SAFETY & ETHICAL ISSUES IN SUICIDE RESEARCH

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Special Interest:

- **Suicide prevention and early intervention,**
- **Health disparities and health equity research,**
- **Diagnostic accuracy including cultural sensitivity in the assessment and treatment of mental and substance use disorders,**
- **Development and use of technology in assessment, diagnosis, and treatment of mental and substance use disorders, and**
- **Strengthening and diversifying the clinician-scientists workforce.**

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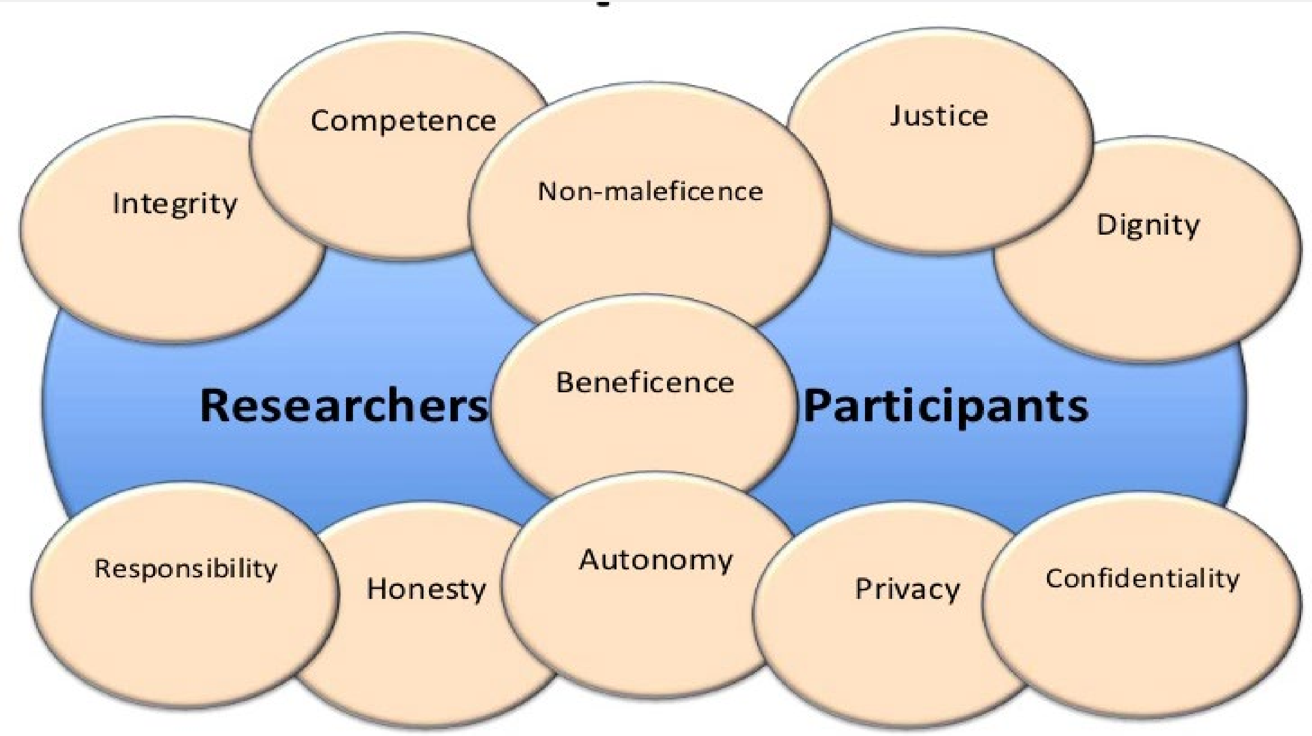
OVERVIEW

- Ethical Principles
  - Autonomy, Beneficence, Justice
- Safety and Ethical Issues in Suicide Research
  - Current Context of Research Priorities
  - Ethics/Safety/Research Design intertwined
- Examples of Suicide Research Approaches
  - Various Ethical and Safety Considerations

PRINCIPLES OF ETHICS



ETHICAL PRINCIPLES IN SUICIDE RESEARCH

- Autonomy = Respect for the individual's right to decide what they will and will not participate in (i.e., self-determination)
  - Is the desire to kill oneself indicative of diminished capacity?
- Beneficence = Doing the greatest good possible
- Non-maleficence = Minimizing or preventing harm
- Justice = those who undertake the burdens to participate in the research must be likely to benefit from the research
  - Avoid exploitation of vulnerable populations who may be easily coerced into participating

AUTONOMY: CONSENT VS. ASSENT

- Informed Consent = voluntary agreement of an individual, or their authorized representative, who is **<u>not induced or coerced</u>**, to participate in research
  - Age of majority – 18 in US except Nebraska & Alabama [19]; Mississippi & PR [21]
  - Language and education
- Assent = voluntary agreement of someone not able to give legal consent to participate in the activity
  - Must possess adequate knowledge & understanding of the proposed study, the risks and potential benefits & importance of making an informed decision
  - Must also have supporting Informed Consent from authorized representative

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AUTONOMY: CONSENT VS. ASSENT

- Parental or authorized representative consent can be “passive” or “active”:
  - Passive consent assumes that a non-response from a parent/guardian or authorized representative indicates latent consent (i.e., permission has been granted for the person to take part in the research)
  - Active consent requires written consent and a non-response indicates an absence of parental/guardian or authorized representative consent.
  - Passive consent is often preferable to researchers because it enhances the likelihood of more robust youth participation but there are ethical implications
- Type of consent sought by the researchers can significantly affect participation rates, study costs, selection biases, and thus, sample representativeness

AUTONOMY: CONSENT VS. ASSENT

- **Person obtaining informed consent must:**
  - be fully aware of the study protocol
  - be trained to ensure that each participant fully understands what's involved and is given ample time to discuss questions/concerns
  - No direct participant contact (e.g., online studies) means participants should be encouraged to contact the researchers with study questions

"The biggest risk in this study is just reading the consent form!"

- Remind participants and their parents/guardians of the **right to withdraw from study** even if they have previously given consent or assent
  - Competent to withdraw??

AUTONOMY: Youth Consent

C. King and A. Kramer, "Intervention research with youths at elevated risk for suicide: meeting the ethical and regulatory challenges of informed consent and assent," Suicide & Life Threatening Behavior, vol. 5, pp. 486-97, 2008.

Intervention research with youths at elevated risk for suicidal behavior and suicide—a vulnerable and high-risk population—presents investigators with numerous ethical challenges. This report specifically addresses those challenges involving the informed consent and assent process with parents/guardians and youths. The challenges are delineated in the context of pertinent laws and regulatory requirements, and guidelines are suggested for their practical resolution. These are illustrated with case examples from NIMH-funded intervention trials.

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BENEFICENCE & NON-MALEFICENCE: CONSIDERATION OF PATIENT’S SAFETY

- Persons with current and past suicidal ideation and behaviors are at enhanced risk for suicide attempts and death

- Persons at risk for suicide and suicidal behavior at elevated risk of death in their everyday lives.

- Does participation in research on suicide and suicidal behaviors increase risk? Will ascertainment bias occur due to patterns of contact with participants?

- Are there known risks for the paradigm/methods/interventions being studied, which can be considered in the risk/benefit calculus?

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BENEFICENCE & NON-MALEFICENCE: CONSIDERATION OF PATIENT'S SAFETY

- Onus on the researcher to ensure the safety of study participants with suicidal ideation and behavior while maintaining the scientific integrity of the study
  - Patient's safety <u>MUST</u> outweigh the needs of the study
- Onus on the institutional review board to ensure that suicidal person is protected.
  - Study protocols for varying levels of risk
- For funded studies:
  - Any onus on the researcher's institution? funder?

BENEFICENCE:
What is your Research Environment

- **Physical environment & clinical environment**
  - Do participants (all) have clinical providers outside of the study who are trained in working with suicidal patients?
  - Are those clinical providers part of the same institution where the research takes place, or community providers?
  - Answers to these questions will impact:
    - Communication between research team and team providing clinical care (if there is one)
    - Options for providing care in case elevated suicide risk identified in the study
    - Communication with study participants about research versus clinical care & safety planning

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BENEFICENCE:
Risk Management & Clinical Monitoring

What are the opportunities for risk ascertainment?

- In person
- By phone / remotely / blinded assessors
- Real time versus retrospective

How is clinical worsening defined? Since last assessment? Since baseline?

  - Who reviews this data?
  - How do these events get reported and to whom?

Do you need a study medical monitor or safety officer?

- Considerations if your safety/risk management data is also study outcome data, e.g. blinding of intervention conditions

JUSTICE: VULNERABLE POPULATIONS?

- Vulnerable populations refers to the disadvantaged sub-segment of the community requiring utmost care, specific ancillary considerations and augmented protections in research
- Individuals with past and current suicidal thoughts and behaviors fall under the category of “vulnerable” populations by the Council for International Organizations of Medical Sciences and the International Ethical Guidelines for Biomedical Research Involving Human Subjects
- The Belmont Report emphasize that:
  - Selection of subjects for research should be based on the problem being studied not the ease of access to individual, their compromised position, or their manipulability!

JUSTICE: VULNERABLE POPULATIONS?

- Double-jeopardy for many suicidal persons in terms of vulnerability
- Difficult to separate research from therapeutic interest
  - Fine line between researcher and “clinician”
  - Impacts the consent process
  - Confidentiality limits conveyed
- Non-clinical/non-therapeutic research studies with the suicidal person extremely challenging
- Care must be taken in approaching, interacting with, and ending the study relationship with the suicidal individuals

JUSTICE --Determining Inclusion/Exclusion Criteria

Suicidal Ideation

- **Passive**
- **Active**
- **Intent/Plan**

Recent Attempt(s)

- **How recent**
- **Severity**

Past History (how far in the past and what history) of ideation and/or attempts

Other risk factors

- **Co-morbid conditions, e.g., substance abuse, depression, trauma**
- **Stressors: interpersonal, economic, involvement in justice system**

CHALLENGES FOR THE ETHICS REVIEW PROCESS

- Scientific integrity of the study important but must be done while maintaining the patient's safety
- Foremost importance is patient's safety:
  - Vulnerable individual is not being exploited
  - Benefits of the study warrants intrusion on the vulnerable person
  - No harm to the individual
  - Competency of the suicidal individual to provide informed consent
  - Competency of the research team to ensure the safety of the individual
  - Issue of maintaining confidentiality; explaining limits of confidentiality
  - Safety protocols in place

SAFETY & ETHICAL ISSUES IN SUICIDE RESEARCH

Suicide/suicide attempt, by definition, involves intent to die, so including people at risk of suicide in intervention research, presents unique and complex ethical dilemmas. Depending on the stage of science, and suicide risk severity, it may not be appropriate to include individuals currently at risk for suicide.

- A person ‘at suicide risk’ is often assumed to be within a ‘vulnerable population’
- In psychiatric clinical trials, suicidal behavior and hospitalization for suicide risk ARE TYPICALLY DEFINED as adverse events
- Drug developers seek safety profiles of their products; there are few FDA indications for pharmaceuticals for suicidal individuals
- However, excluding those ‘at risk’ for suicide can be considered unethical since it prevents us from conducting research that would benefit this at-risk and vulnerable population

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Current US Federal Context

National Institute of Mental Health (NIMH)

- Prioritized Research Agenda for Suicide Prevention (2014)
- Zero Suicide Initiative (RFA-MH-16-800 Applied Research Toward Zero Suicide Healthcare Systems)
- Suicide Prevention Research Priorities in Health Care (JAMA Psychiatry, Gordon et al 2020)
- NIMH FOAs encourage: *assessment of suicidal behavior to advance understanding of how effective prevention and treatment of mental disorders might impact suicide-relevant outcomes*

Food and Drug Administration

- June 2018 Draft Guidance on Developing Drugs for Treatment of MDD: "Patients with a history of suicidal ideation and behavior need not be systematically excluded from trials."
- August 2012 Draft Guidance: Suicidal Ideation and Behavior Prospective Assessment of Occurrence in Clinical Trials

SAFETY & ETHICAL ISSUES IN SUICIDE RESEARCH

…are identified when you define your research aims, and your research environment

- Who is your subject population? What is the base rate of the suicidal events you wish to study (in what time frame)?

- How are suicide behaviors/thoughts likely perceived in your subject populations, and *in the context* for your study? Expected?

- Does your study involve risk in the paradigm or research methods used? (experimental device with good safety profile vs pharmaceutical with significant side effects)

- Is your institution/study team equipped with experienced staff to manage risk?

Aspects of Staff Training to Consider

Pilot tested protocols that define staff duties- researchers and available clinicians (and clinician researchers)

- Level of Training
- Supervision
  - Research team able to debrief and explore emotions related to suicide
  - Consider involvement of stakeholders in study development
  - Plans for postvention if suicide events occur (e.g., support for staff; outreach to family; school setting)

Recognize that empathetic, well trained staff conducting informed consent/and interviews, can have a therapeutic effect

Examples of Research Topics/ Designs
BIG DATA

- **Benefits of big data:**
  - Information can be drawn from electronic health records, wearables, electronic surveys/assessments, social media
  - Larger sample size for rare events = ↑ power
  - Reach many more people as well as those who might not otherwise participate in research or receive care
  - Machine learning – predictive analytics

BIG DATA

- **Challenges:**
  - Web-based surveys or interventions may likely prohibit the same level of assessment and response as is possible in face-to-face interviews
  - Best practices for big data studies and for assuring that the needs of researchers, participants, and institutions are met, still need to be clarified
  - If, when, who & how to intervene for those at risk is difficult to determine

BIG DATA

- Protection against potential unintended consequences:
  - Risk of re-identification
  - In social media studies, cyberbullying of those at risk for suicide
  - Monetization of data
  - Misuse of predictive analytics
    - Use of race/ethnicity in clinical algorithms for other areas of medicine has been found to be problematic
    - Potential for suicide prevention research

EMA & Passive Data Collection

- Ethics, regulatory guidance, nor safety best practices/common standards not in place
- If the goal = understand trajectories leading to intentional self-harm, as well as signals of imminent crisis, 'safety interventions' will interrupt processes under study
- What are the initial research questions the field can pursue to help address ethical and safety processes to address the goal?

  E.g., are there safer contexts to examine this initially?

ETHICAL ISSUES IN SUICIDE RESEARCH – Global Studies:

Some challenges with respect to international studies:

- Differences in legal age to give consent
- Legality of suicidal behavior
- Cultural differences in:
  - Risk factors & willingness to self-report suicidal risk
  - Crisis and mental health resources
  - Expectations for research and clinical care

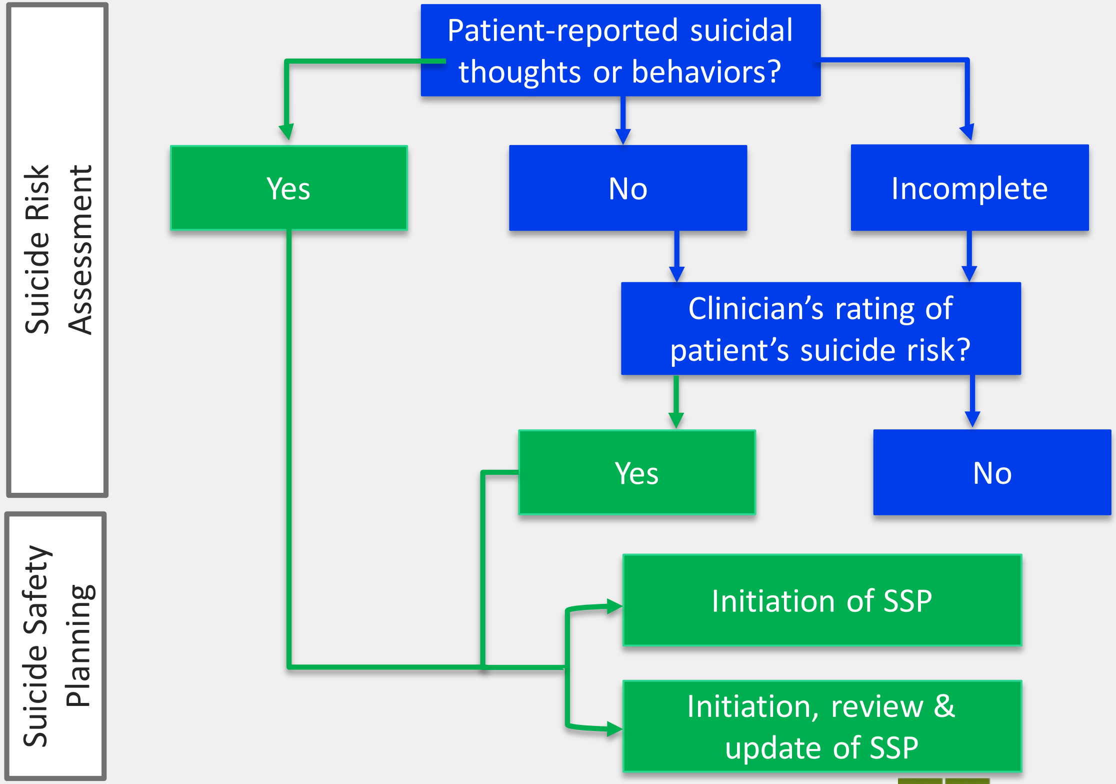
AN EXAMPLE OF GLOBAL ISSUES TO CONSIDER

A Canadian woman was turned back at the U.S. border after information about her suicide attempt was inappropriately shared with American officials through an RCMP-administered database, the federal privacy watchdog says.

Part of the 1952 Immigration and Nationality Act, the section stipulates, in part, that the U.S. shall not admit people who "have a physical or mental disorder and behavior associated with the disorder that may pose, *or has posed* [our emphasis], a threat to the property, safety, or welfare of the alien or others."

In Canada, some improvements have been made to limit access to non-criminal mental health information in police databases. After a scathing report from the Ontario privacy Commissioner, the Toronto police worked with the RCMP to develop a new CPIC function that blocks U.S. border officials from accessing this type of information except in certain specific circumstances, such as when a suicide attempt involved serious violence or harm of others, or appeared to be intended to provoke a lethal response by police. The Ontario Chiefs of Police have also updated their guidelines for

Healthcare Implementation Research



What is the standard of care?
What aspects of care are being improved?
What constitutes risk in current and 'new' practices being studied?

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SOME TAKE AWAY POINTS:

- Suicide research is critical for improved clinical and public health advancement, and requires deliberate considerations of safety and ethical concerns
- It is important to have adequate training when conducting research with individuals who have suicidal thoughts, plans, past attempts or are bereaved by suicide
  - Challenges exists but not including individuals at risk could be considered unjust
  - Including individuals with 'lived experience' and other stakeholders in the planning stage can improve protocols
- Efforts should be made to anticipate what factors contribute to suicide research challenges and to help develop solutions when possible
  - Not doing so risks building barriers to research in an area in need of more evidence

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Analyzing The Incidence And Severity Of Suicidal Behavior And Ideation

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October 29, 2020

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Disclosure

Dr. Galfalvy and her family own stocks in IBM, Inc, which owns the rights to the statistical software package SPSS. Some of the analyses presented in this talk used SPSS.

Topics addressed

A. Models for the risk and severity of suicide attempt in retrospective studies

B. Models for suicidal ideation

C. Modeling short-term changes in suicidal ideation from high-frequency (Ecological Momentary Assessment) data

A. Models For Suicidal Behavior

Most studies collect data on several aspects of suicidality: number, type and severity of attempts, severity/frequency of ideation etc.

Opportunity: analyzed jointly, or separately, the models for these can both inform and qualify each other

Challenge: even among mental health patients, suicide attempt and suicidal ideation are relatively rare events, which may lead to violations of assumptions for certain statistical models, as well as low statistical power

A. Models For Suicidal Behavior (2)

Consequence: Researchers decide to combine levels of outcome (i.e. incidence with severity of attempt; or interrupted , aborted and actual attempts, etc.)

Problem: combining disparate measurements may not be warranted for methodological and conceptual reasons

Proposed solution: Choose appropriate measurement scale and more sophisticated statistical modeling strategy.

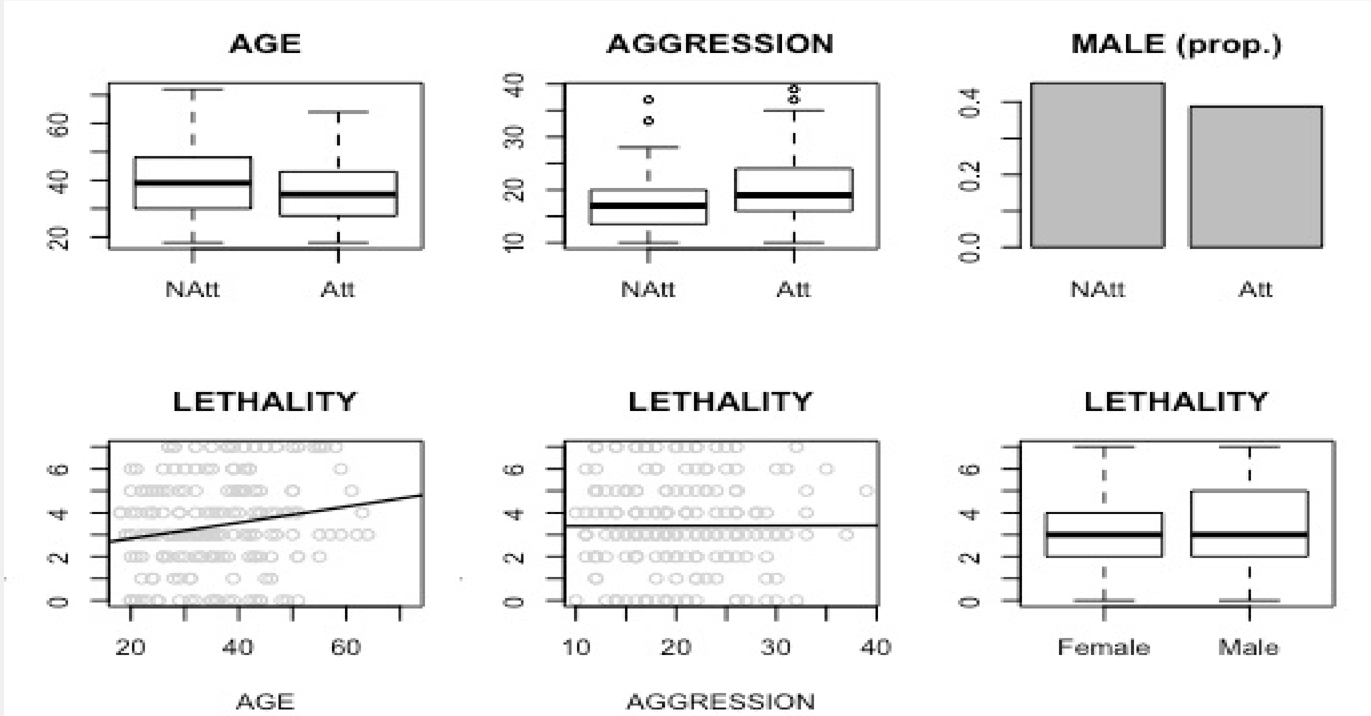
Example 1: Risk and severity of suicide attempt in depressed patients

Retrospective study of mood disorder patients (N=384), approx. 50% with history of suicide attempt. Maximal lethality (severity) of attempts are recorded.

Aim: Identify risk and protective factors for suicide attempt, and for the severity of attempt (age, sex and aggression are discussed here)

Data Analysis Plan: Step 1: Binary logistic regression for attempter status; Step 2: Ordinal logistic regression for the lethality (severity) in the attempter subset. Step3: Combine attempter status with severity (?)

Suicide attempt status and lethality



Step 1: Binary Logistic regression for attempter status (yes/no)

	B	S.E.	Wald	df	Sig.	Exp(B)
MALE	-.564	.229	6.094	1	**.014**	.569
AGGTOT	.124	.023	29.04	1	**.000**	1.132
AGE	-.019	.010	3.981	1	**.046**	.981
Constant	-1.290	.595	4.697	1	**.030**	.275

Interpreting the binary LR model

Logistic Regression estimate B<0 protective factor, B>0 risk

Odds ratio Exp(B) : OR<1 protective, OR>1 risk

Male vs. Female OR= .569, protective factor

AGGTOT : OR= 1.132/1 point increase, risk factor

AGE: OR= .981/ 1 year increase, protective factor

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Step 2: Lethality of suicide attempt

Medical severity measure for suicide attempt: range 0-8

- Severity above 3 required hospitalization, 8 is death, 0 is no medical damage
- Maximal severity is computed for patient's lifetime
- Differences between levels are not considered equal → ordinal, not continuous measure: use **Proportional Odds Logistic Regression (POLR)**

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POLR vs. least squares regression

Use POLR when response is ordered, but differences between levels are not necessarily equal

Practical rule: Likert scales with 3 or 4 levels - definitely use ordinal regression, 5 levels- inspect distribution

POLR assumption: for each of the predictor variables, the odds ratio comparing the response level 1 to response level 2 (for 1 point increase in the predictor) is the same as the one comparing response level 2 to response level 3 etc.

Step 2: POLR results for lethality

	Estimate	Std. Error	z value	Pr(>|z|)
AGE	0.03118	0.01237	2.520	**0.0117**
MALE	0.21724	0.27437	0.792	0.4285
AGGTOTN	0.01153	0.02260	0.510	0.6099

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Interpretation of POLR results

In suicide attempters:

-Older age is a RISK factor ($B=0.025 > 0$) for higher lethality of attempt

- Higher aggression and male sex are non-significant predictors, although the effects of both are in the risk direction.

Contradictory results?

Younger age, higher aggression and female sex are risk factors for the PROBABILITY of suicide attempt

Among attempters, older age is associated with higher lethality (SEVERITY) of attempt, and the others are non-significant

What would happen if the PROBABILITY and the SEVERITY of attempt is combined into a single scale, i.e. high-lethality, low-lethality, non-attempter?

Can we combine probability and the severity into 1 ordinal variable?

- Technically, yes.
- The assumption of proportional odds is almost certainly violated for the combined outcome
- Effects in opposite directions may cancel out, depending on the sample composition, the logistic regression or POLR may dominate

Step 3: POLR for “combined” outcome

DV: high-lethality attempter (n_3=85), low-lethality attempter (n_2=111) and non attempter (n_1=188).

	Estimate	Std. Error	z value	Pr(>|z|)	
AGE	-0.01153	0.00893	-1.291	0.1966	
MALE	-0.43253	0.20647	-2.095	**0.0362**	*
AGGTOTN	0.09586	0.01886	5.083	**<0.0001**	***

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Proportional Odds assumption check:

	Df	logLik	AIC	LRT	Pr(>Chi)	
AGE	1	-377.88	767.77	10.1013	**0.001482**	**
MALE	1	-382.51	777.01	0.8597	0.353826	
AGGTOTN	1	-378.60	769.20	8.6733	**0.003229**	**

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Conclusion: Example 1.

Predictors of the incidence and the severity of suicidal behavior are often different

Combining the two into a single scale may lead to incorrect conclusions

It can not be fixed statistically (i.e. by treating it as ordinal vs. continuous scale)

Need to check two different models→ use two-part model

Two-part Models

Combined incidence and severity is a zero-inflated variable

Allows different predictors for incidence and severity

- Best-known example: Zero-inflated Poisson regression (ZIP) for counts

Related to the family of "hurdle models"

For uncorrelated observations of attempt incidence/severity, can be fit without special software, as above.

B. Models For Suicidal Ideation

Quantitative suicidal ideation severity scales are often zero-inflated. Analytic choices:

1. Non-parametric statistics always applicable, but have limited ability for adjusting for covariates
2. Run LS regression/ANOVA , use a robust method for calculating significance levels
3. Two-part models: logistic regression for incidence of ideation+ Least Squares regression model for severity of ideation

Example 2: Suicidal Ideation As Treatment Outcome

Secondary analysis of a naturalistic treatment study that compared two antidepressants (N=85)

Dependent variable: Beck Scale for Suicidal at 3 months

- No main effect of group at 3 month

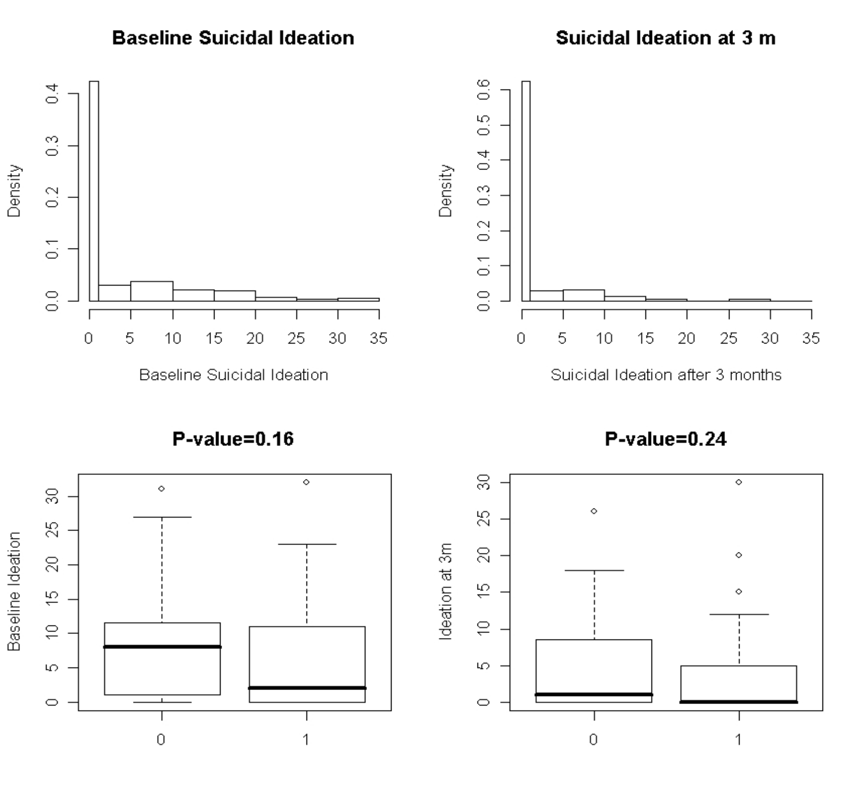
Question: do subjects with higher ideation at baseline do better on one of the treatments, i.e. does baseline ideation moderate the effect of treatment

Example 2 (cont.)

Statistical Analysis Goal: Test interaction between baseline score and treatment group in a model of ideation at 3m, adjusted for 1 pre-selected covariate.

Challenge: Most subjects show no ideation at 3 months

Plan: try the 3 methods listed previously, compare results!



Distribution of ideation scores at baseline and 3 month, by group. Group differences were tested using the 2-sample Wilcoxon test.

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Method 1. Non-parametric analysis: compare 2 Spearman correlations

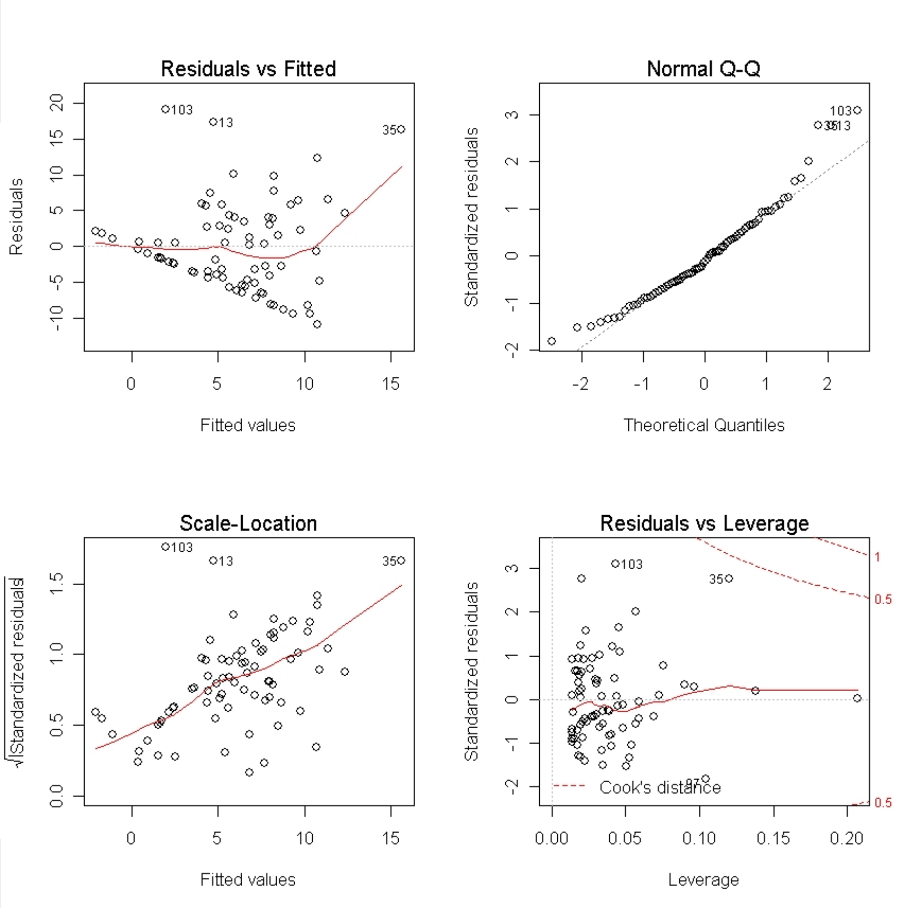
Idea: Interaction of a group and a continuous predictor same as different correlations with the outcome, by group.

Correlation between baseline and 3 month ideation scores:

- Treatment group 1: $r=0.66$, $p=0.0006$
- Treatment group 2: $r=0.40$, $p=0.0012$
- Test for equal correlations $p=0.15$ not significant

Method 2. Least Squares Model

	Estimate	Std. Error	Pr(>|t|)
(Intercept)	4.60817740	2.45609730	0.0647356277
SSI_BL	0.68755350	0.16816642	**0.0001128998**
TREAT	2.79653806	1.70045632	0.1044771126
NCOVAR	-0.03926753	0.01305796	**0.0036449956**
SSI_BL:TREAT	-0.36126616	0.18484025	0.0545833412



LS regression is robust to violation of normality assumption
- but less robust to heterogeneity of variances –also 0 inflation presents as a line in residual plot
- no transformation of the ideation scale can solve this problem

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Method 2 improved

Use the bootstrap to compute p-value

Resample cases: interaction p=.0833

Resample residuals: interaction p=.0654

- Conclusions do not change from LS model
- Did not address the problem of possibly different predictors for the 0 vs.1 and the severity part

Method 3. Two-part Model

	Part 1		Part 2	
	LOGREst	LOGRPr(>|z|)	OLSEst	OLSPr(>|t|)
(Intercept)	1.17584434	0.42436965	2.91398426	0.61073715
SSIBL	0.30383832	0.02029414	0.76513882	0.01706085
Treatm	0.97138361	0.35949735	5.25556144	0.17353157
NCOVAR	-0.02039354	0.01179831	-0.02637649	0.37473973
SSIBL:Treatm	**-0.23699656**	**0.08836396**	**-0.35228892**	**0.28701273**

Conclusion Example 2

There are practical choices for analyzing even severely zero-inflated data!

In this example, conclusions were similar from all methods.

Bootstrap significance level for the LS model was very similar to the LS p-value.

- But bootstrap p-value will be regarded as more believable because of the LS assumption violations

C. Analysis Of High-frequency Data On Suicidal Ideation/Behavior

Ecological Momentary Assessment (EMA) can collect data on suicidal ideation and behavior several times/day and…

1. Estimate suicidal behavior frequency/ ideation severity, and/or classify of individuals by risk
2. Estimate subject-level variability in ideation/behavior
3. Test the effects of time-varying events (triggers),

Good Analytic Practices For EMA Data

Check missing data mechanism

Account for diurnal variability, day-of-the-week and seasonal effects, if applicable

It is best to check models fit on person-level aggregated data against results from hierarchical/mixed effect models

Consider using location-scale models to test effects on both severity/variability

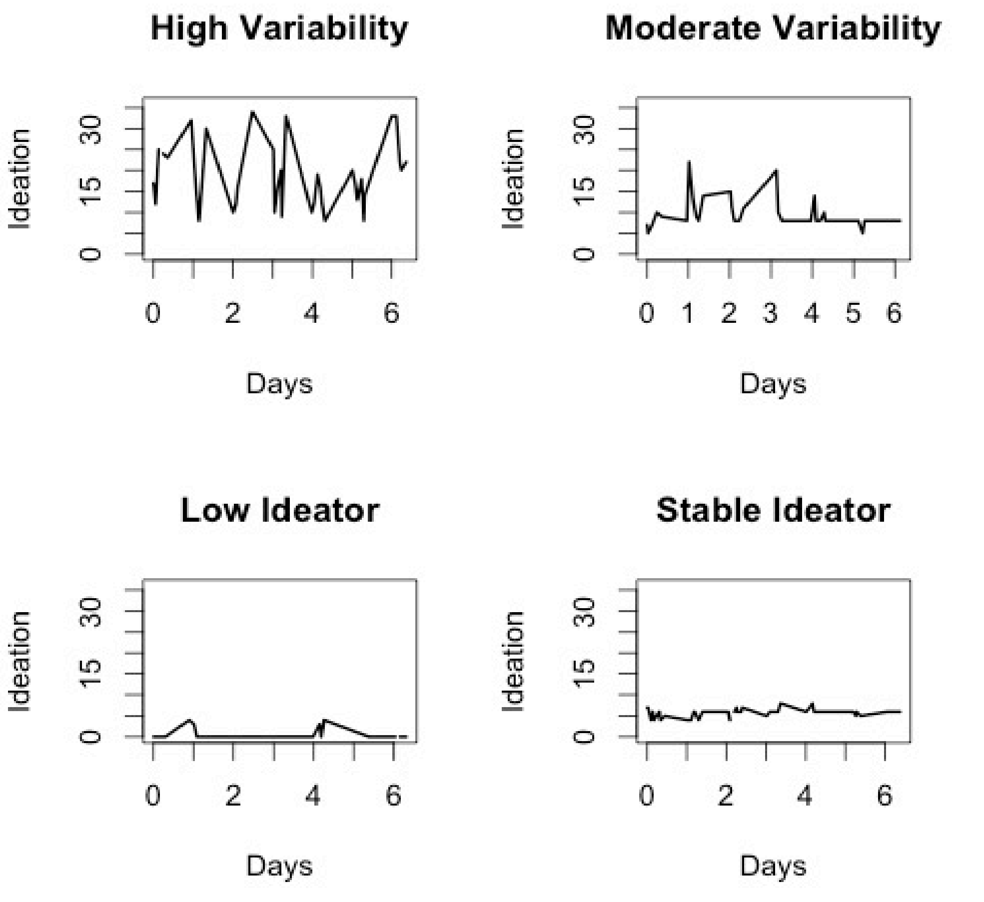
Example 3: EMA study of suicidal ideation

N=84 participants with Borderline Personality Disorders with recent attempt or NSSI

Randomly timed prompts 6 times a day, 76 questions

81 completed at least 5 prompts in one week (68% of prompts answered)

<u>Hypothesis</u>: Ideation increases following negative life events, depending on depression severity and traits



EMA Suicidal Ideation

Score is total of 9 questions from the Beck Scale for Suicidal Ideation, on 5-pt Likert scale: *a wish to live; a wish to die; a wish to escape; thoughts about dying; thoughts about suicide; urge to die by suicide; thoughts about hurting self; urges to hurt self;* and whether they had *reasons for living*.

4 subjects' 1-week time course

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Between-Subject Differences In SI:

Subject's average EMA ideation can be tested for correlation with baseline traits and state variables

-the BL measures can also be tested as predictors of suicidal ideation during EMA using mixed effect models:

Example: Beck Depression Inventory

$SI_{i,t} \sim BDI_i$: b=0.31 (SE=0.05), $t_{76}=6.24$, $p<0.0001$.

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Measures of within-subject change in EMA-SI

Point-to-point difference score at time t: $SI_t\text{-}SI_{(t-1)}$

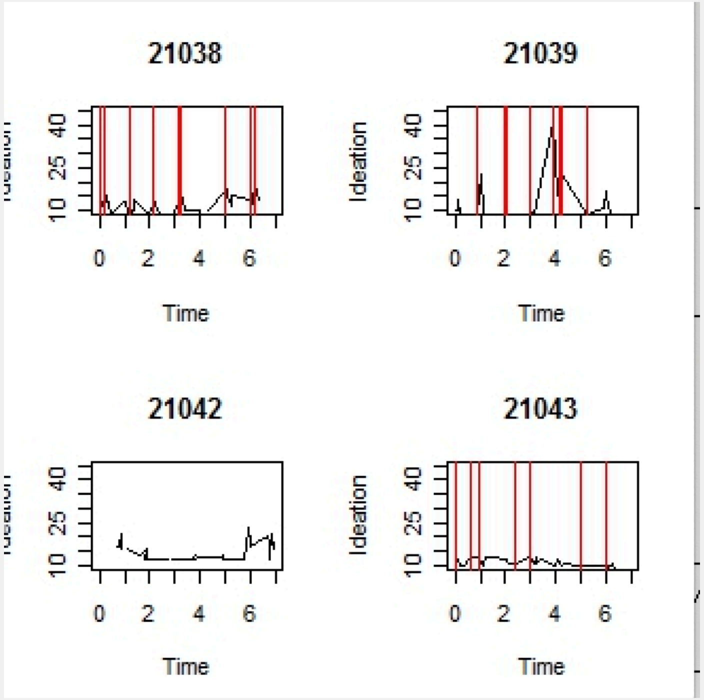
- assumes that 5 point increase is the same whether it starts from SI=0 or from SI=30

Percent increase in ideation at time t : $SI_t/SI_{(t-1)}$

- emphasizes changes that start from lower SI value

Aggregate variability: root mean successive squared deviations (RMSSD)

Change in SI after a disagreement



4 subjects' 1-week time course. Red vertical line denotes disagreement. Note the variability in frequency and in the response.

Change in SI after a trigger event

Mixed effect models can test time-varying predictors' effect on ideation change score:

$(SI_{i,t}\text{-}SI_{i,t-1}) \sim Disagreement_{t,I}$ (b=2.68, p<0.0001)

Baseline traits can also be tested as moderator the response to trigger: $(SI_{i,t}\text{-}SI_{i,t-1}) \sim BDI_i + Disagr_{t,I} + BDI_i{*}Disagr_{t,I}$

- interaction b= -0.09, t=-2.42; df=930; p=0.0200

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Conclusion, Example 3.

EMA can quantify both between-subject and within-subject differences in ideation severity.

Can test effect of stress and coping on within-subject change in suicidal ideation.

Extension: depending on temporal granularity, analysis can establish the sequence of trigger→change in affect→change in suicidal ideation/behavior.

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Resources online

Two-part model: R: https://devinincerti.com/2015/09/11/twopart.html

SAS: https://support.sas.com/resources/papers/proceedings15/3600-2015.pdf

Bootstrap: R: https://www.statmethods.net/advstats/bootstrapping.html

SAS: https://blogs.sas.com/content/iml/2018/12/12/essential-guide-bootstrapping-sas.html

SPSS https://www.ibm.com/products/spss-bootstrapping

Location-scale model for EMA: https://reach-lab.github.io/MixWildGUI/MixWild_User_Guide.pdf

Thank You!

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DATA ANALYTIC METHODS:

Natural Language Processing

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Disclosures

Last three years:

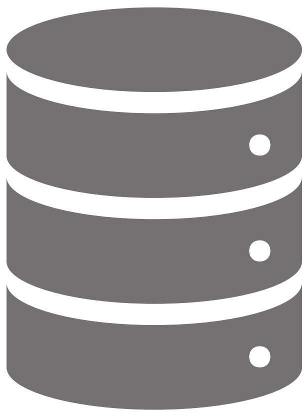
- Grant support, American Psychiatric Association/Foundation (APA/F)
- Writing honoraria, Carlat Publishing

Data Structures

Structured:

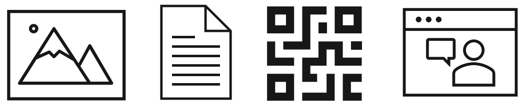
- Regular internal structure
- Minimal labor required for downstream use
- Smaller storage footprint (e.g., tables, relational databases)
- <20% of data

ID	Age	Gender	Diagnosis
001	22	M	MDD
002	55	F	GAD



Unstructured:

- Irregular internal structure
- Significant labor required for downstream use
- Large storage footprint (e.g., data lakes)
- ~80% data



Electronic Health Record (EHR) = **Semi-Structured**

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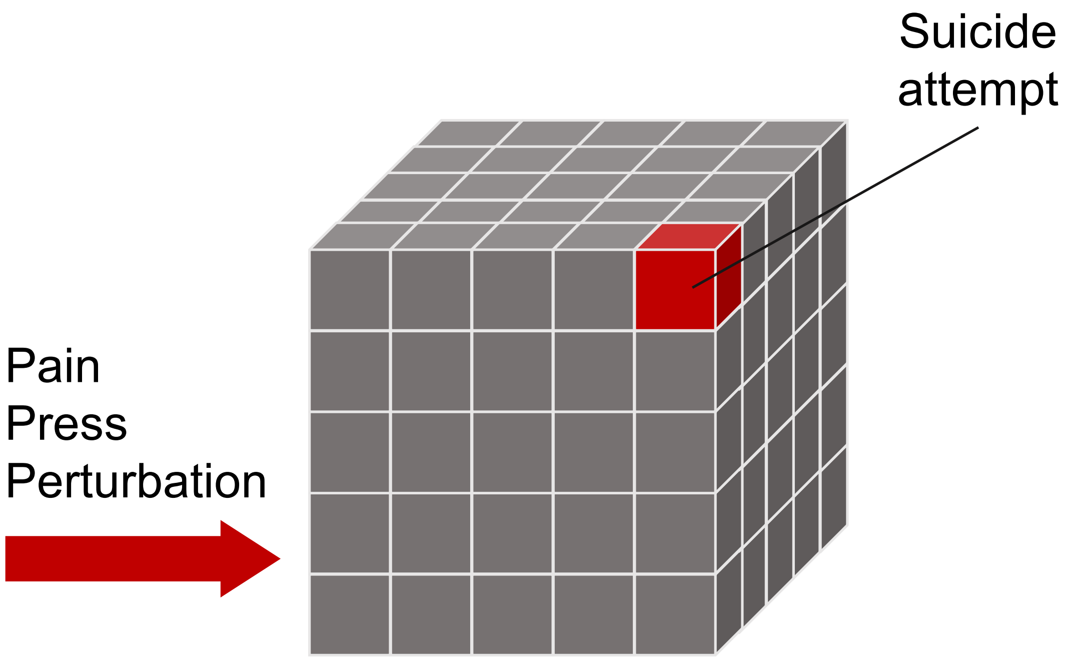
Unstructured Suicide Data

- **Suicide notes / other writing**
  - Rare <30%, variable length & depth, frequently instructional, destroyed in cases of no attempt / survival, <u>curated</u>
- **EHR**
  - Quotes often rare, <u>curated</u> by two parties, mis-coding, Blois' funnel
- **Interviews, free text survey responses**
  - Limited to survivors, retrospective, <u>curated</u>



Shneidman's Cubic Model

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Unstructured Suicide Data

- **Suicide notes / other writing**
  - Rare <30%, variable length & depth, frequently instructional, destroyed in cases of no attempt / survival, curated
- **EHR**
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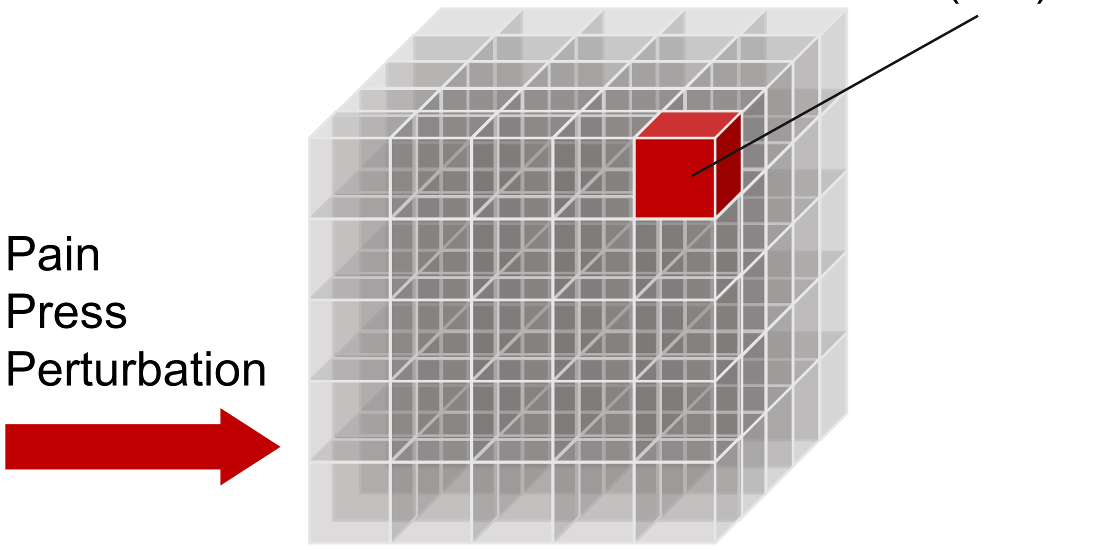


Distilled Narrative Problem

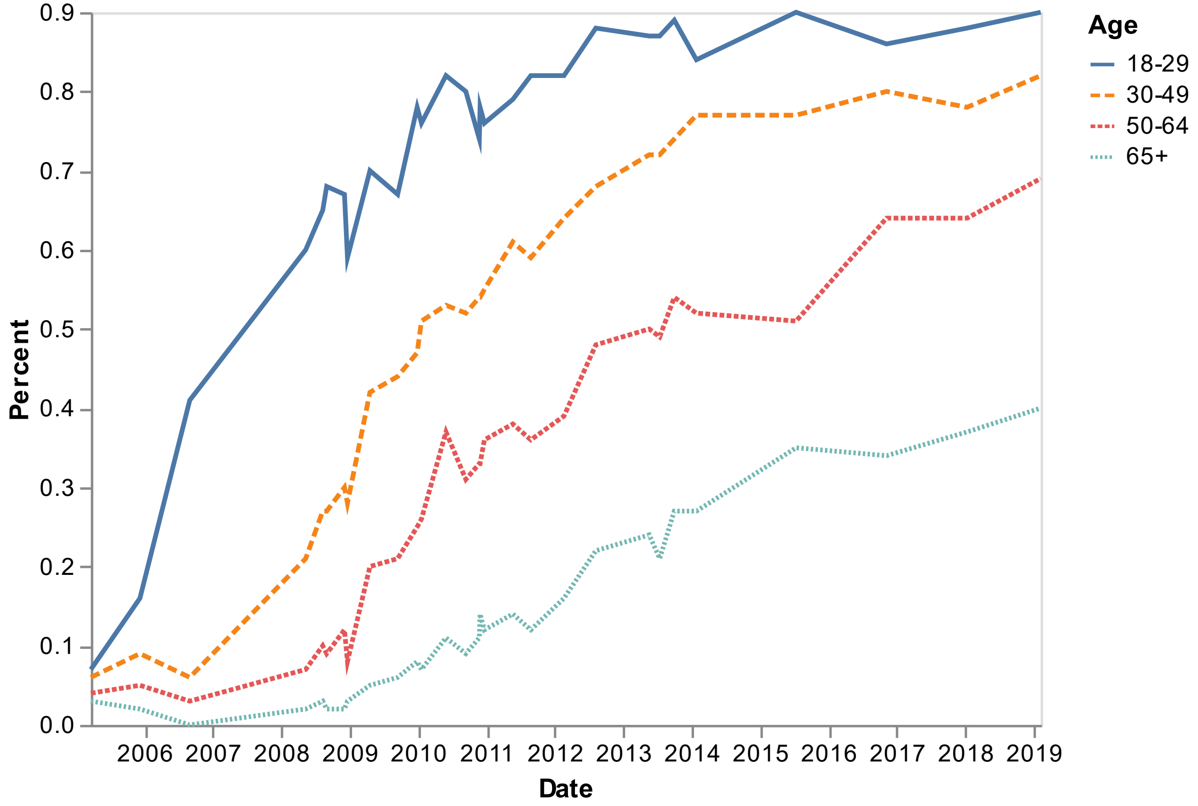
“In almost every case, the results have reflected **more the method of analysis** than the suicidal state of man.”

—Shneidman, *Suicide as Psychache*

- Mixed results
- Generalizability?

Social Media = New Suicide "Note"

- **72% of US adults** use at least one SM platform (Pew Institute, 2/2019)
- Earliest and **highest utilization among adolescents** (high risk group for suicide)
- Many **readily divulge distress and suicidality online** (but may not disclose to clinicians)
- Preliminary data indicates **fair correlation** with psychometrically assessed suicidal risk



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Social Media = New Suicide "Note"

Advantages:

- Ubiquitous, public, "free"
- **IRB exempt**: 45 CFR 46.101(b)(4) applies unless direct contact
- **Access to rare populations**
- Uniquely identifiable users can be tracked over time
- Meta-data (platform dependent)
- Observe user-community interactions & group-level reactions (**social microcosms**)

Disadvantages:

- Mostly **unstructured**
- **BIG** data (Twitter = 12 terabytes of data daily), costly to store
- **Volatile**: always evolving
- Ethics: what if you detect a suicidal individual? (*Cyberpsychol Behav Soc Netw*. 2013 Sep; 16(9): 708–713)

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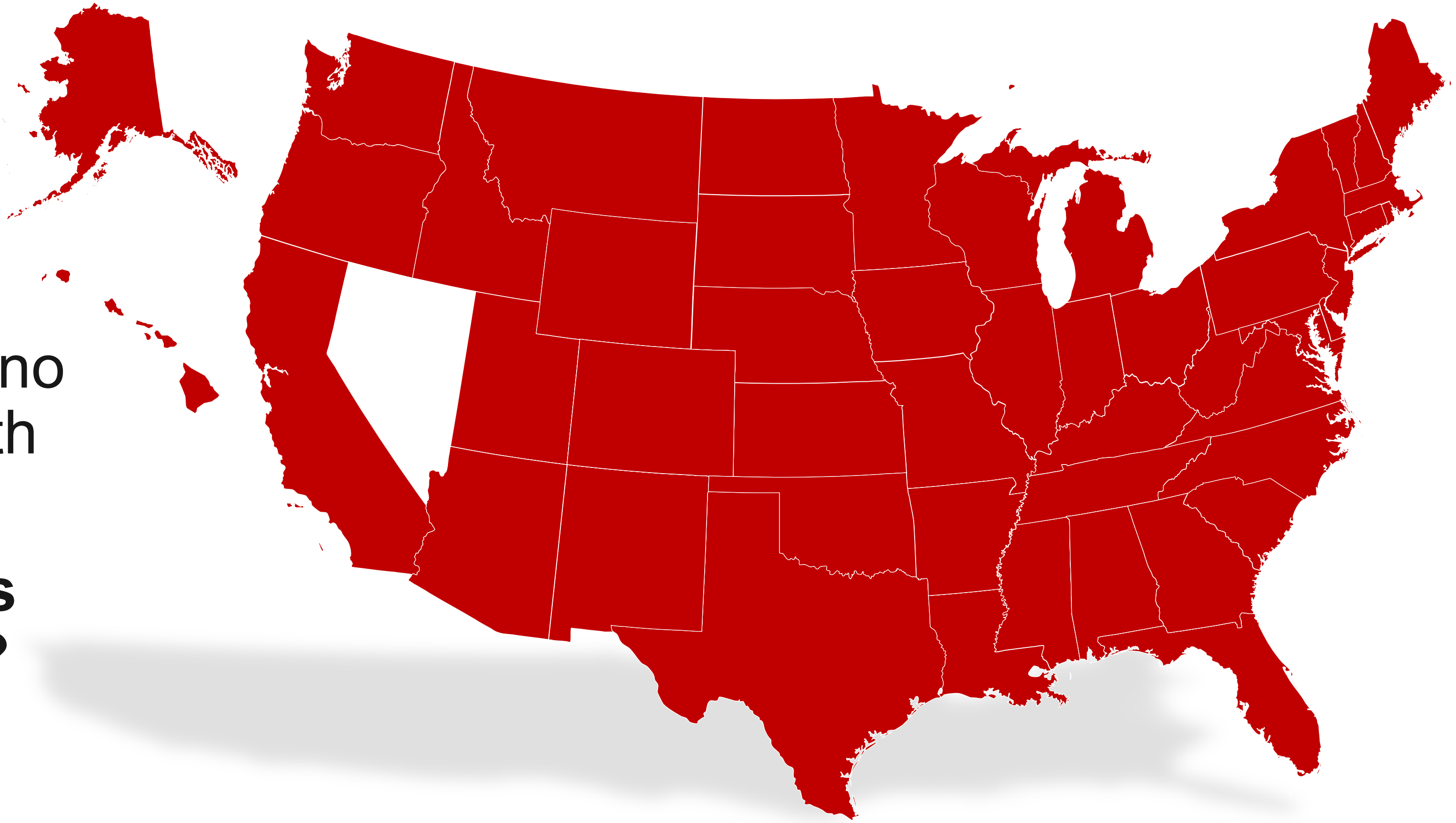
CDC VitalSigns—1999-2016

- Suicide rates increased in nearly every state
- 54% who died had no known mental health condition
- **How do we access these individuals?**



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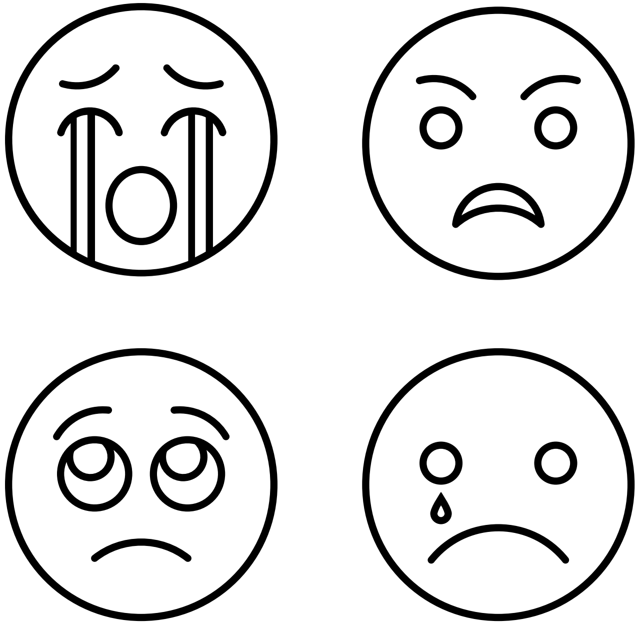
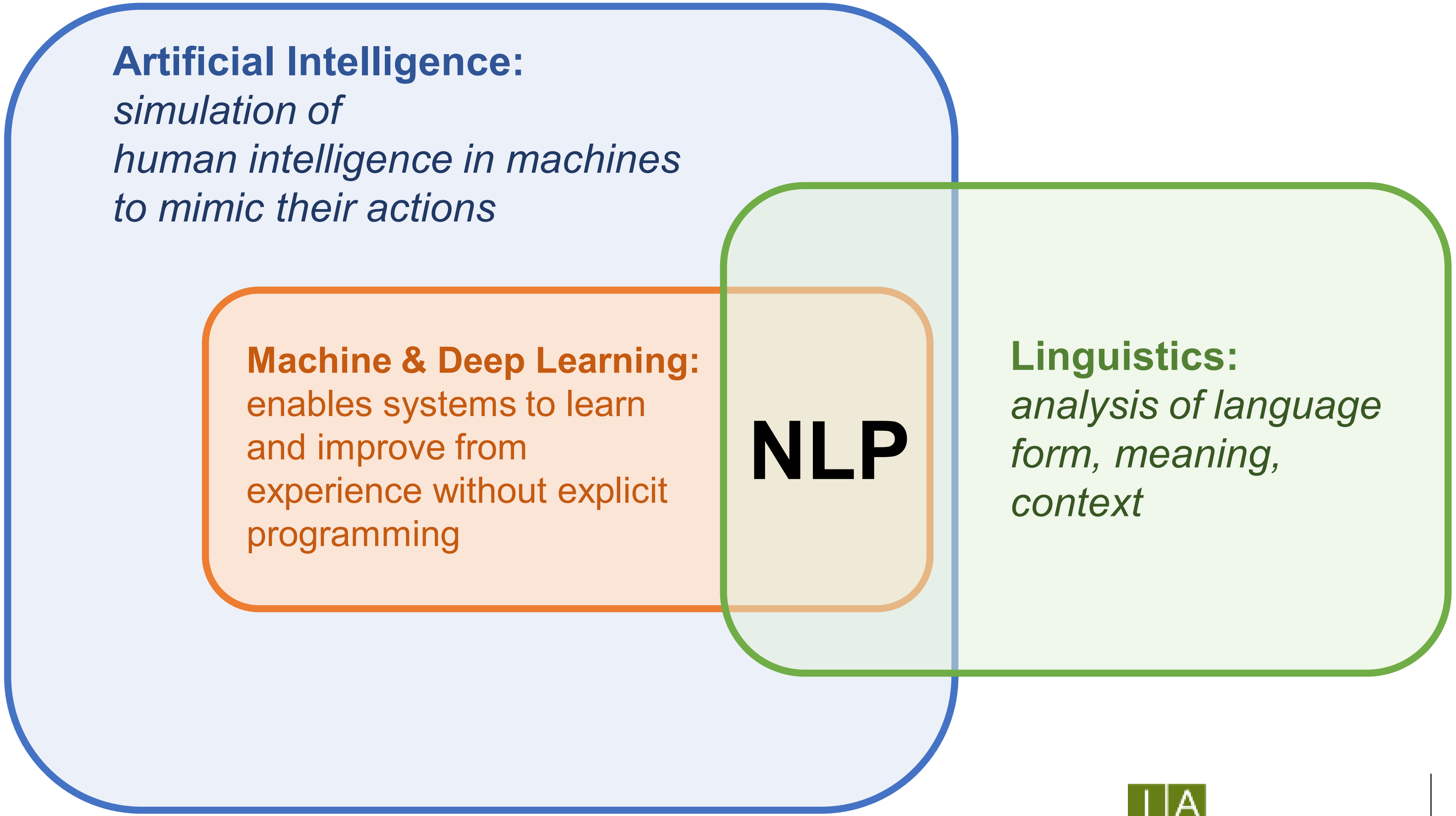
Text Data != Suffering



- **“Traditional” Process:**
  - Set annotation criteria
  - **Manual** labelling
  - Comparison with other annotators, resolve disagreements, repeat
- **Issues:**
  - **Slow, labor-intensive, costly**
  - Prone to **bias**, difficult to reproduce
  - **Limited** to pre-set criteria
  - Never leverage the full breadth & depth of the data

Natural Language Processing



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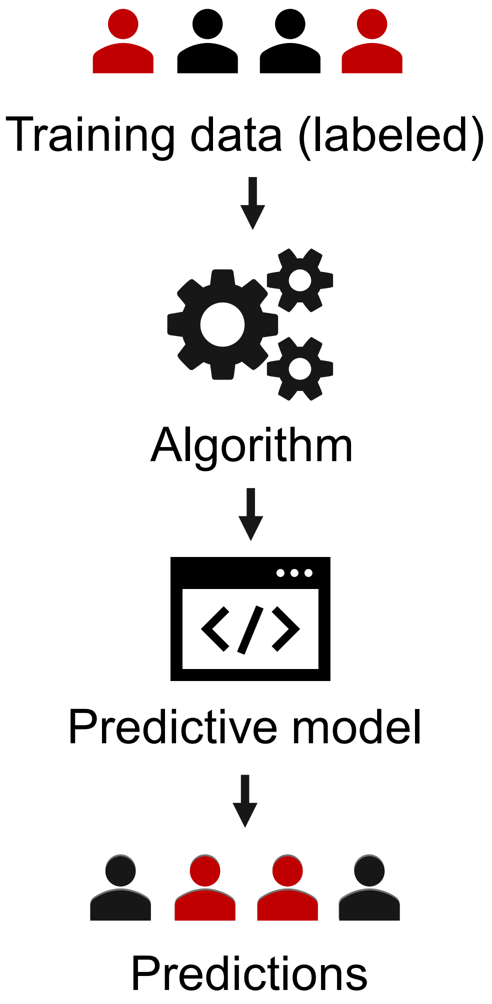
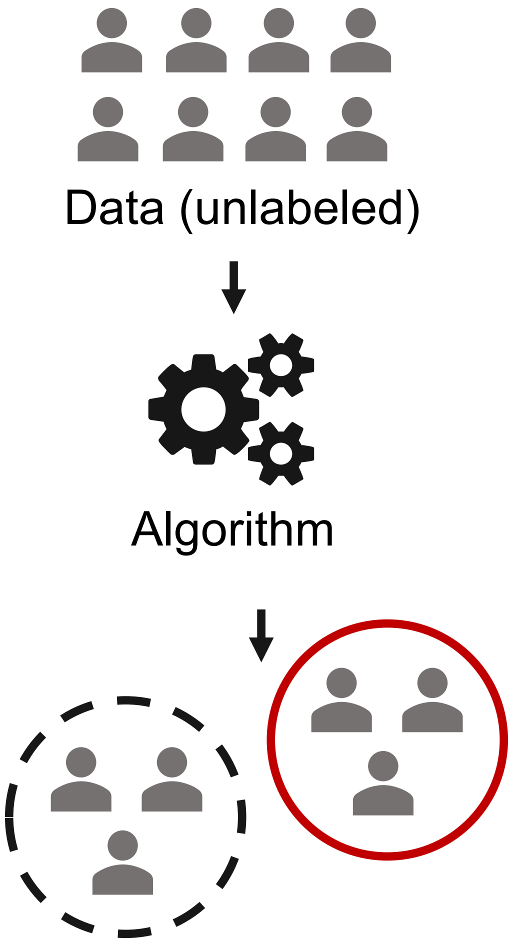
Learning Types

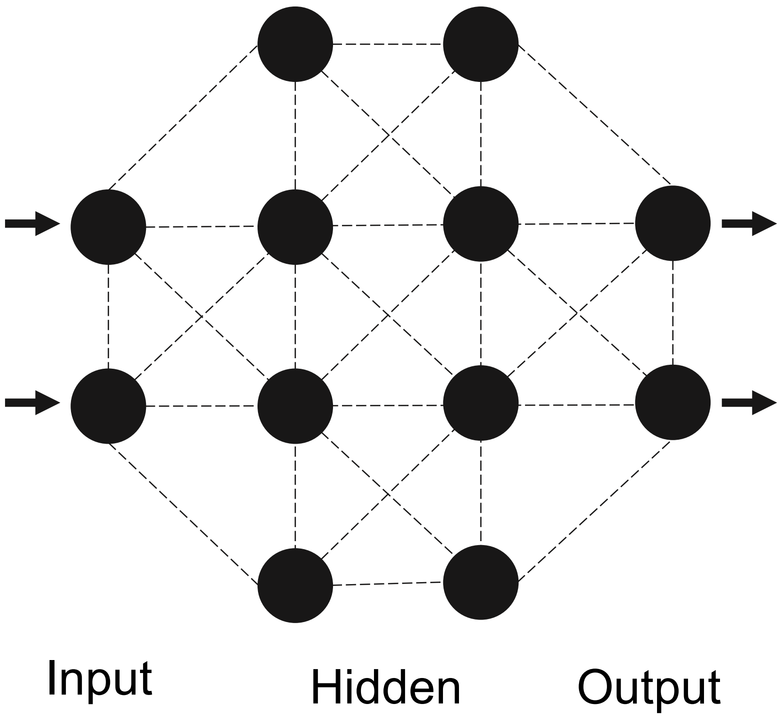
Supervised



Unsupervised



Deep



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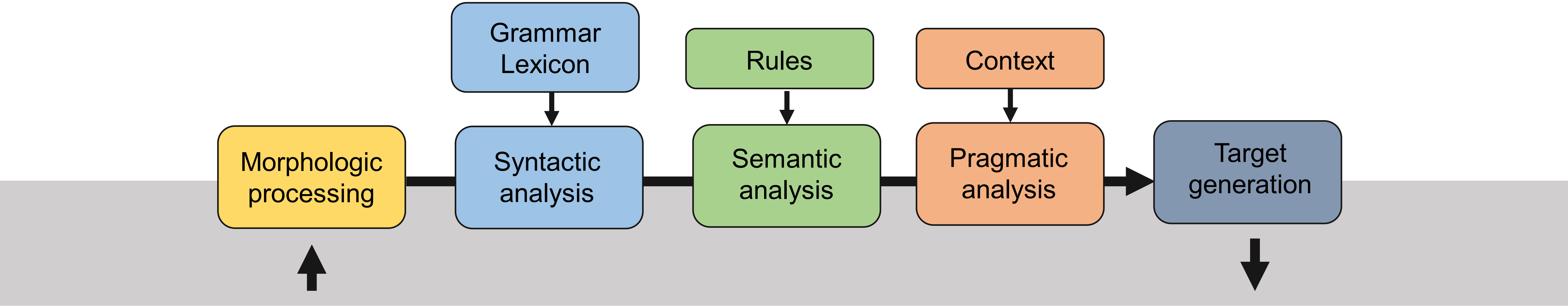
NLP vs. NLU vs. NLG



Input:
"Hey Google, turn on lights."

Output:
"Welcome home."

Series of encapsulated machine/deep learning problems, insight individually, for features extraction, or as a system

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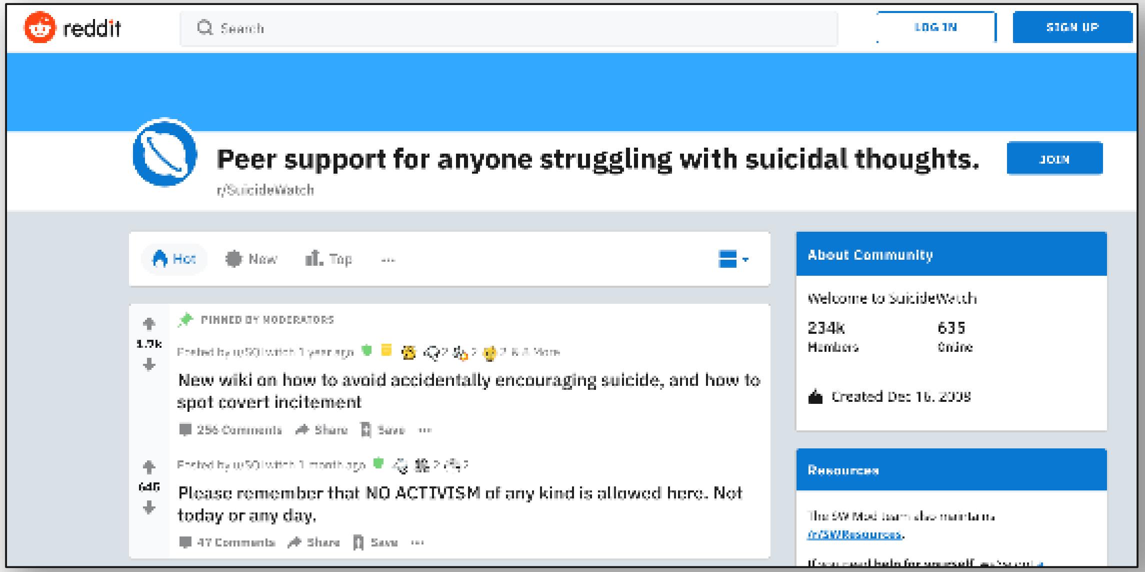
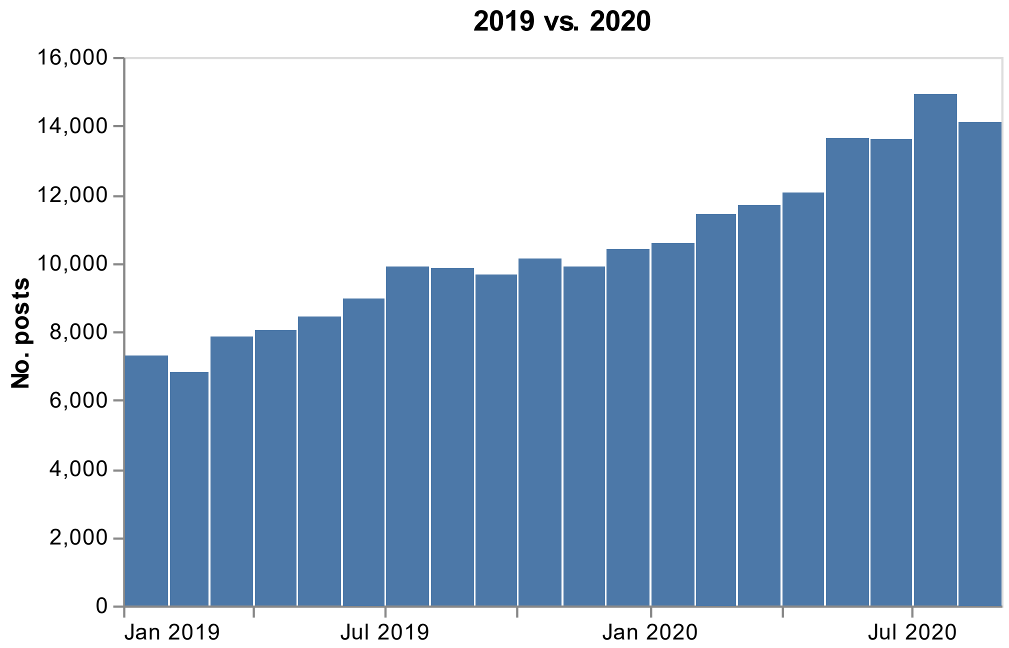
Reddit r/SuicideWatch

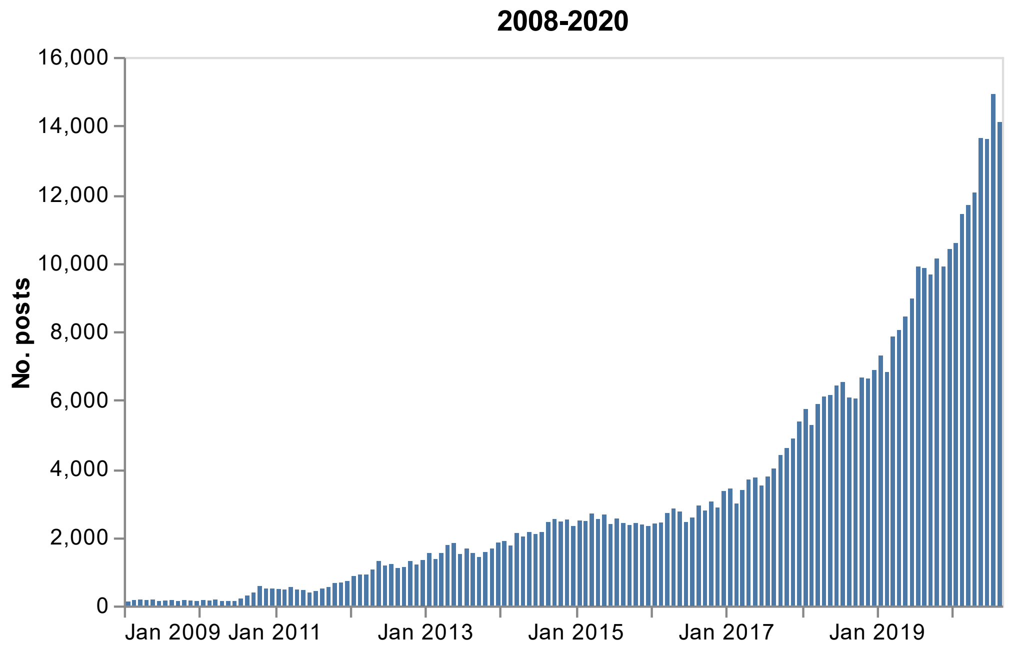
- **Reddit, public API, Pushshift.io**
- **69 meta-data fields**
  - Username = including if deleted
  - Post time (UTC)
  - Number of comments, cross-posts, guildings
- **Derived meta-data**
  - Post frequency & removals
  - Post length & word count
  - Frequency of posting by user (some in the 100s)
  - User activity in other forums – drill-down cohort characterization



Meta-Data Insights

Are people posting to SW more post-COVID?





2019: N=107,094
2020 (T-4 mo.): N=101,959

Does the rate of repeat posting differ?
More removal of posts?
New users or previous posters?

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NLP PIPELINE

Preprocessing → Parsing & EDA → Text Representation & Feature Engineering → Modeling → Evaluation

- Words, misspellings, emojis, numbers, contractions, URLs, #s, @s, code artifacts username mentions, processing artifacts, etc.
- **Parallel & distributed processing enables rapid execution** of even highly complex cleansing pipelines to regularize, de-identify, de-clutter (often iterative)
- Depth and extent of cleansing depends on downstream analysis / applications (e.g., emotional state can be derived from emojis)

COVID example:
N=209,053 (raw) → 173,227 (clean/intact)

NLP PIPELINE

Preprocessing → **Parsing & EDA** → Text Representation & Feature Engineering → Modeling → Evaluation

Syntactic analysis: *analyzing words according to formal grammar*

- **Sentence segmentation**
  - Sentence > clauses > Phrases > Words
  - Punctuation removal is an information loss (e.g., !)
- **Tokenization**
  - Digesting corpus into individual words or *n*-grams
- **Part-of-speech tagging**
  - Noun vs. adverb vs. adjective
- **Stemming vs. Lemmatization**
  - Removing word affixes = reduces size of dataset
  - Run, Runs, Running
- **Stop words**
  - a, the, in, of, etc.
  - Context dependent (self & distancing language)
- **Dependency parsing**
  - Grammatical structure

Pre-Post Stop Word Removal

	Term	Frequency
0	i	2696523
1	to	1214375
2	and	986657
3	not	774891
4	my	714422
5	the	702119
6	a	626022
7	it	551530
8	am	542309
9	is	511996

	Term	Frequency
0	want	205464
1	like	188186
2	life	161259
3	feel	156167
4	know	147641
5	would	141013
6	get	117131
7	even	108037
8	people	103580
9	one	97723

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Preprocessing → Parsing & EDA → **Text Representation & Feature Engineering** → Modeling → Evaluation

Text representation: *Mapping of words/phrases to real numbers, vectors (algorithm friendly)*

Bag-of-Words

Term	Doc1	Doc2
want	2	15
hope	0	1
self	10	2
work	1	1

Sparse matrix problem, no preservation of surrounding context

Term Document – Inverse Document Frequency (TD-IDF)

$$w_{i,j} = tf_{i,j} \times \log\left(\frac{N}{df_i}\right)$$

$tf_{i,j}$ = number of occurrences of i in j

df_i = number of documents containing i

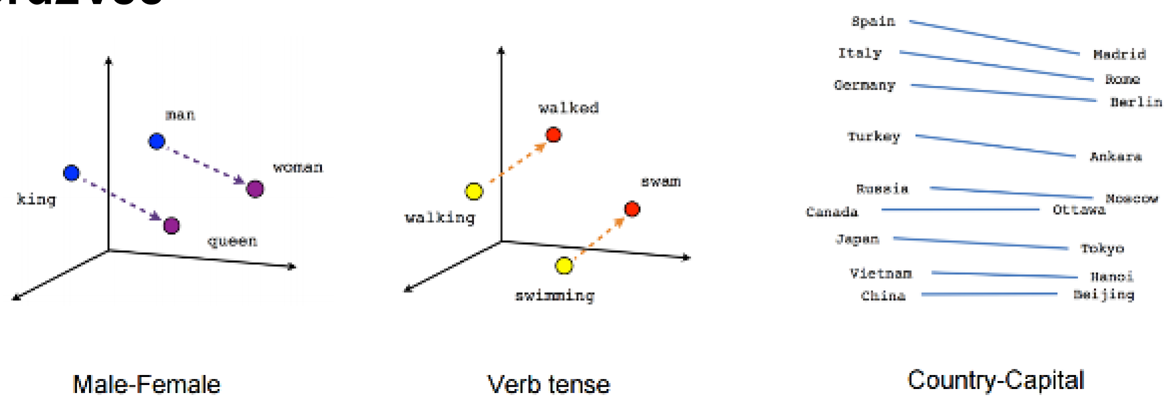
N = total number of documents

NLP PIPELINE

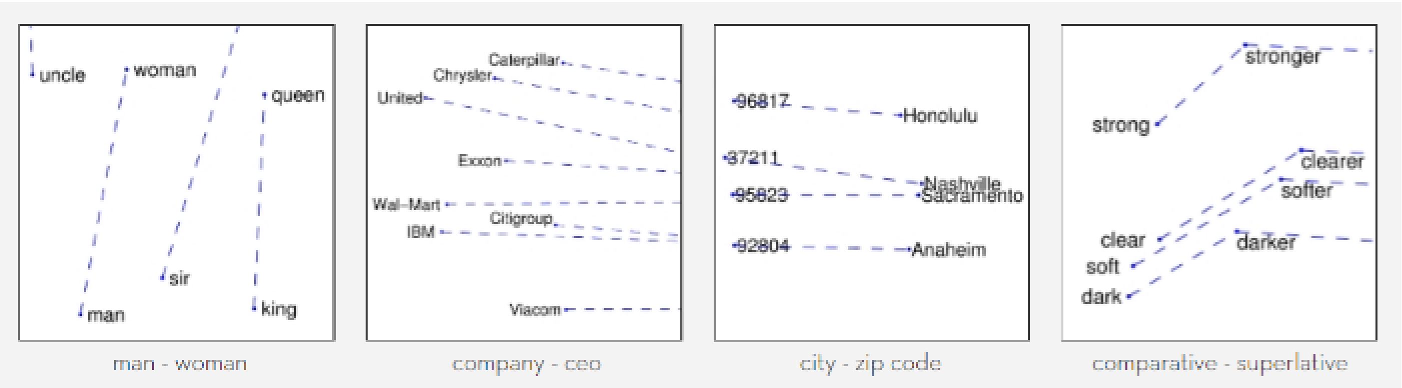
Preprocessing → Parsing & EDA → **Text Representation & Feature Engineering** → Modeling → Evaluation

- Sparse matrix solved by mapping high dimensional space into low dimensional space = unsupervised learning
- **Dimensionality reduction techniques** (e.g., PCA, nearest neighbor) bring semantically similar items together
- **Word2Vec** (CBOW, skip gram) = neural network algorithm for training word embeddings, preserves context
- **GloVe:** Global Vector for word representation (matrix factorization, LSA)

Word2Vec



GloVe



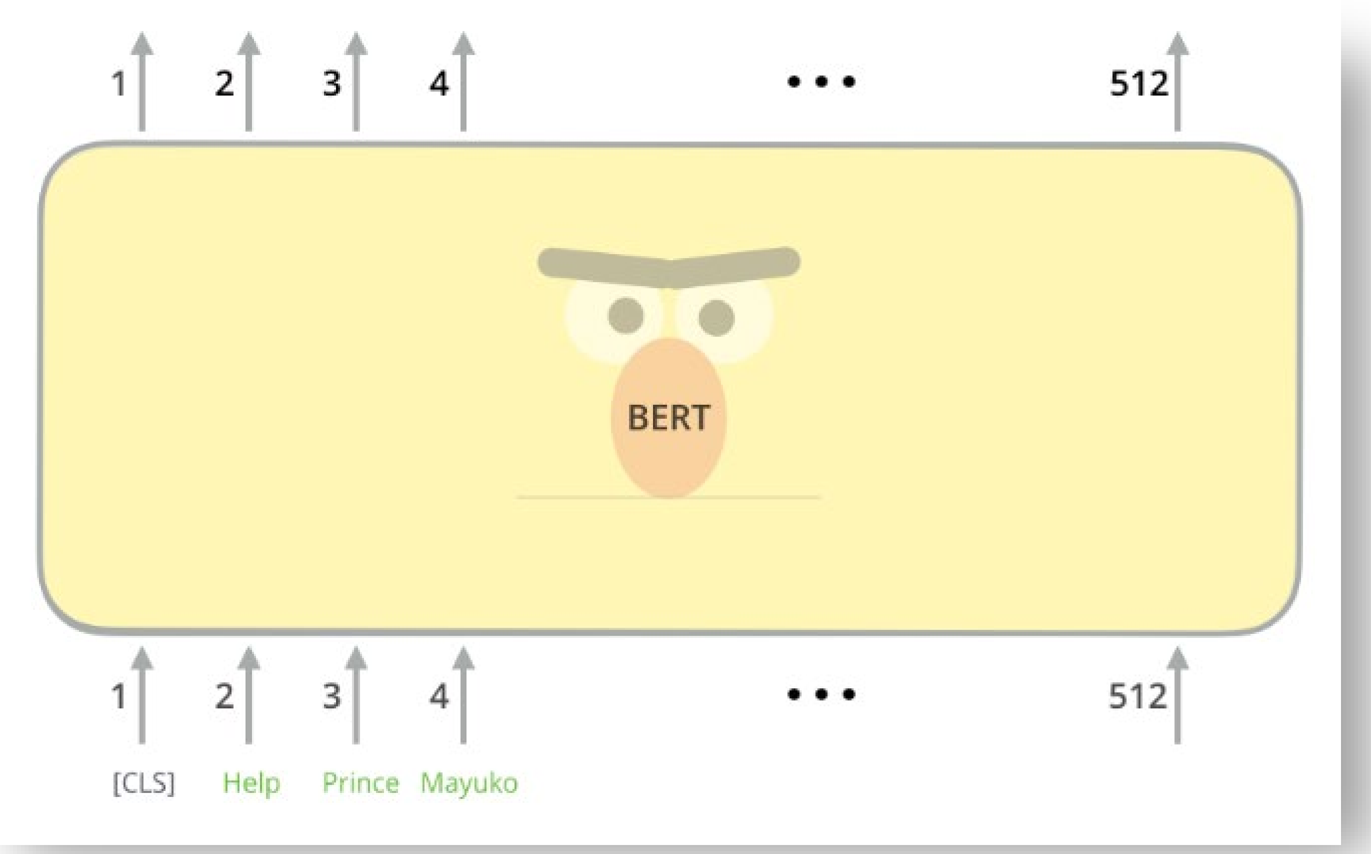
NLP PIPELINE

Preprocessing → Parsing & EDA → Text Representation & Feature Engineering → **Modeling** → Evaluation

Semantic analysis = *meaning from text*

Named-Entity Recognition: extract and classify entities according to defined categories (e.g., names, organizations, places, diagnoses)

Historically brittle, need for manually annotated lexicons → move toward semi-supervised and transfer learning approaches (pre-trained models, unsupervised learning)



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Named-Entity Recognition

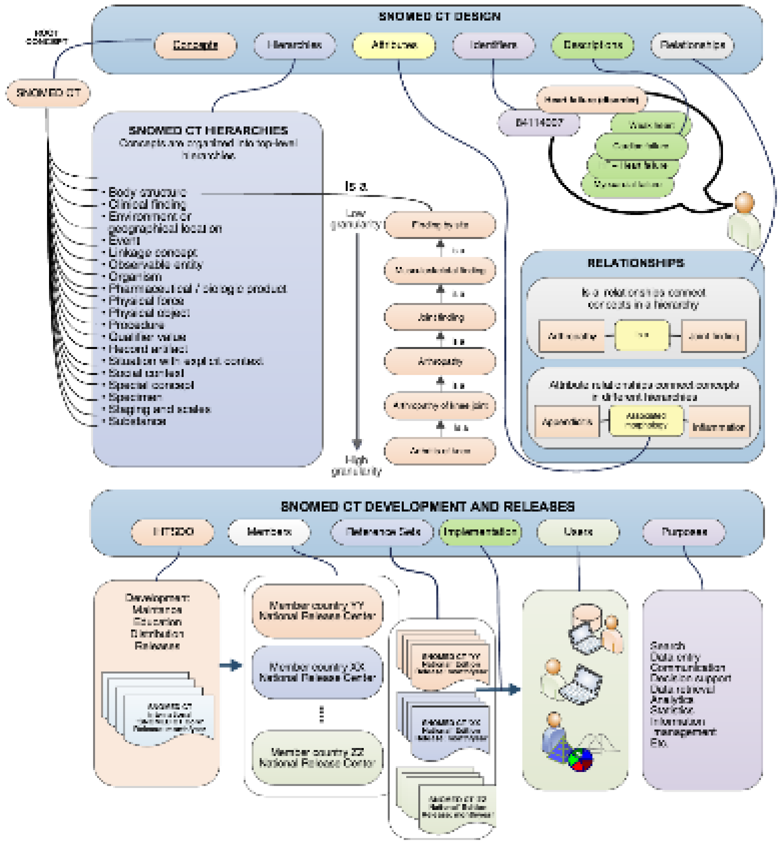
- **Rapid structuring of unstructured data** (e.g., demographic data, substance abuse, admission of prior trauma, reported prior diagnoses, etc.)
- **High-level of customization** to task
- Many publicly available models and lexicons

COVID example:

- NER here identified 6551 individuals reporting issues related to the pandemic
- F > M (opposite of Reddit demographics)
- 25-45 years of age (slightly older than site demographic)
- Great deal of prior MH diagnosis and current contact

Medical Lexicons

- Systematized Nomenclature of Medicine (**SNOMED**)
- Unified Medical Language System (**UMLS**)
- **RxNorm** provides semantic structure for drug formulations



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Linguistic Inquiry & Word Count

http://liwc.wpengine.com/

Affective or emotional processes
1. Positive Emotions
   a. Positive Feelings
   b. Optimism and energy
2. Negative emotions
   a. Anxiety or fear
   b. Anger
   c. Sadness or depression

Cognitive processes
1. Causation
2. Insight
3. Discrepancy
4. Inhibition
5. Tentative
6. Certainty

Sensory and perceptual processes
1. Seeing
2. Hearing
3. Feeling

Social processes
1. Communication
2. Other references to people
3. Friends
4. Family
5. Humans

Occupation
1. School
2. Job or work
3. Achievement

Leisure activity
1. Home
2. Sports
3. Television and movies
4. Music

Money and financial issues

Metaphysical issues
1. Religion
2. Death and dying

Physical states and functions
1. Body states, symptoms
2. Sex and sexuality
3. Eating, drinking, dieting
4. Sleeping, dreaming
5. Grooming

- *Pennebaker et al.*
- Software that analyzes each word in the text against a dictionary of pre-defined words associated with psychologically-relevant categories and quantifies proportion.
- 6,400 words, word stems, and selected emoticons
- “If It Ain't Broke, Don't Fix It” = great for EDA

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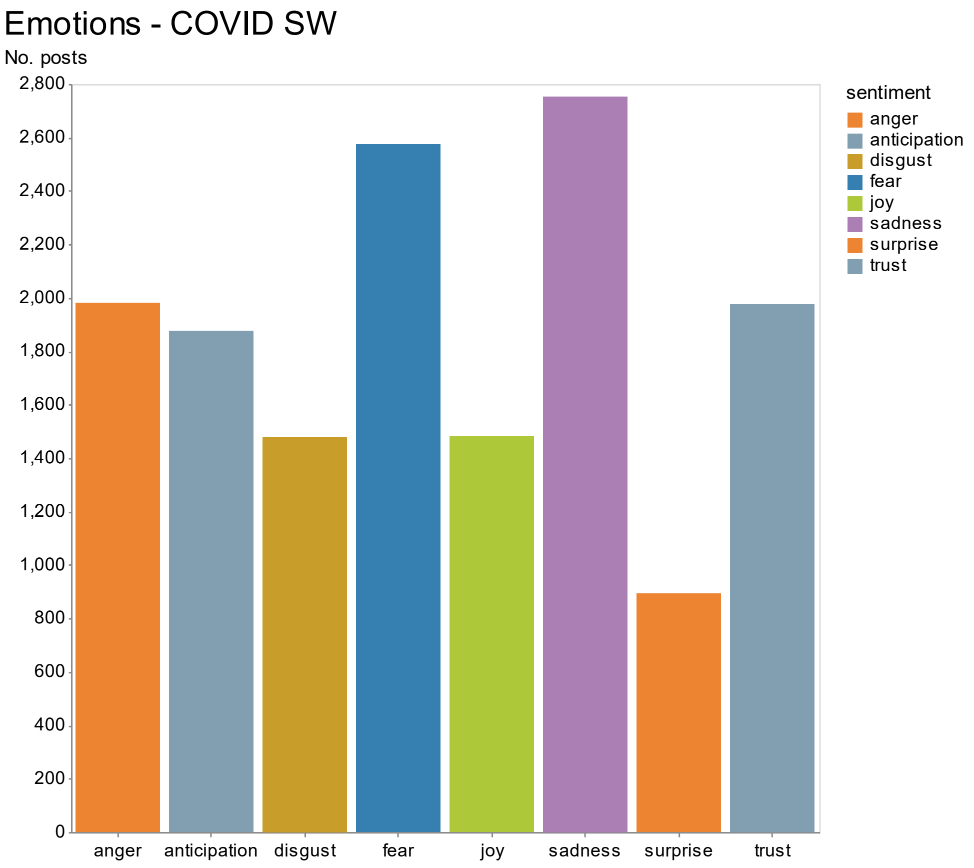
NLP PIPELINE

Preprocessing → Parsing & EDA → Text Representation & Feature Engineering → **Modeling** → Evaluation

Emotion & Sentiment Analysis

- Determine emotional content of text
    - Positive, negative, neutral (most common)
    - Anger, disgust, fear, joy, sadness, surprise (Ekman)
- Algorithm trained on a lexicon (supervised learning, classification problem, Naïve Bayes popular option)
- Rule, feature, or embedding-based options
- Length of training text to be considered (e.g., letter vs. a tweet)
- Variable level for scheme for scoring



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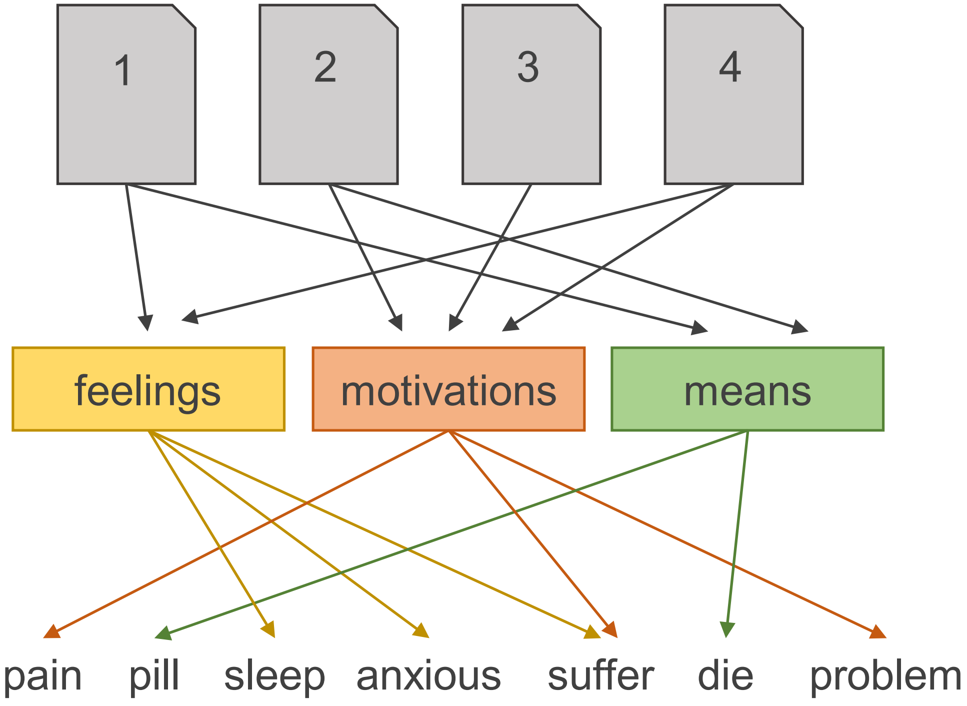
Preprocessing → Parsing & EDA → Text Representation & Feature Engineering → **Modeling** → Evaluation

Topic modeling

- Many options, same assumptions:
  - Each document consists of a mixture of topics,
  - Each topic consists of a collection of words
- **Latent Dirichlet Allocation:** popular, generative probability model, output is a per document topic distribution, and per topic word distribution
- **Others:** PLSA, LSA (uses TD-IDF scores), lda2vec (word2vec + LDA), top2vec (BERT + UMAP/HDBSCAN cluster)
- Time element may be added to track changes over time (**dynamic**)



Document-Topic Probability Matrix

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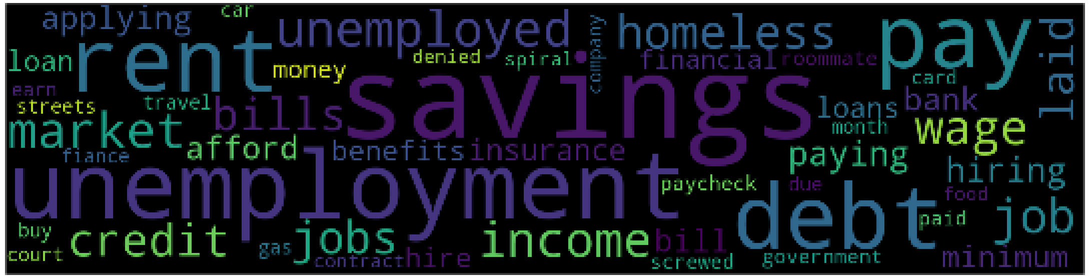
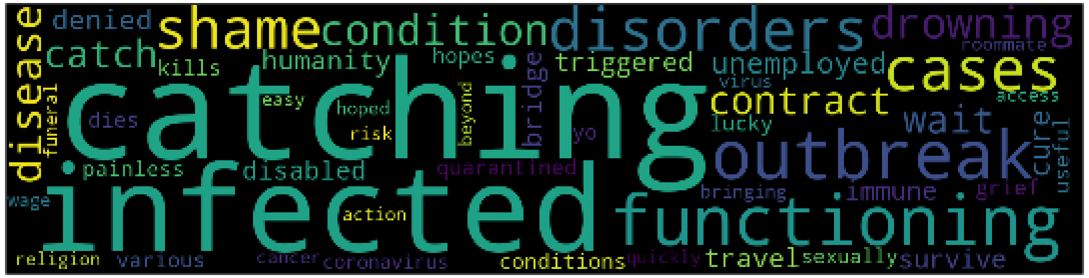
COVID Example (41 topics identified)

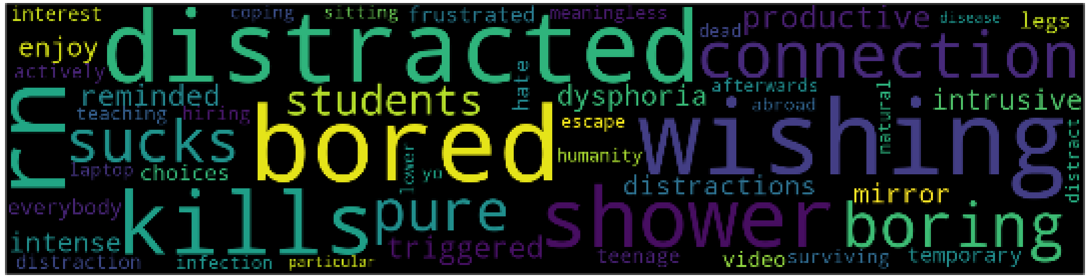
Topic 1 N=723



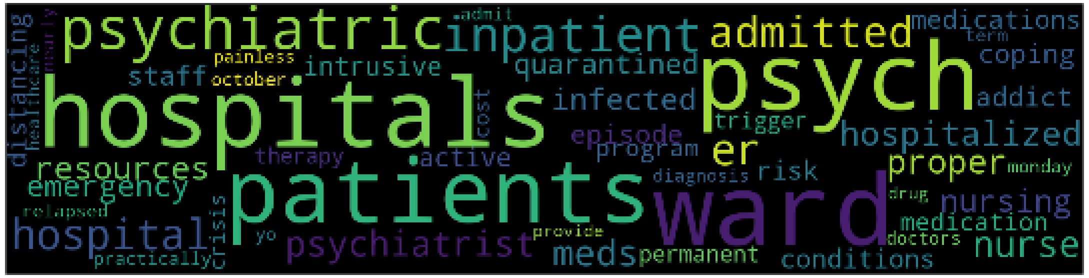
Topic 3 N=379



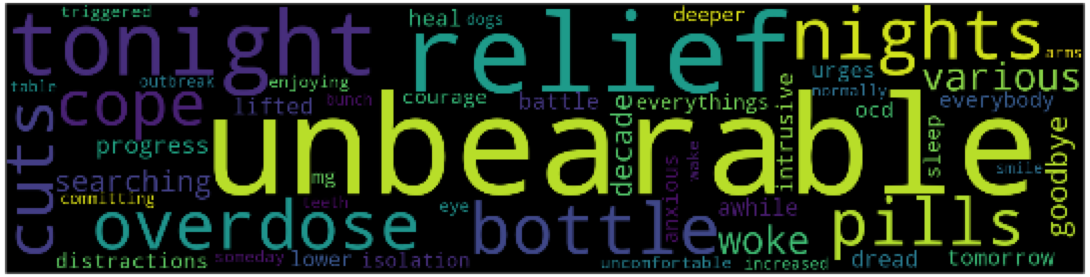
Topic 2 N=451



Topic 4 N=273



Topic 5 N=258



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Highest similarity to Topic 4

Topic	Words	Cosine similarity score
13	'inpatient', 'er', 'admitted', 'hospital', 'nurse', 'meds', 'psychiatrist', 'hospitalized', 'proper', 'resources', 'nursing', 'emergency', 'infected', 'quarantined', 'episode', 'addict', 'staff', 'coping', 'risk', 'conditions', 'medications', 'distancing', 'intrusive', 'active', 'medication', 'program', 'permanent', 'trigger', 'therapy', 'crisis', 'cost', 'practically', 'term', 'october', 'monday', 'diagnosis', 'nearly', 'relapsed', 'healthcare', 'doctors', 'admit', 'painless', 'yo', 'drug', 'provide'	0.3443
4	'appointments', 'practice', 'steps', 'finding', 'ward', 'distraction', 'services', 'bill', 'meds', 'psych', 'psychologist', 'research', 'crisis', 'effort', 'exercise', 'impact', 'local', 'responsibility', 'academic', 'cases', 'meaningful', 'hello', 'however', 'sessions', 'appointment', 'cancelled', 'therapy', 'psychiatric', 'proper', 'currently', 'psychiatrist', 'mid', 'spiral', 'hotline', 'rely', 'episodes', 'current', 'savings', 'knowledge', 'practically', 'coworkers', 'direction', 'service', 'lack', 'depressing', 'therapists', 'peers', 'christian', 'medical', 'perspective'	NA

NLP Use Cases

- Features for predictive models
- Document classification and comparison
- Screening subjects for study inclusion
- Diagnostic re-classification of subjects
- Rapid synthesis of literature, policies, etc.
- Speech-to-text
- Chat bots
- Many, many, more…
- Well supported community (R, Python), numerous validated packages (NLTK, Spacy, OpenNLP)

Take Home

- Extracting meaning from text is hard, but NLP makes it easier, faster, and more systematic
- Social media data holds promise in innovating suicide research and prevention, particularly when powered by NLP

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Thank you!

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