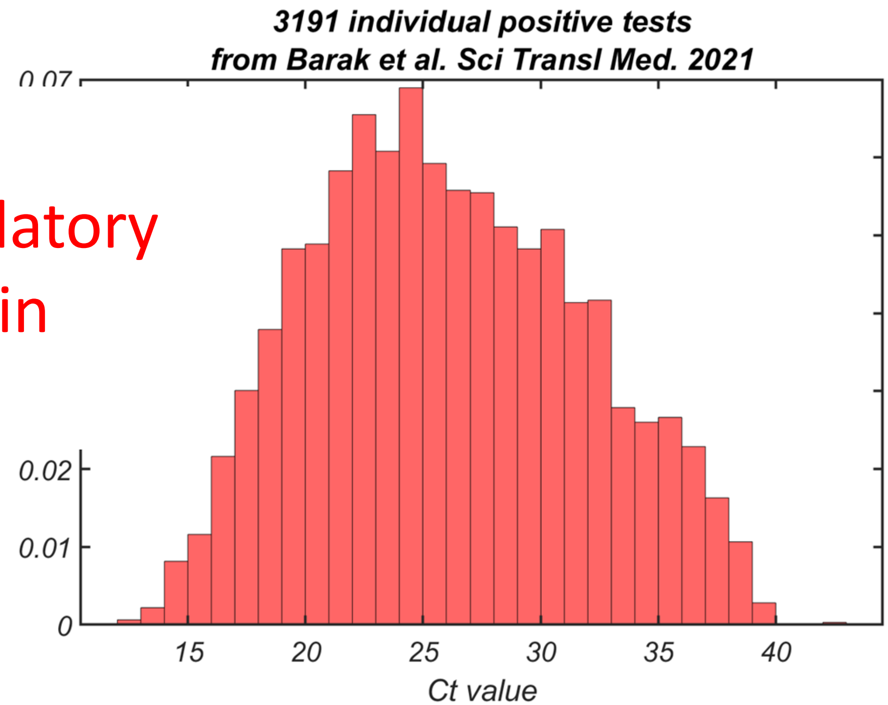
Figure 3 Distribution of cycle threshold (CT) values. The total number of specimens with indicated CT values for Target 1 and 2 are plotted. The estimated limit of detection for (A) Target 1 and (B) Target 2 are indicated by vertical dotted lines. Horizontal dotted lines encompass specimens with CT values less than 3× the LoD for which sensitivity of detection may be less than 100%. This included 19/1,180 (1.6%) reported CT values for Target 1 and 81/1,211 (6.7%) reported CT values for Target 2. Specimens with Target 1 or 2 reported as "not detected" are denoted as a CT value of "0."

Distribution of SARS-CoV-2 PCR Cycle Threshold Values Provide Practical Insight Into Overall and Target-Specific Sensitivity Among Symptomatic Patients

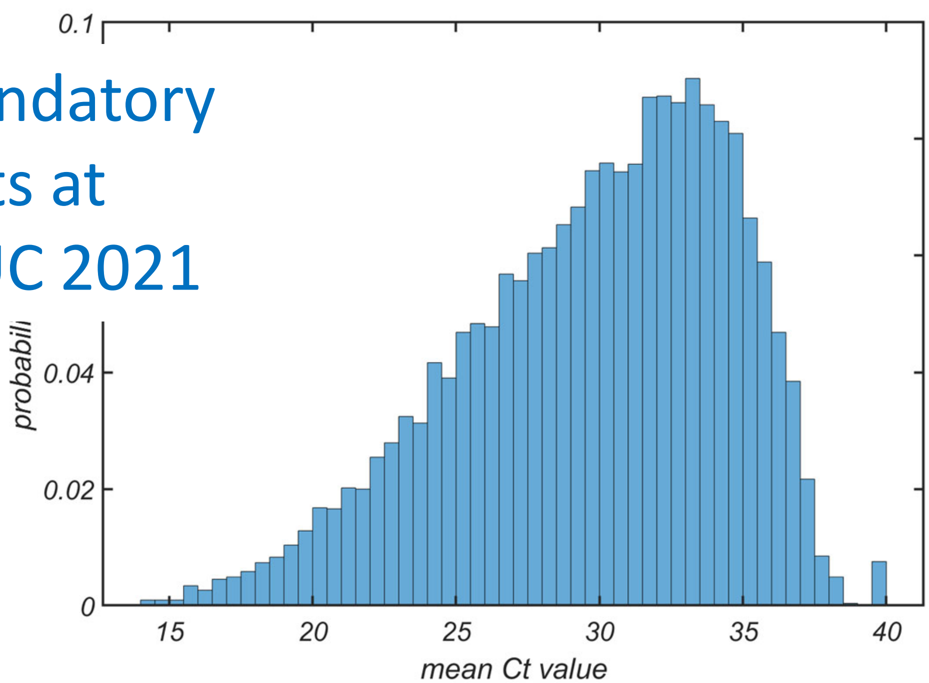
Blake W Buchan, PhD, Jessica S Hoff, PhD, Cameron G Gmehlin, Adriana Perez, Matthew L Faron, PhD, L Silvia Munoz-Price, MD, PhD, Nathan A Ledeboer, PhD *American Journal of Clinical Pathology*, Volume 154, Issue 4, 1 October 2020, https://academic.oup.com/ajcp/article/154/4/479/5873820

Why should we care?

Non-mandatory tests in Israel



Mandatory tests at UIUC 2021



- High Ct value means we identified the infected individual early, hopefully before transmission to others

- When testing is mandatory, and people are tested frequently – the mean Ct value is shifted towards higher values