

Handout Disclaimer

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What we will cover today:

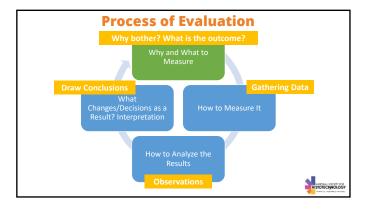
Part 1: What is Data? Part 2: Preparing Data for Analysis Part 3: Analyzing Data

HISTOTECHNOLOGY

Part I: What is Data?

- **1.** Summarize where data fits into the evaluation cycle.
- 2. Identify what data is present and available to you.
- 3. Define data
- 4. Classify types of data





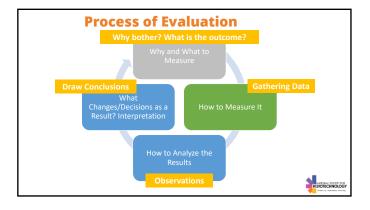
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Examples of Questions

- How does my staff feel about work schedules?
- Should my lab use an automated embedder?
- Should we invest in a new database?





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4. Classify types of data



What Data Do You Already Have Access To?

- LIS canned reports
- Emails
- Error logs
- Budgets (current and past)
- Page viewsSearch terms
- Invoices
- Sign out logs
- Staff meeting agendas





Okay, so data exists all over the place. But how do I know what I am looking at?

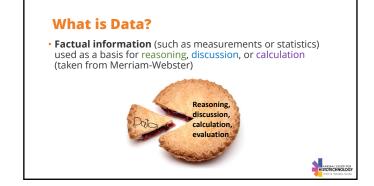
HISTOTECHNOLOGY

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Types of Data

Quantitative: its numerical in nature and can include things like, test scores, temperatures, click rates. Qualitative: its descriptive in nature, like color, types of college degrees, and frequency can be calculated. Also known as categorical.



Identify if the following are Qualitative or Quantitative

- 1. The baby weighs 20 pounds
- 2. The workshop attendees rated the event highly effective
- 3. The sky is blue
- 4. There were 200 IHC requests this month
- 5. The lab is cold today
- 6. Joe is 6 foot 2







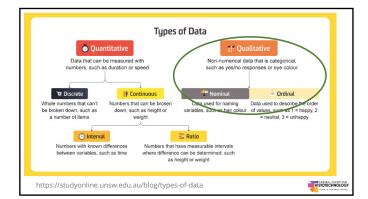


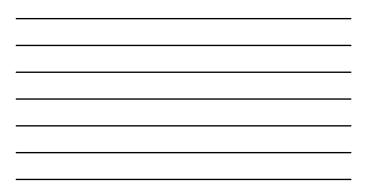
Part I: What is Data?

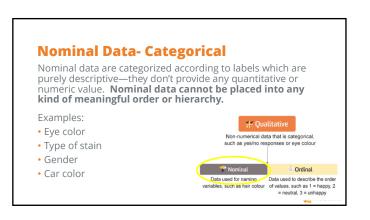
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Why does type of data matter? It determines the kinds of statistical tests and measures that can be used.











Ordinal Data- Categorical

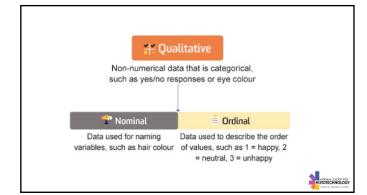
Ordinal data are categorical (non-numeric) but may use numbers as labels – BUT CAN BE RANKED NATURALLY.

Examples:

- Grades/Marks (A,B,C,O,ME,etc)
- Education level
- Income level (low, middle, upper middle class, etc.)
- Satisfaction levels



Phonity	Block		Container		Task	Lab Responsible Pathole	Z.
Embedded Priority	PS20-	A1	PS20-	A1-1	H&E	And the second s	
Embedded Priority	PS20-	A1	PS20	A1-4	H&E		
Embedded Priority	PS20-	A1	PS20-	A1	H&E		
Embedded Priority	PS20-	A1	PS20-	A1-1	H&E		
mondded Priority	PS20-	A1	PS20	A 4	ERG	transport of the second second	CHECK IN
Embedded Priority	PS20-	A1	PS20-	A1-7	H&E	Contract of Contract of Contract	
Embedded Priority	PS20-	A1	PS20	A -1	H&E FS		
mbedded Priority	PS20-	A1	PS20	A14	H&E		
Embedded Priority	PS20-	A1	PS20-	A1	H&E		
Embedded Priority	SS20-	A1	SS20-	A1-T	H&E		ENT Service
Embedded Priority	SS20-	A1	SS20-	A1-13	H&E		ENT Service
Embedded Priority	SS20-	A1	SS20-	A1-9	H&E		ENT Service
Embedded Priority	SS20-	A1	SS20-	A1-1	ERG		Derm Service
Embedded Priority	SS20-	A2	SS20-	A2-1	ERG		Derm Service
Embedded Priority	SS20-	A3	SS20-	A3-1	H&E		Derm Service
Embedded Priority	SS20-	A4	SS20-	A4-1	H&E		Derm Service
Embedded Priority	SS20-	A5	SS20-	A5-1	H&E		Derm Service
Embedded Priority	SS20-	A6	SS20	A6-1	ERG		Derm Service
Embedded Routine Surgical	SS20-	A1	SS20	A1-2	H&E FS Permanent		GYN Surg Service FS/TP Slides
Embedded Routine Surgical	SS20-	A10	SS20	A10-1	HER2 IHC		GYN Surg Service FS/TP Slides
Embedded Routine Surgical	SS20-	A11	SS20	A11-1	H&E		GYN Surg Service FS/TP Slides
Embedded Routine Surgical	SS20-	A12	SS20	A12-1	H&E		GYN Surg Service FS/TP Slides
Embedded Routine Surgical	SS20-	A2	SS20	A2-1	H&E		GYN Surg Service FS/TP Slides
Embedded Routine Surgical	SS20-	A3	SS20	A3-1	HER2 IHC		GYN Surg Service FS/TP Slides
Embedded Routine Surgical	SS20-	A4	SS20	A4-1	H&E		GYN Surg Service CO FS/TP Slides
Embedded Routine Surgical	SS20-	A5	SS20	A5-1	H&E		GYN Surg Service







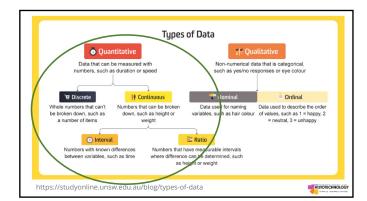
Is the Question Nominal or Ordinal?



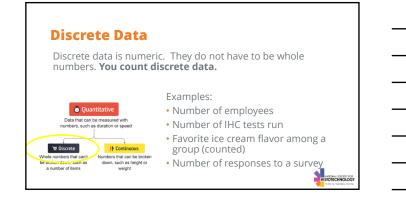
- 1. Are you left handed or right handed?
- How satisfied are you with your pizza delivery service? 1 not satisfied, 2 – satisfied, 3 – very satisfied
- 3. What kind of house do you live in?
- 4. What kind of pet do you have?
- Are you willing to work extra shifts? I am willing to work any extra shifts, I am willing to work extra shifts if given notice, I am willing to work extra shifts occasionally, I am not willing to work extra shifts.

Remember, nominal has no hierarchy...







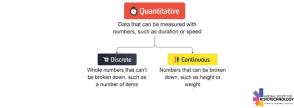




Priority	Block		Containe		*3 Task	Lab Responsible Pathologist	Case Flags	
Embedded Priority	PS20	A1	PS20	A1.1	HAF	Cab Responsible Pathologist	RENAL	
Embedded Priority	PS20-	A1 A1	PS20 PS20	A1-1	HAE		RENAL	
Embedded Priority	PS20- PS20-	A1	PS20 PS20	A1-4 A1-7	HAE		RENAL	
Embedded Priority	PS20-	A1	PS20	A1.1	H&E		REIPE	
Embedded Priority	PS20- PS20-	A1	PS20- PS20	A1-1 A1-4	FRG	<u> </u>		
Embedded Priority	PS20-	AI	PS20-	A1.7	H&E	Goes from		
Embedded Priority	PS20-	A1	PS20-	A1.1	HAEFS	0000 11011		
Embedded Priority	PS20-	AI	PS20-	A1-1	HAEFS			
Embedded Priority	PS20-	AI	PS20-	A1-4	H&E	ordinal da	to to	
Embedded Priority	SS20-	AI	SS20-	A1-11	HAE	Uluildi üd		
Embedded Priority	SS20-	AI	SS20-	A1-13	HAE			
Embedded Priority	SS20-	A1	SS20-	A1-9	HAE	diagnatal		
Embedded Priority	SS20-	A1	SS20-	A1-1	FRG	discrete		
Embedded Priority	SS20-	A2	5520	A2-1	ERG			
Embedded Priority	SS20-	A3	5520	A3-1	HAE		Derm Service	
Embedded Priority	SS20-	Ad	5520	A4-1	HAE		Derm Service	
Embedded Priority	SS20-	AS	SS20-	A5-1	HAE		Derm Service	
Embedded Priority	SS20-	A6	SS20	A6-1	ERG		Derm Service	
Embedded Routine Surgical	SS20-	A1	SS20	A1-2	H&E FS Permanent		GYN Surg Service FS/TP Slides	
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Embedded Routine Surgical	SS20-	A12	SS20-	A12-1	H&E		GYN Surg Service FS/TP Slides	
Embedded Routine Surgical	SS20-	A2	SS20	A2-1	H&E		GYN Surg Service FS/TP Slides	
Embedded Routine Surgical	SS20-	A3	SS20-	A3-1	HER2 IHC		GYN Surg Service FS/TP Slides	TECHNOLO
Embedded Routine Surgical	SS20-	A4	SS20	A4-1	H&E		GYN Surg Service	with theorem and



Continuous data is numeric and you measure it (height, weight, temperature). It can be measured over time and be put in the context of time.





- 1. The baby weighs 7 lbs 6 ounces pounds
- 2. There were 200 IHC requests this month
- 3. The lab was 65 degree Fahrenheit
- 4. The lab has 6 employees
- 5. It took the staff 2 days and 3 hours to complete the safety training.

Remember, counting vs measuring...



between variables, such as time where differ	The Nominal
Interval:	Ratio:
Year	Weight
Credit score	Error rates
SAT test	Crime rate
Temperature (C or F)	Length of time

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Provides:	Nominal	Ordinal	Interval	Ratio
The "order" of values is known		~	~	~
"Counts," aka "Frequency of Distribution"	~	~	~	~
Mode	~	~	~	~
Median		~	~	~
Mean			~	~
Can quantify the difference between each value			~	~
Can add or subtract values			~	~
Can multiple and divide values				~
Has "true zero"				~

Part 1 Recap!



- 1. The baby weighs 7 lbs 6 ounces pounds
- 2. There were 200 IHC requests this month
- 3. The lab was 65 degree Fahrenheit
- 4. The lab has 6 employees
- 5. It took the staff 2 days and 3 hours to complete the safety training.





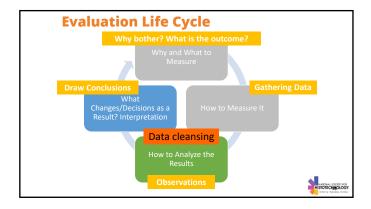
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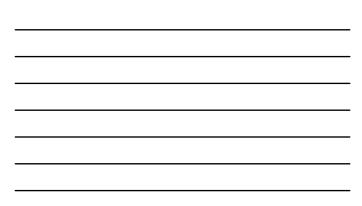
- ✓ Summarize where data fits into the evaluation cycle.
- ✓Define data.
- ✓ Classify types of data.
- ✓Identify what data is present and available to you.



- 1. Explain the impact of dirty data
- 2. Perform a data cleanse

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Preparing the Data: Cleansing

60-80% of a data scientists time is spent cleaning data.



• Data Scrubbing: "The procedure of modifying or removing incomplete, incorrect, inaccurately formatted, or repeated data in a database." (Technopedia).

- AKA: Cleaning, scrubbing, dirty data, unclean data
- Extractions of data or databases



Connie's Customized Checklist

1. Remove duplicates (if you are not counting frequency)



Duplicate Values

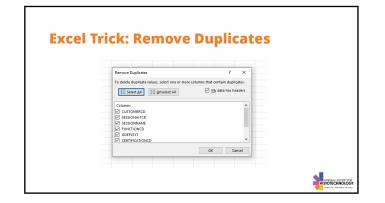
- When you have one qualified response entered more than one time.
- CRMs, CMXs, etc typically have a duplicate value finder or preventer but they are far from perfect.

Tip: Have protocols/SOPs in place to remove duplicates. Staff turnover and people unfamiliar with your database may not understand what to do when they encounter a duplicate and that can cause dirty data!





0000835391	SC2021	47th NSH (WS10	HistogoncNSH	09/14/21	1 A	Allison Eck; Brad Flowers
0000835391	SC2021	47th NSH (WS11	Adhesive NSH	09/14/21	1 A	David Prine
0000835391	SC2021	47th NSH (WS21	Diagnosti NSH	15-Sep	1 A	Richard Ormesher
0000835391	SC2021	47th NSH (WS32	Discovery NSH	09/16/21	1 A	Kim Pickard; Michele Levitt
0000835391	SC2021	47th NSH (WS40	Using The NSH	09/16/21	1 A	Gerelyn Henry
0000835391	SC2021	47th NSH (WS11	Adhesive NSH	09/14/21	1 A	David Prine
0000835391	SC2021	YOGADAY	Morning 1N3H	09/15/21	1.4	Gerelyn Henry
0000835391	SC2021	47th NSH (YOGADAY	Morning \NSH	09/15/21	1 A	Gerelyn Henry
0000835391	SC2021	47th NSH (YOGADAY	Morning \NSH	09/16/21	1 A	Gerelyn Henny
0000820781	SC2021	47th Non-12105	Stains BeNCH	00/15/21	0.5 A	Jean Mitchell; Surena Becraf
	SC2021	47th NSH (ET01	Modificat NSH	09/21/21	0.5 A	Elizabeth Chlipala
	SC2021	47th NSH (ET01	NSH	09/25/21	0.5 A	Elizabeth Chlipala
	SC2021	47th NSH (ET01	Modificat NSH	09/27/21	0.5 A	Elizabeth Chlipala
	SC2021	47th NSH (ET01	Modificat NSH	09/30/21	0.5 A	Elizabeth Chlipala
	SC2021	47th NSH (ET02	Chemical NSH	09/15/21	0.5 A	Steven Goodman
	SC2021	47th NSH (ET02	Chemical NSH	09/15/21	0.5 A	S Goodman
	SC2021	47th NSH (ET02	Chemical NSH	09/20/21	0.5 A	
	SC2021	47th NSH (ET02	Chemical NSH	09/24/21	0.5 A	Steven Goodman
	SC2021	47th NSH (ET02	Chemical NSH	09/25/21	0.5 A	Steven Goodman
	SC2021	47th NSH (ET02	Chemical NSH	09/27/21	0.5 A	Steven Goodman
	SC2021	47th NSH (ET02	Chemical NSH	09/27/21	0.5 A	Steven Goodman



Connie's Customized Checklist

- 1. Remove duplicates (if you are not counting frequency)
- 2. Identify formatting issues:
- Formatting for quantitative entries like dates, decimals • Formatting for categorical information like states, names, etc.





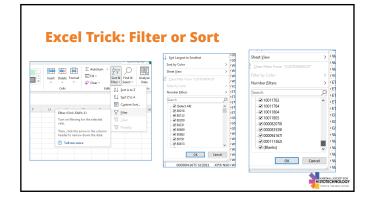
Formatting Issues

- Inconsistencies with data fields.
- Open ended fields will always need attention.

Tip: Consider drop downs, and prefilled items when you can. Test with people to see if there are issues that are preventable (i.e. are dropdowns missing fields, etc.)



0000835391	SC2021	47th NSH (WS10	Histogono	NSH	09/14/21	1	Α	Allison Eck; Brad Flowe	ers
0000835391	SC2021	47th NSH (WS11	Adhesive	NSH	09/14/21	1	A	David Prine	
0000835391	SC2021	47th NSH (WS21	Diagnosti	NSH 【	15-Sep	1	A	Richard Ormesher	
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0000835391	SC2021	47th NSH (WS40	Using The	NSH	09/16/21	1	A	Gerelyn Henry	
0000835391	SC2021	47th NSH (WS11	Adhesive	NSH	09/14/21	1	A	David Prine	
0000835391	SC2021		YOGADAY	Morning \	NSH	09/15/21	1	A	Gerelyn Henry	
0000835391	SC2021	47th NSH (YOGADAY	Morning \	NSH	09/15/21	1	A	Gerelyn Henry	
0000835391	SC2021	47th NSH (YOGADAY	Morning \	NSH	09/16/21	1	Α	Gerelyn Henry	
0000820781	SC2021	47th NSH (ET05	Stains Be	NSH	09/15/21	0.5	Α	Jean Mitchell; Surena I	Becra
	SC2021	47th NSH (ET01	Modificat	NSH	09/21/21	0.5	Α	Elizabeth Chlipala	
	SC2021	47th NSH (ET01		NSH	09/25/21	0.5	A	Elizabeth Chlipala	
	SC2021	47th NSH (ET01	Modificat	NSH	09/27/21	0.5	A	Elizabeth Chlipala	
	SC2021	47th NSH (ET01	Modificat	NSH	09/30/21	0.5	A	Elizabeth Chlipala	
	SC2021	47th NSH (ET02	Chemical	NSH	09/15/21	0.5	A	Steven Goodman	
	SC2021	47th NSH (ET02	Chemical	NSH	09/15/21	0.5	Α	S Goodman	
	SC2021	47th NSH (ET02	Chemical	NSH	09/20/21	0.5	Α		
	SC2021	47th NSH (ET02	Chemical	NSH	09/24/21	0.5	Α	Steven Goodman	
	SC2021	47th NSH (ET02	Chemical	NSH	09/25/21	0.5	A	Steven Goodman	
	SC2021	47th NSH (ET02	Chemical	NSH	09/27/21	0.5	A	Steven Goodman	
	SC2021	47th NSH (ET02	Chemical	NSH	09/27/21	0.5	A	Steven Goodman	







Connie's Customized Checklist

- 1. Remove duplicates (if you are not counting frequency)
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 - Formatting for quantitative entries like dates, decimals
 - Formatting for categorical information like states, names, etc.
- 3. Find missing data and fill in or remove.



Missing Data

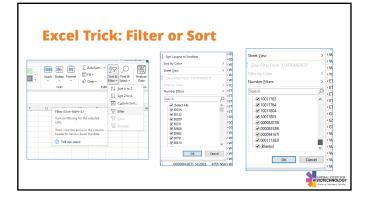


- Data fields that are not complete.
- "Missing data can reduce the statistical power of a study and can produce biased estimates, leading to invalid conclusions."

Tip: Collection desires vs realities (think about the amount of time it would take a person to enter fully the information, or accurately)

HistogoncNSH 09/14/21 1 A Allison Eck; Brad Flow	1 A	09/14/21	Histogonch	47th NSH (WS10	SC2021	0000835391
Adhesive NSH 09/14/21 1 A David Prine	1 A	09/14/21	Adhesive N	47th NSH (WS11	SC2021	0000835391
Diagnosti NSH 15-Sep 1 A Richard Ormesher	1 A	15-Sep	Diagnosti N	47th NSH (WS21	SC2021	0000835391
DiscoveryNSH 09/16/21 1 A Kim Pickard; Michele	1 A	09/16/21	DiscoveryN	47th NSH (WS32	SC2021	0000835391
Using TheNSH 09/16/21 1 A Gerelyn Henry	1 A	09/16/21	Using TheN	47th NSH (WS40	SC2021	0000835391
Adhesive NSH 09/14/21 1 A David Prine	1 A	09/14/21	Adhesive N	47th NSHLWS11	SC2021	0000835391
Morning NSH 09/15/21 1 A Gerelyn Henry	1 A	09/15/21	AY Morning \N	VOGAD/	SC2021	0000835391
Morning NSH 09/15/21 1 A Gerelyn Henry	1 A	09/15/21	AY Morning \N	47th NSH (YOGADA	SC2021	0000835391
Morning \NSH 09/16/21 1 A Gerelyn Henry	1 A	09/16/21	AY Morning \N	47th NSH (YOGADA	SC2021	0000835391
Stains Be NSH 09/15/21 0.5 A Jean Mitchell; Surena	0.5 A	09/15/21	Stains Be N	47th NSH (ET05	SC2021	0000820781
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NSH 09/25/21 0.5 A Elizabeth Chlipala	0.5 A	09/25/21		47th NSH (ET01	SC2021	
Modificat NSH 09/27/21 0.5 A Elizabeth Chlipala	0.5 A	09/27/21	Modificat N	47th NSH (ET01	SC2021	/ \
Modificat NSH 09/30/21 0.5 A Elizabeth Chlipala	0.5 A	09/30/21	Modificat	47th NSH (ET01	SC2021	
Chemical NSH 09/15/21 0.5 A Steven Goodman	0.5 A	09/15/21	Chemical N	47th NSH (ET02	SC2021	
Chemical NSH 09/15/21 0.5 A SGoodman		09/15/21	Chemical N	47th NSH (ET02	SC2021	
Chemical NSH 09/20/21 0.5 A	0.5 A	09/20/21	Chemical N	47th NSH (ET02	SC2021	
Chemical NSH 09/24/21 0.5 A Steven Goodman	0.5 A	09/24/21	Chemical N	47th NSH (ET02	SC2021	
Chemical NSH 09/25/21 0.5 A Steven Goodman	0.5 A	09/25/21	Chemical N	47th NSH (ET02	SC2021	
Chemical NSH 09/27/21 0.5 A Steven Goodman	0.5 A	09/27/21	Chemical N	47th NSH (ET02	SC2021	\mathbf{X}
Chemical NSH 09/27/21 0.5 A Steven Goodman	0.5 A	09/27/21	Chemical N	47th NSH (ET02	SC2021	$\mathbf{\nabla}$





Connie's Customized Checklist

- 1. Remove duplicates (if you are not counting frequency)
- 2. Identify formatting issues:

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- Formatting for quantitative entries like dates, decimals
 Formatting for categorical information like states, names, etc.
- 3. Find missing data and fill in or remove.
- 4. Remove duplicates again!



Instructions

- Open the data file (see chat)
- As a team, have one person open the excel and share screen in the break out.
- Answer the following questions.
 How many unique records exist in the data set?
 - In which column(s) did
 - formatting issues exist?In which column(s) was there missing data?



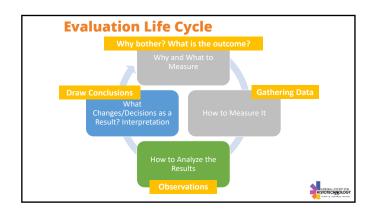




Part III: Analyzing Data

- 1. Interpret measures of central tendency.
- 2. Analyze data







Two Types of Quantitative Analysis

 Descriptive: focus on describing a sample of a population.





"In other words, we use one group of statistical methods – descriptive statistics – to investigate the slice of cake, and another group of methods – inferential statistics – to draw conclusions about the entire cake." *-Karyn Warren, PhD*





Frequency

The rate at which something occurs or is repeated (over time or in a sample).

Central Tendency

- A measure of central tendency is a single value that attempts to describe a set of data by identifying the central position within that set of data.
- A single measure may not give you the full picture because extreme values can impact each measurement.



Mean

- Average
- Total all numbers in the data set and divide by the number of responses.





Median

- The value that appears in the center of the data set.
- If the number of data points is odd, the median is the middle data point in the list.
- If the number of data points is even, the median is the average of the two middle data points in the list



Mode

• The number that appears the most in the data set.



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Range

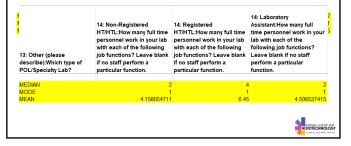
• Range: describes the difference between the smallest and largest value.

 To calculate this, you first need to use numeric codes to represent each grade, i.e. A = 1, A- = 2, B = 3, etc. The range would be 5 - 1 = 4. So in this simple example, the range is 4. This is an easy calculation to carry out. The range is useful because it offers a basic understanding of how spread out the values in a dataset are.





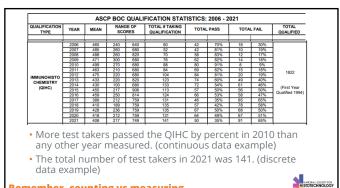
Why Central Tendency Matters



OBSERVATION - Analysis

- Observation = FACTS
- Analysis is just what the numbers or information say.





Remember, counting vs measuring...



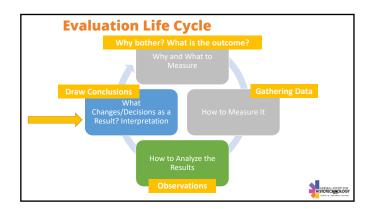


Why can't I make conclusions like...

The QIHC exam is too hard.

- Because the data doesn't show us that. Maybe the test takers didn't have enough study tools, maybe the technology is outdated for taking the exam.
- More importantly, we aren't at that step yet!







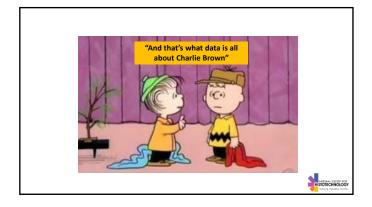




	Total	Hospital	Private Independent						
Sample Size	1,088	809	279						
Grossing Questions									
Who performs grossing in your lab?									
Non-Registered HT/HTL	9%	7%	15%						
Registered HT/HTL	31%	26%	44%						
Laboratory Assistant	3%	2%	5%						
Laboratory Technician	8%	7%	11%						
Grossing Assistant	22%	20%	27%						
Supervisor	9%	9%	11%						
Manager	3%	3%	3%						
Pathologist	31%	35%	21%						
Pathologist's Assistant	53%	62%	25%						
Resident	12%	16%	2%						
Other (please specify)	2%	2%	2%						
What are the average number of cassettes grossed per hour?									
Mean	46.9	46.1	48.7						
Median	30.0	30.0	35.0						
What are the average num	ber of container	s grossed per hour?							
Mean	27.6	23.3	36.1						

Diversity of Thought Makes Data Better!

- We all look at things differently, even numbers
- Using many sets of eyes and brains can analyze data better





For Your Reading Pleasure

- https://uxdesign.cc/data-for-design-f33fd7419cc8
- <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7886543</u>
- https://towardsdatascience.com/9-common-mistakesbeginner-data-scientists-make-91255ddd1311

HISTOTECHNOLOGY

References

- Evaluation, A Systematic Approach: Seventh Edition, Rossi, Lipsey, and Freeman
- DataFloq, 10 Really Cool Data Cartoons You Have to See! <u>https://datafloq.com/read/10-really-cool-data-cartoons-you-have-to-see/</u>
- Merriam-Webster Dictionary, 2022
- ASCP QIHC Pass Rates published Jan 18, 2022
- 2022 NSH Workload Study
- Kang H. The prevention and handling of the missing data. Korean J Anesthesiol. 2013 May64(5):402-6. doi: 10.4097/kjae.2013.64.5.402. Epub 2013 May 24. PMID: 23741561; PMICID: PMC3668100.