Estimating adolescent suicide attempt likelihood and moderating pathways from depressive symptoms

Incorporating high-dimensional risk and protective factors using the UK Millennium Cohort Study

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Background

- Suicide 2nd leading cause of death among adolescents aged 15-19; critical public health challenge worldwide (Yan et al., 2024)
  - Suicide rates: 9.1 per 100,000 in 15-24-year olds in UK in 2018 (ONS Mortality Statistics)
  - Suicide attempts: 1 in 14 (7%) in 17-year-olds in UK in 2018 (Patalay & Fitzimons, 2021)

- Depression one of the most robust predictors of suicide attempts in youth (Richardson et al., 2024)
- However, ~2/3rds of adolescents with depressive symptoms do not engage in suicidal behaviors (de Araújo Veras et al., 2016)

Clinical & Public Health Motivation

- UK Clinical Guidelines
  - do not support screening for suicide risk (NG225: NICE 2022)
  - recommend screening adolescents for depression (e.g., in primary care, schools) (NG134: NICE, 2019)
  - when assessing depression risk, important to consider multiple psychosocial factors (NG134: NICE, 2019)

- unclear **which factors** most strongly **shape link between depressive symptoms** and **adolescent suicide attempts**
- Elucidating these pathways is critical for improving prevention, early identification, and targeted interventions

Research Gap

Moderators of the depression-suicide relationship

- Individual moderators tested (e.g. self-esteem: Yang et al, 2024)
- Complex interplay among multiple variables not tested

Traditional statistical methods (e.g., multilevel regression or path analysis) limited in:

- detecting complex, multidimensional interactions (Abbasi et al., 2021)
- accounting for heterogeneous influences (Cohen et al., 2013)
- capturing underlying non-linear relationship without pre-defined assumptions (Andersen, 2009)

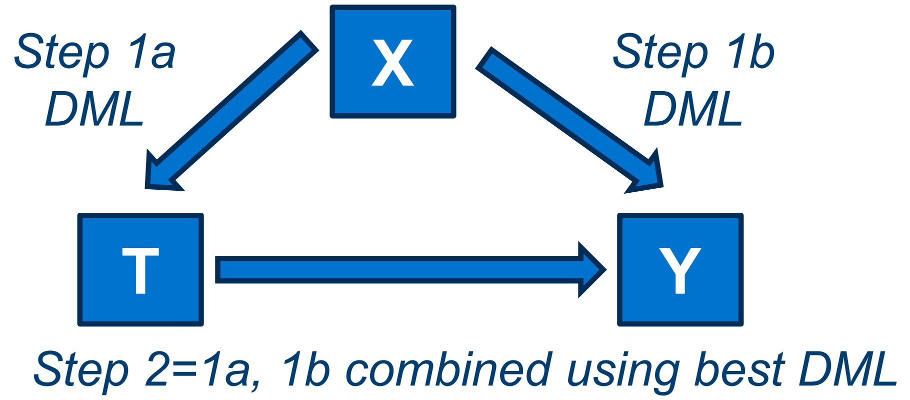
Machine Learning

- Algorithms handle high-dimensional variables
- Allow for interactions without pre-defined functional forms
- Capture linear and non-linear relationships
- **Accuracy of models in predicting suicide risk** based on high-dimensional data (Liu et al, 2025 systematic meta-analyses in adolescents)

- ML & other suicide risk assessment tools: lack of quality evidence
  - wide CIs, risk of bias, inadequate comparison groups, few meaningful outcomes, lack of effectiveness studies, risk of withholding care (NG225: NICE 2022)

Double Machine Learning: Introduction

- a double de-biasing **causal inference** method (Jacob, 2021)
- estimates **Average Treatment Effect** (ATE) between a treatment/exposure (T) and an outcome (Y)
- allows estimation of **Conditional Average Treatment Effect** (CATE) based on high-dimensional observed characteristics (X) (Jacob, 2021)



- Used to estimate **absolute risk** in a population based on treatment or exposure

Aim and Research Questions

Aim: to elucidate how multiple risk and protective factors may contribute to suicide attempts in adolescents with depressive symptoms, key for early identification & effective intervention

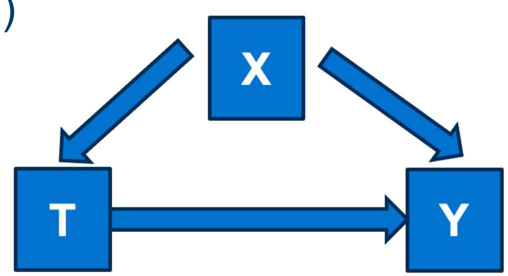
Research questions:

- How do depressive symptoms contribute to the emergence of suicide attempts?
  - **What are the primary factors** linking depressive symptoms to suicide attempts?
  - **How do the interactions** among different factors manifest in this relationship, **shaping high & low risk** of suicide attempts?

Li, Yip, Neufeld in prep

Method

- Data
  - UK Millennium Cohort Study → UK nationally representative birth cohort study (Connelly & Platt, 2014)
  - Sweep 6 (aged 14 in 2015) and 7 (aged 17 in 2018)
- Measurement
  - T: Depressive symptoms at age 17: past 30 days, Kessler Psychological Distress Scale, K6 (Kessler et al, 2002)
  - Y: Suicide attempts by age 17 (lifetime)
  - X: 63 risk and protective factors (age 14 & 17)



- Model
  - Contemporaneous model → DML: limit unmeasured confounding over a long interval (Lerner et al, 2009)

Key Risk & Protective Factors

63 theoretically supported variables, ages 14 & 17

Demographic (5)	*Mental & Physical health (12)*	*Relationships & social support (8)*	*Addictive behaviors (9)*
Sex at 14	Emotional symptoms at 17	Social support at 14	Smoking at 14
Sex orientation at 17	Conduct problems at 17	Relationship mother at 14	E-cigarette at 14
Religion at 14	Hyperactivity at 17	Relationship father at 14	Drinking at 14
Ethnicity at 14	Longstanding physical or mental illness at 17	Wellbeing family at 14	Illegal drug use at 14
Poverty at 14	Mental wellbeing at 17	Wellbeing friends at 14	Gambling at 14
	Self-esteem at 17	Close friends area at 14	Smoking at 17
Leisure activities & screen time (11)	Depression at 14	Close friends school at 14	E-cigarette at 17
Activity: cinema at 14	Self-esteem at 14	Peer problems at 17	Drinking at 17
Activity: live sport at 14	Wellbeing: schoolwork at 14		Illegal drug use at 17
Activity: music group at 14	Wellbeing: appearance at 14	***Psychological/behavioral traits (9)***	***Victimization (9)***
Activity: reading at 14	Wellbeing: school at 14	Prosocial behavior at 17	Victimization emotional at 14
Activity: youth clubs at 14	Wellbeing: life at 14	Openness at 17	Victimization_physical at 14
Activity: museums at 14		Conscientiousness at 17	Victimization_property at 14
Activity: religious service at 14		Extraversion at 17	Victimization sexual at 14
Activity: stay with friends at 14		Agreeableness at 17	Victimization emotional at 17
Screentime: watching films at 14		Neuroticism at 17	Victimization_physical at 17
Screentime: playing games at 14		Importance be well liked at 14	Victimization property at 17
Screentime: social networking at 14		Importance work hard at 14	Victimization_sexual at 17
		School motivation at 14	Victimization_cyber at 17

Double Machine Learning Analyses

- Model selection:
  - linear DML, sparse linear DML, DML, causal forest DML
    - Training set (60%) & validation set (40%)
    - Evaluate models using Rscorer: Goodness-of-fit statistic like R^2
    - five-fold cross-validation to mitigate overfitting
- Estimation of ATE and CATE
- Interpretation of CATE:
  - SHAP values (SHapley Additive exPlanations) & tree interpreters
- Analysed in Python
  - EconML and DoWhy modules

Li, Yip, Neufeld in prep

Sensitivity Tests

Sensitivity tests of ATE

1) Random common cause:
   - introduce a randomly generated confounder.
2) Unobserved common causes: add an unobserved confounder
3) Data subset validation: remove a random subset of the data
4) Placebo treatment:
   - replace treatment with a randomly generated placebo variable

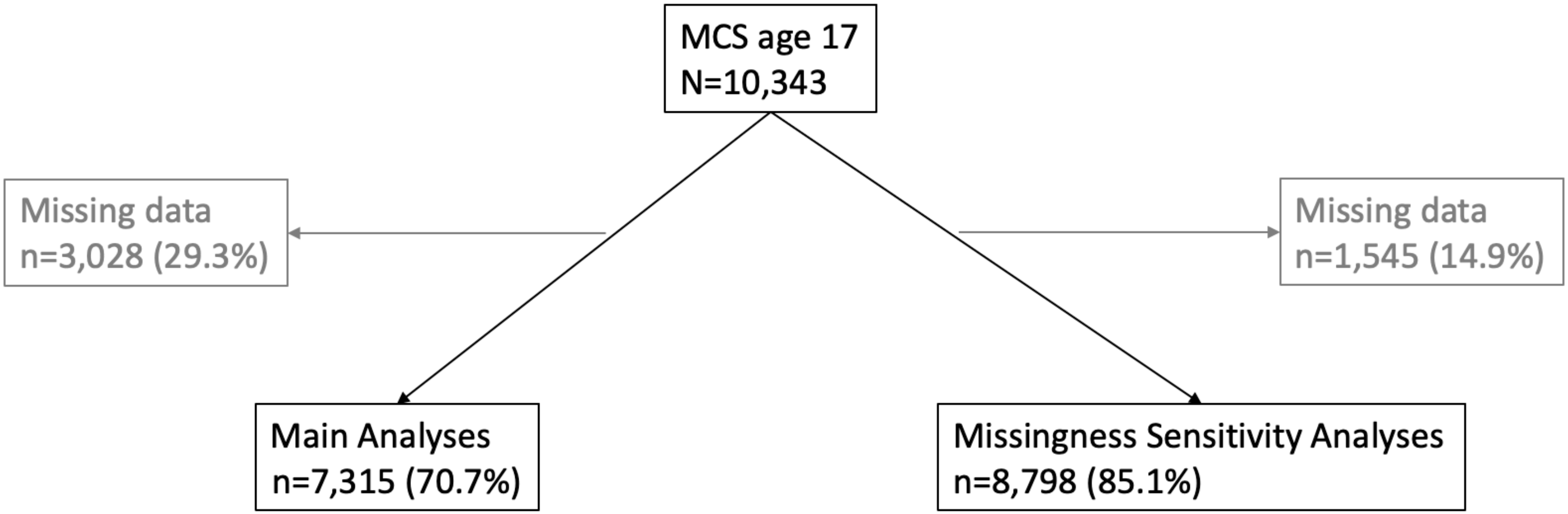
Additional sensitivity tests

1) Reverse Model and 2) Prospective Model (43 covariates)

Missingness: Complete cases

- Imputing missing values in T or Y could violate identification assumptions and introduce estimation bias (Chernozhukov et al, 2018)
- Imputing X in high-dimensional settings:
    - introduce additional data distortions, imputation models depend on unverifiable assumptions (Varol et al, 2025)
- Limiting analysis to complete cases:
    - prevents underestimation of standard errors
    - preserves internal consistency of input data
        - essential DML's reliance on sample splitting and cross-fitting procedures (Ross et al, 2020)

Addressing Missingness



Sensitivity Analyses: most covariates as auxiliary variables (W)

- X=five demographic variables without missing values
- W=remaining 58 risk & protective factors (ages 14 & 17) with missing values
- W is solely for debiasing in the first stage
- W does not contribute to the interpretation of treatment effect heterogeneity.

Representative of Full Dataset

- Negligible differences in analysed vs. excluded sample (all model variables)

Results: Model Comparison

Best model captures complex nonlinear relationships

- RScorer highest for causal forest DML
- Negative RScorer suggests potential overfitting during model training

Table 1. RScorer test of four DML algorithms

Algorithm	RScorer (10^{-2})
Linear double machine learning	-0.65
Sparse linear double machine learning	-0.96
Double machine learning	-0.99
Causal forest double machine learning	**0.86**

Li, Yip, Neufeld (in prep). Table created by Sijia Li using Python (3.9.18). Data source: Millennium Cohort Study, Sweeps 6 & 7, 2015 and 2018.

Table 2. Sensitivity tests of the ATE

Method	Value
Estimated ATE	0.040
Random common cause	0.040
Unobserved common causes	0.040
Data subsets validation	0.042
Placebo treatment	0.001

95% CI = [0.011, 0.068]

Reduced Missingness Model
ATE=0.039

Table 3. Sensitivity tests of two alternative models

	Reverse Model	Prospective Model
Algorithm	RScorer (10^{-2})	RScorer (10^{-2})
Linear double machine learning	-2·60	-4·30
Sparse linear double machine learning	-2·30	-3·67
Double machine learning	-2·60	-4·33
Causal forest double machine learning	-0·21	-0·42

Li, Yip, Neufeld (in prep). Tables created by Sijia Li using Python (3.9.18). Data source: Millennium Cohort Study, Sweeps 6 & 7, 2015 and 2018.

Interpreting ATE of 0.040

One standardized unit increase in depression score
→ 4% increased likelihood of a suicide attempt

- One standardized unit = 12 points on K6; depression cut-off: 13+ (Tomitaka, 2020)
- transitioning from **non-depressed to clinically depressed** state for all but the lowest-scoring participants

ATE reflects increase in **absolute** risk

- 7% prevalence in suicide attempts in 17-year-olds in UK (Patalay & Fitzsimmons, 2021)

Interpretation: effectively intervening on depression could **more than half** prevalence of suicide attempts in adolescence

Depression to Suicide Attempts: Key Risk and Protective Factors among 63

Interpret Conditional Effects with SHapley Additive exPlanations (SHAP) values

- Leading factors of effect heterogeneity

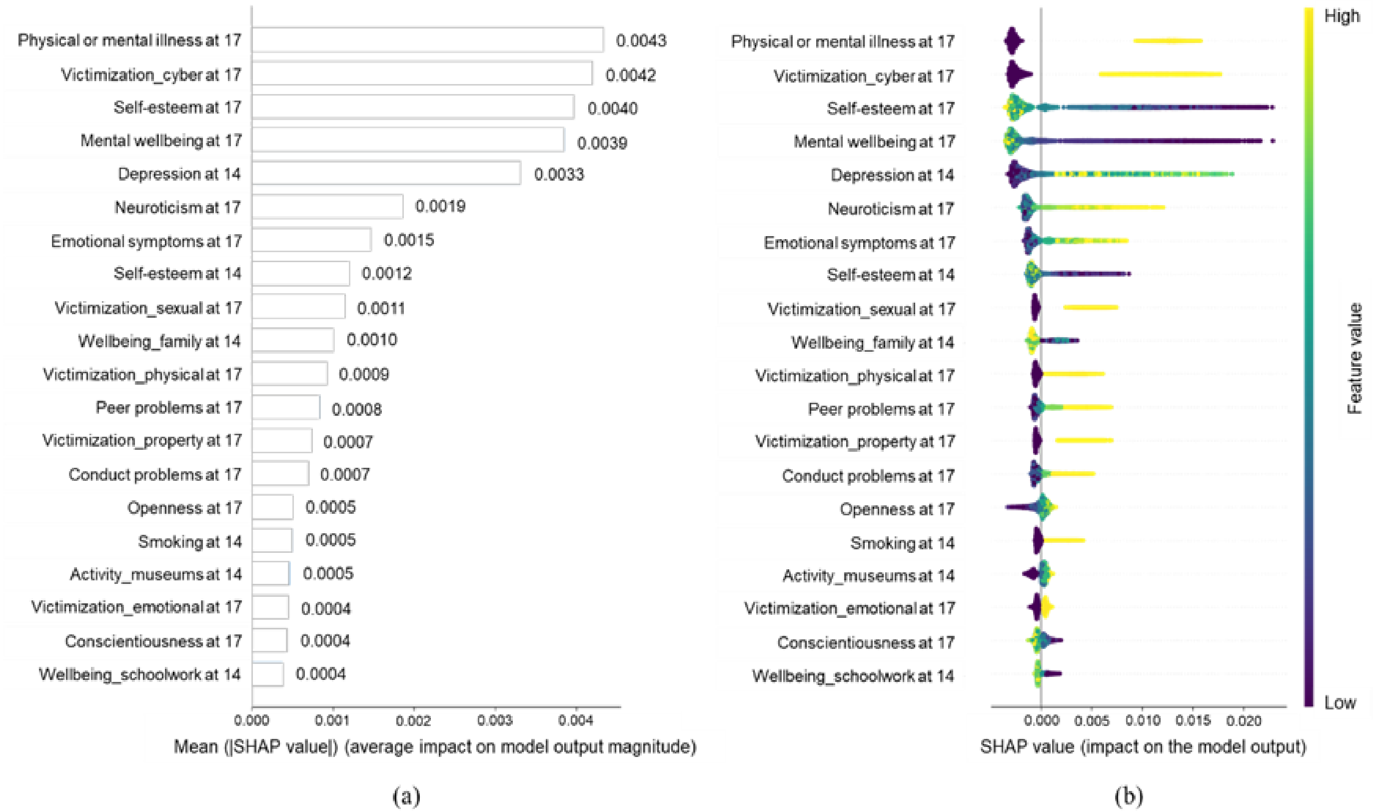


Fig. 1. SHAP values of CATE model (a) Bar chart of SHAP values; (b) Beeswarm chart of SHAP values.

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Interpret CATE with a three-depth tree interpreter

- 100+ individuals per leaf (over 1% of total)
    - capture key covariates but prevent overfitting
- All but 3 subgroup comparisons yielded significantly different CATEs

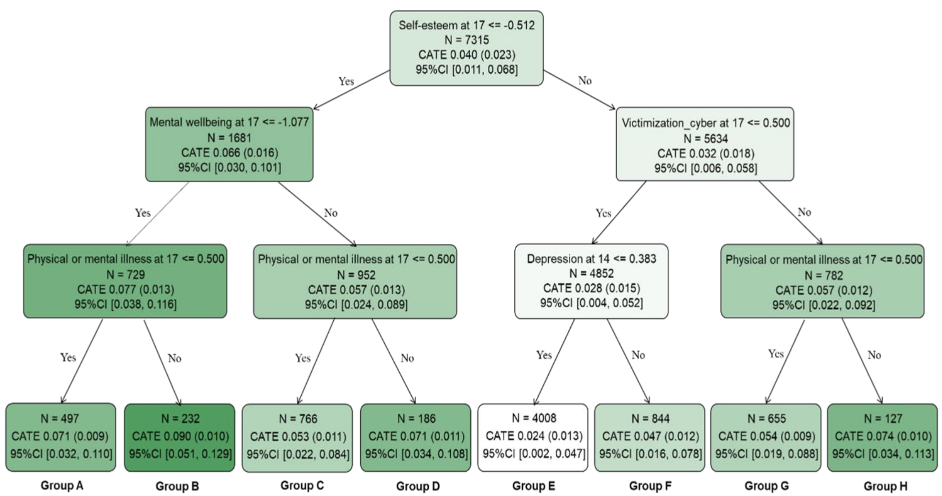


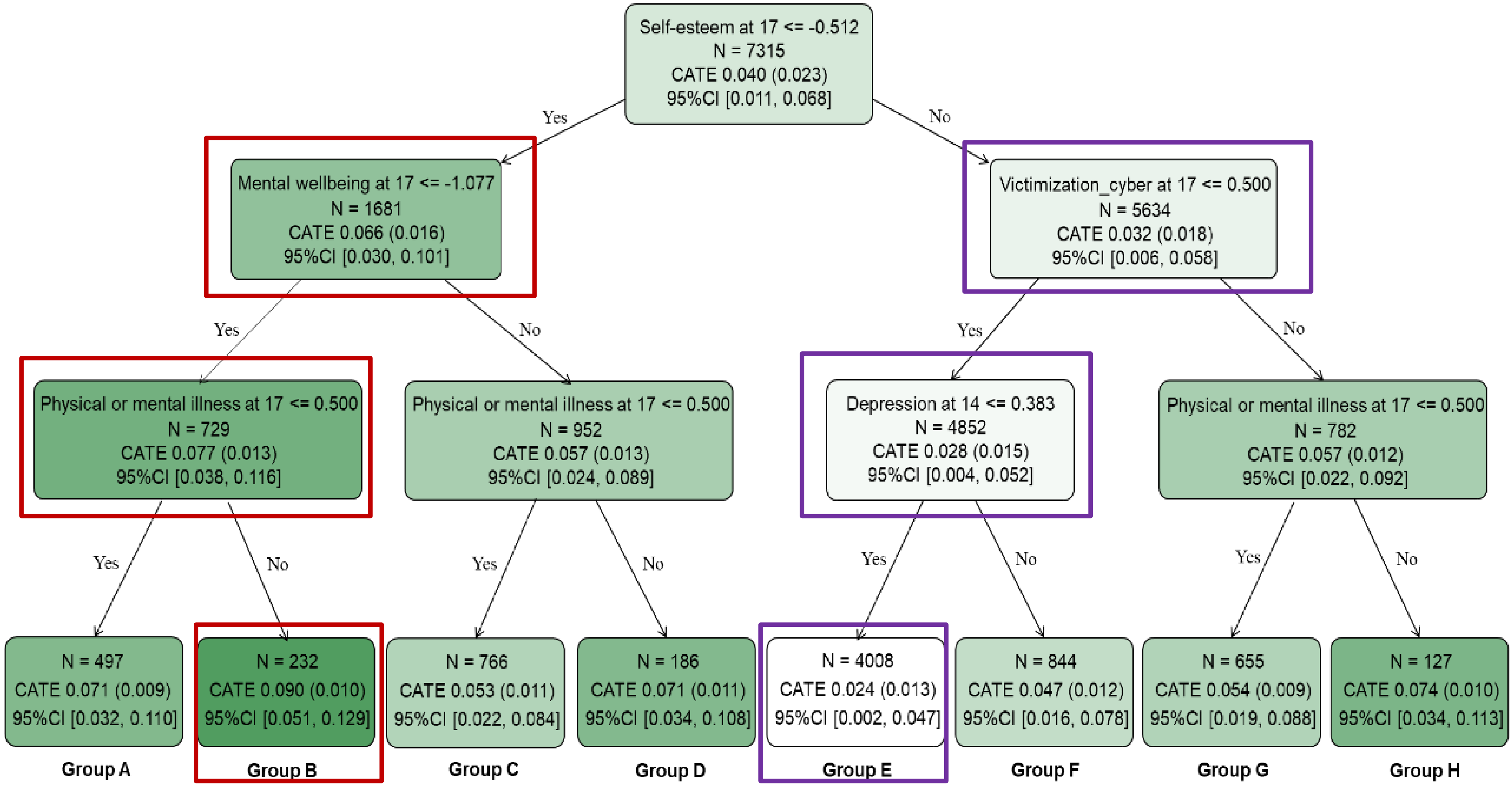
Fig. 2. Three-depth tree interpreter of the CATE model

	Group A CATE=0·071 N=497	Group B CATE=0·090 N=232	Group C CATE=0·053 N=766	Group D CATE=0·071 N=186	Group E CATE=0·024 N=4008	Group F CATE=0·047 N=844	Group G CATE=0·054 N=655	Group H CATE=0·074 N=127
Group A CATE=0·071 N=497	-							
Group B CATE=0·090 N=232	**0·019***** [0·018, 0·020] d=2·00	-						
Group C CATE=0·053 N=766	**0·018***** [0·017, 0·019] d=1·72	**0·037***** [0·035, 0·039] d=3·46	-					
Group D CATE=0·071 N=186	0·000 [-0·002, 0·002] d=0·00	**0·019***** [0·017, 0·021] d=1·76	**0·018***** [0·016, 0·020] d=1·65	-				
Group E CATE=0·024 N=4008	**0·047***** [0·046, 0·048] d=4·15	**0·066***** [0·065, 0·067] d=5·61	**0·029***** [0·028, 0·030] d=2·43	**0·047***** [0·045, 0·049] d=3·97	-			
Group F CATE=0·047 N=844	**0·024***** [0·022, 0·026] d=2·14	**0·043***** [0·041, 0·045] d=3·61	**0·006***** [0·005, 0·008] d=0·52	**0·024***** [0·022, 0·026] d=2·08	**0·023***** [0·022, 0·024] d=1·87	-		
Group G CATE=0·054 N=655	**0·017***** [0·016, 0·018] d=1·89	**0·036***** [0·034, 0·038] d=3·86	0·001 [-0·000, 0·002] d=0·10	**0·017***** [0·015, 0·019] d=1·78	**0·030***** [0·029, 0·031] d=2·79	**0·007***** [0·006, 0·008] d=0·63	-	
Group H CATE=0·074 N=127	**0·003**** [0·001, 0·005] d=0·30	**0·016***** [0·013, 0·019] d=1·13	**0·021***** [0·019, 0·023] d=2·01	**0·003*** [0·000, 0·006] d=0·28	**0·050***** [0·047, 0·053] d=4·25	**0·027***** [0·025, 0·029] d=-2·36	**0·020***** [0·018, 0·022] d=2·27	-

Fig. 3. Differences (t-tests) among groups at 3rd level of tree interpreter

Li, Yip, Neufeld (in prep). Figures created by Sijia Li using Python (3.9.18). Data source: Millennium Cohort Study, Sweeps 6 & 7, 2015 and 2018.

Depression to Suicide Attempts: combined factors help predict high and low risk profiles



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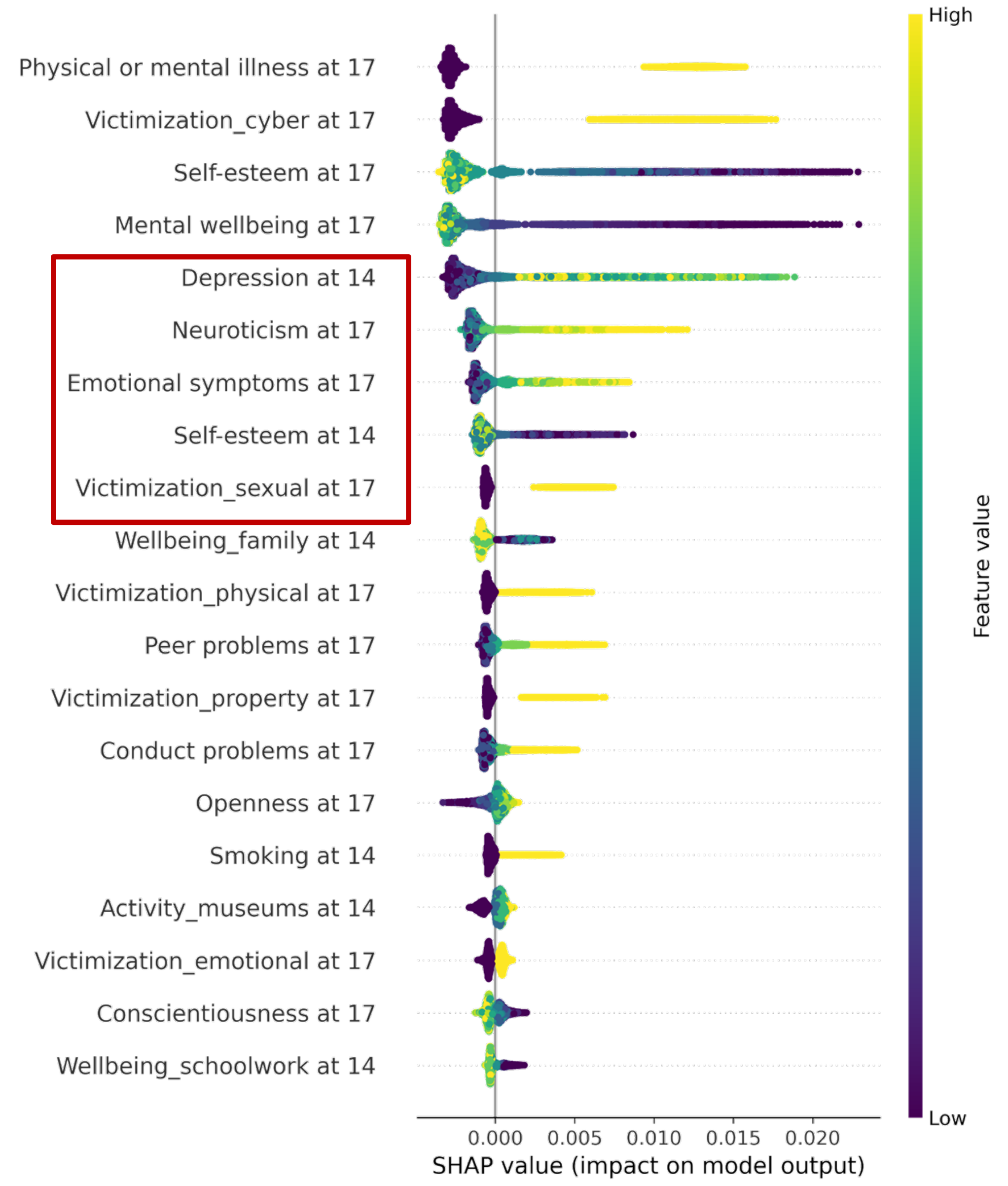
Other factors that need more attention

Risk factors:

- Neuroticism at 17
- Emotional symptoms at 17
- Sexual victimization at 17

Protective factors:

- Self-esteem at 14
- Family wellbeing at 14



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Implications for Prevention

- Early screening and intervening on depressive symptoms is crucial
- Public programmes nurturing **positive family environments** may confer long-term resilience against suicide risk (Liu & Wang, 2024)
- Establishing a secure and resilient **digital mental health ecosystem** is paramount for mitigating evolving digital-era risks (Perret et al, 2020)
- **Educational programmes** which age-appropriately equip students with an understanding of **respectful relationships, online risks**, and criminal behaviour in these domains, as well as **how to get help and stay safe** (Department for Education, 2019)
  - all domains of victimisation were in the top 20 most influential of 63 covariates contributing to the link from depression to suicide attempts

Implications for Depression Treatment

1. **Self-esteem** included in psychosocial assessments & inform treatment plans, e.g. CBT targeting self-esteem (Berg et al, 2022)
2. Depression treatment in early adolescence is crucial (Neufeld et al, 2017)
3. Make treatment more effective by prioritising alleviating **emotional symptoms** & nurturing **positive family environments** (Neufeld, 2020)
4. **Trauma informed care** & processing traumatic experiences (Brown & Hoffman, 2018)
5. Importance of **integrated physical & mental health care** in young people (Bennett et al, 2024)

Thank you!

- People with lived experience & participants
- Sijia Li, MSc and Prof Paul Yip

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