

PDF hosted at the Radboud Repository of the Radboud University Nijmegen

The following full text is a publisher's version.

For additional information about this publication click this link.

<https://hdl.handle.net/2066/222145>

Please be advised that this information was generated on 2021-06-13 and may be subject to change.



Identification and validation of risk factors for antisocial behaviour involving police



Gido H. Schoenmacker^{b,e,*}, Katre Sakala^{g,h,i}, Barbara Franke^{a,b}, Jan K. Buitelaar^{b,c,d},
Toomas Veidebaum^g, Jaanus Harro^f, Tom Heskes^e, Tom Claassen^e, Arias Vásquez Alejandro^{a,b}

^a Department of Human Genetics, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, the Netherlands

^b Department of Psychiatry, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Geert Grooteplein Zuid 10, Route 836, room 4.84, Nijmegen 6525, GA, the Netherlands

^c Department of Cognitive Neuroscience, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, the Netherlands

^d Karakter Child and Adolescent Psychiatry University Centre, Radboud University Medical Centre, Nijmegen, the Netherlands

^e Faculty of Science, Radboud University, Nijmegen, the Netherlands

^f Division of Neuropsychopharmacology, Department of Psychology, University of Tartu, Tartu, Estonia

^g Department of Chronic Diseases, National Institute for Health Development, Tallinn, Estonia

^h Department Family Medicine and Public Health, University of Tartu, Tartu, Estonia

ⁱ School of Natural Sciences and Health, Tallinn University, Tallinn, Estonia

ARTICLE INFO

Keywords:

Antisocial behaviour
Prediction
Risk factors
Mediation
Aggression
Substance use

ABSTRACT

Adult antisocial behaviour has precursors in childhood and adolescence and is most successfully treated using childhood interventions. The aim of this study was to identify and validate robust risk factors for antisocial behaviour involving police contact in a data-driven, hypothesis-free framework. Antisocial behavior involving police contact (20/25% incidence) as well as 554 other behavioural and environmental measures were assessed in the longitudinal general population Estonian Children Personality Behaviour and Health Study sample (n = 872). The strongest risk factors for antisocial behaviour included past substance use disorder, gender, aggressive mode of action upon provocation, and concentration difficulties and physical fighting in school at age 15 years. Prediction using the selected variables for both methods in the other, unseen cohort resulted in an area under the receiver operating characteristics curve of 0.78-0.84. Our work confirms known risk factors for antisocial behaviour as well as identifies novel specific risk factors. Together, these provide good predictive power in an unseen cohort. Our identification and validation of risk factors for antisocial behaviour can aid early intervention for at-risk individuals.

1. Introduction

Antisocial behaviour can be defined as actions that disregard the well-being of others (Fairchild et al., 2013). It includes a wide range of disruptive behaviours ranging in severity from nuisances such as loud or unruly behaviour to criminal behaviour including (but not limited to) vandalism or physical violence. Individuals with antisocial behaviour incur a high cost for society, with some estimates ranging between \$9000-\$15,000¹ USD increased annual public costs per child diagnosed with antisocial behaviour (Foster et al., 2005; Scott et al., 2001). In addition to the substantial costs to society, antisocial behaviour also has high economic as well as quality-of-life costs at an individual level for victims as well as perpetrators (Black et al., 2010;

Romeo et al., 2006; Ttofi et al., 2011).

While the full developmental path remains unclear, a common precursor to adult antisocial behaviour is aggressive and disruptive behaviour in childhood (Calkins and Keane, 2009; Fairchild et al., 2013). Moreover, antisocial behaviour benefits from early intervention: while treatment of adults remains difficult and often inconclusive or unsuccessful (Gibbon et al., 2010; Khalifa et al., 2010), intervention in childhood may be both cost-effective and more successful (Foster et al., 2006; Scott et al., 2010).

Because of the benefits of early intervention and treatment, the idea of predicting the occurrence of antisocial behaviour later in life is not new. A longitudinal study assigning preschool children into three risk groups showed predictive power for police contact at age 15 years, with

* Corresponding author.

E-mail address: Gido.Schoenmacker@radboudumc.nl (G.H. Schoenmacker).

¹ Adjusted for an average inflation of 2.12% per year to 2019 costs.

the best predictors including externalising behaviour and motor coordination. However, the false positive rate was too high to support an early intervention policy (White, Jennifer L. Moffitt, Terrie E. Earls, Felton Robins, Lee Silva, 1990). In another longitudinal study, White and coworkers found that the best childhood precursors of antisocial behaviour included economic deprivation, poor parenting, an antisocial family, and ADHD-like symptoms (Farrington, 1993). A longitudinal twin study performed by Farrington and colleagues found that lower IQ, reading problems, conduct problem symptoms, and ADHD symptoms in childhood predicted adult antisocial personality disorder (Simonoff et al., 2004). In a cross-sectional study, Bender and Lösel identified bullying behaviour as a strong risk factor for later antisocial behaviour (Tofi et al., 2012).

While the previous studies have identified risk factors that predicted antisocial behaviour later in life, none of the studies to date (to our knowledge) included a validation in a second, independent sample. Building predictive models without an independent testing sample is sensitive to overfitting (e.g. (Reunanen, 2003)), which means that the best predictors from one study may not predict antisocial behaviour in a new sample. Identifying a robust set of predictors and demonstrating that these have discriminative power in an unseen sample will be essential to work towards inclusion of such prediction into early intervention policy and fills a hole in existing literature. It is important to note that identifying robust predictors does not necessarily contribute to the understanding of the causal relationship(s) between predictors and outcome. One approach to untangle direct and indirect effects of the predictors is with a mediation model.

Based on the above, the aim of the current study was two-fold: *first*, to identify and validate the best predictors for antisocial behaviour involving police contact (ABPC) using a hypothesis-free approach in two longitudinal cohorts of ages 9-33 years. This means that all individual items as well as subscales from available questionnaires were treated as potential predictors without making a prior selection. The chosen approach permitted the use of all available data (in our case 555 variables) without prior selection. *Second*, we used a causal discovery approach to test whether our validated predictors had a mediated or unique effect on ABPC.

2. Methods and materials

2.1. Study population

The study was performed using the longitudinal Estonian Children Personality Behaviour and Health Study (ECPBHS) sample consisting of two independent cohorts. The younger cohort ($n=583$) was born between 1988-1989. The elder cohort ($n=655$) was born in between 1982-1983. More detailed information about the design and collection methods of the ECPBHS can be found in (Harro et al., 2001; Tomson et al., 2011). Briefly, ECPBHS is a general population longitudinal multidisciplinary study of (at the time) school-aged children from Tartu County in Estonia. Data was collected in four waves at ages 9, 15, 18, and 25 years for the younger, and ages 15, 18, 25, and 33 years for the elder cohort. Written informed consent was obtained from participants and parents and the study was approved by the Ethics Review Committee on Human Research of the University of Tartu, Estonia.

2.2. Measurements

The data available for this study included multiple types of descriptive and questionnaire data. Some of these were completed by parents and teachers, others by participants about themselves and about other participants. A complete overview can be found in Table 1.

2.2.1. Outcome measure for antisocial behaviour involving police contact

ABPC was measured using the Life History of Aggression (LHA;

(Coccaro et al., 1997)) interview by clinical psychologist. The LHA measures the timing and frequency of aggressive behaviour over the lifetime. One LHA item measured frequency of ABPC. For this study, this was converted to a binary variable. Other LHA items (such as physical assault on people) were excluded from the analyses, because these items partially target the same ABPC.

With regards to police contact, Estonia is a member of the European Union (EU), Europol, and Interpol and its justice system follows generally recognised principles of international law. Crime rate has declined over the last couple of decades (Criminal Policy Department of the Estonian Ministry of Justice, 2019) and trust in police is high at 87% in 2018 (Kivirähk, 2018; Sööt et al., 2014; Tabur and Sepp, 2020) with trust ratings similar to other European countries like Norway, Spain, the UK, Switzerland, and the Netherlands (Jackson et al., 2011). With a prison population rate of 184 per 100,000 inhabitants in 2020, Estonia is on the higher end of EU prison population rates yet comparable to other Eastern European countries such as Czechia (197), Poland (195), Slovakia (195), and Latvia (179) (Institute for Crime and Justice Policy Research, 2020).

2.2.2. Aggression measures

Multiple aggression measures were available for analysis. First, the Buss-Perry rating scale measures aggression and consists of four aggression components (Buss and Perry, 1992). Second, the driver anger scale (DAS; (Lajunen et al., 1998)) measures driver anger. Third, the University of Illinois bully scale (UIBS; (Espelage and Holt, 2001)) measures bullying behaviour and consists of three subscales. For the UIBS, participants were asked to retrospectively rate themselves and selected classmates, so that each participant was rated by at least two raters. Fourth, the aggressive provocation questionnaire (APQ; (O'Connor et al., 2001)) measures aggressive behaviour and consists of 12 scenarios where participants indicate levels of anger, frustration, irritation, and select a response behaviour. Lastly, the aggressiveness subscale of the Hyperactivity Scale of af Klinteberg (HSK; (af Klinteberg, 1988)) was rated by class teachers.

2.2.3. ADHD and impulsivity measures

The adult ADHD self-report scale (ASRS) measures adult ADHD (Kessler et al., 2005) and was completed by participants. The Swanson, Nolan and Pelham (SNAP) rating scale measures ADHD symptom severity (Swanson, 1981). The SNAP was completed by teachers and individually by both parents. The Adaptive and Maladaptive Impulsivity Scale (AMIS; (Laas et al., 2010)) measures impulsivity. Lastly, class teachers rated hyperactivity using the HSK.

2.2.4. Other measures

The ECPBHS includes information on other measures that we used in order to achieve our aim: First, lifetime substance use disorders were assessed by the MINI psychiatric interview (Sheehan et al., 1998). Second, stressful life events were assessed using the stressful life events inventory (Akkermann et al., 2012). Third, family relations were measured using the Tartu adult family relationships scale (TFRS; (Paaver et al., 2008)), consisting of 49 items. Fourth, general mental abilities were assessed using sets C and D of the Raven Standard Progressive Matrices Test (RSPM; (Raven et al., 1998)) and completed by participants. An assortment of general items, including environmental factors such as family income and education was gathered and included in our analysis.

2.3. Variable selection and prediction

As the main goal of this study was to identify informative variables for ABPC, we followed a two-stage approach in order to select the most informative predictors with 7 steps in total. The full process is illustrated in Fig. 1. We did this because standard approaches might identify risk factors within a group, but generally do not exclude the

Table 1
Overview of all questionnaires and the ages at which they were measured in the two Estonian children personality behaviour and health study cohorts.

	Questionnaire	Age at assessment, younger cohort (years)	Age at assessment, elder cohort (years)
Aggression	Life History of Aggression	25	33
	Driver Anger Scale	25	25,33
	University of Illinois Bully Scale	25	33
	Aggressive Provocation Questionnaire	25	33
	Buss-Perry rating Scale	25	33
ADHD	Adult ADHD self-report	25	25,33
	Swanson, Nolan, and Pelham Rating Scale	15,18	18
	Adaptive and Maladaptive Impulsivity Scale	15,18,25	18,25,33
	Hyperactivity Scale of af Klinteberg	9,15,18	15,18
Other	Mini International Neuropsychiatric Interview	25	25
	Tartu adult family relationship scale	18,25	18,25,33
	Raven Standard Progressive Matrices Test	18,25	25
	Stress & Stressful life events*	15,18,25	15,18,25,33
	General, socioeconomic, and substance use*	9,15,18,25	15,18,25,33

* Unnamed rating scales, see Section 2.2.4.

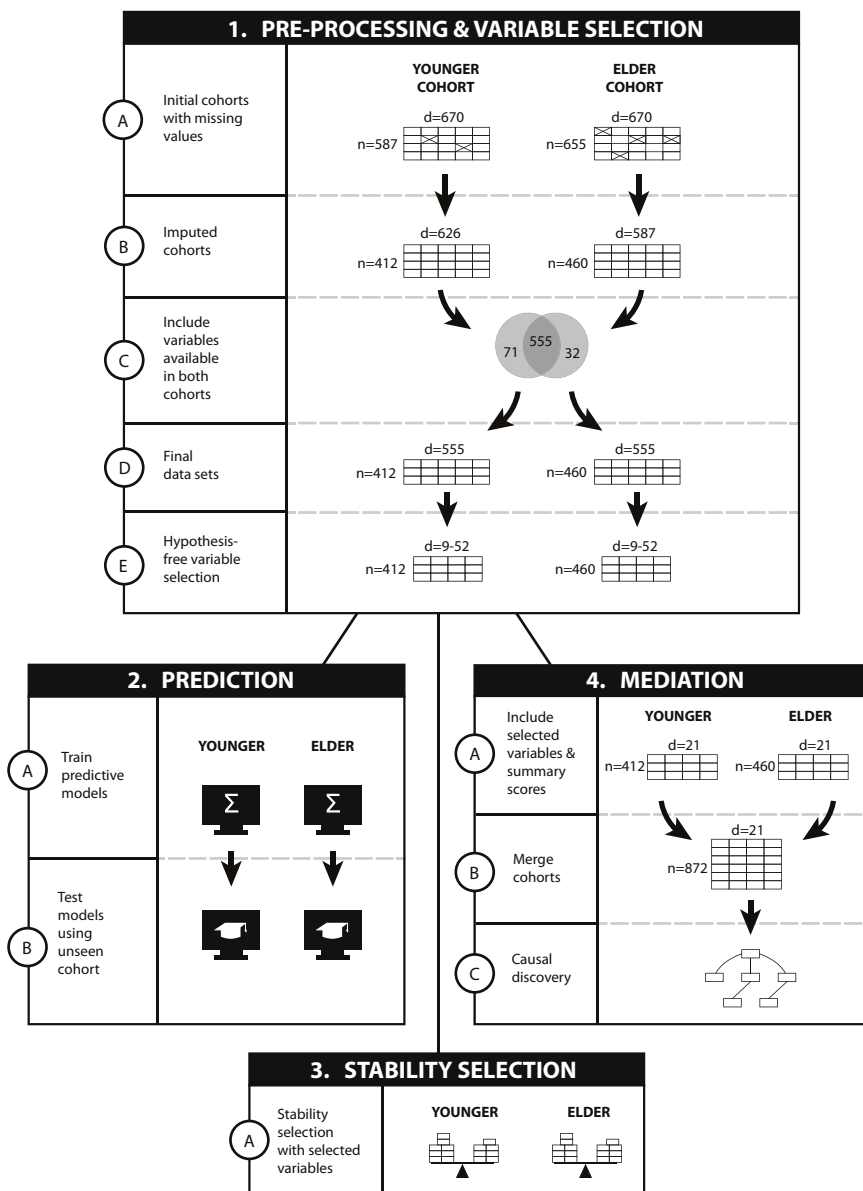


Fig. 1. Schematic overview of imputation, quality control, and variable selection steps. Panel 1 show the imputation and quality control steps for both cohorts, as well as the variable selection step. Next, we continue with three parallel processes to examine and validate the variable selection results. This is illustrated in panels 2, 3, and 4. Panel 1: Schematic overview of the pre-processing and variable selection. Initially in step 1A, the younger cohort consists of n = 587 individuals and d = 670 variables. The elder cohort consists of n = 655 individuals and 670 variables. Secondly in step 1B, imputation, quality control, and normalisation within cohort is performed. Thirdly in step 1C, the available variables from the two cohorts are compared and only the overlapping variables are kept. Fourthly, in step 1D the end result for the younger cohort is n = 412 with 555 variables and n = 460 for the elder cohort with 555 (identical) variables. Lastly step 1E shows the variable selection.

Panel 2: Schematic overview of the model training and prediction. In step 2A the selected variables from step 1E are used to train predictive models using the discovery cohorts. Next, in step 2B, the models are tested in the other, unseen cohort. This is the first time in the process that we “cross over” from one cohort to the other.

Panel 3: Schematic overview of the stability selection process. After steps 1-5 shown in Fig. 1, in step 3A we further investigate the 9 variables that were selected by at least three out of four models. This involves testing the stability of the variable selected process (1E) with respect to changes in our particular sample.

Panel 4: Schematic overview of the mediation analysis. In step 4A we include 21 variables for mediation analysis (see 3.5). Next in step 4B we join the two age cohorts together to create one large sample of n = 872 individuals. Lastly in step 4C, a causal discovery algorithm is used to produce a full mediation model.

possibility of the findings being limited to their very specific sample. To address this, we tested the stability of risk factors, their predictive power in new individuals, and possible mediation effects.

2.3.1. Preprocessing and imputation

In the preprocessing stage, we started with two initial cohorts containing missing values (Fig. 1-1A). The missing data points were imputed using a non-parametric imputation random forest approach with the “MissForest” R package version 1.4 (Stekhoven and Bühlmann, 2012). Next (Fig. 1-1B), variables and individuals with >50% missing data (before imputation) were excluded, as well as individuals with missing ABPC outcome. Only variables available in both cohorts were included (Fig. 1-1C). If the variables were measures at different ages, the closest age match was selected. This resulted in the final data sets of $n=412$ individuals for the younger and $n=460$ individuals for the elder cohort, with 555 variables overlapping between the cohorts (Fig. 1-1D). Importantly, during this process, the two cohorts were treated separately as to avoid introducing bias.

2.3.2. Variable selection

A hypothesis-free variable selection process was performed in each cohort (Fig. 1-1E). Two methods were used for variable selection and prediction. The first method was elastic net regularised logistic regression, which is a standard method for variable selection and prediction that creates a linear model (Zou and Hastie, 2005). The second method was random forest classification, which performs variable selection and prediction in high-dimensional data (see e.g. Boulesteix et al., 2012) and builds a non-linear model (Breiman, 2001).

For elastic net logistic regression, optimal variable selection was achieved using cross-validation in the training cohort. This optimal selection was defined as the most regularised model within 1 standard error of the minimum mean cross-validated error. The elastic net parameter α , which defines the balance between ridge and LASSO regression, was tested for eleven values.

Variable selection for random forest was done using the permuted out-of-bag prediction error for a forest of 15,000 trees. The optimal model was defined as all variables above 1 standard deviation of the mean out-of-bag prediction error. The random forest parameter *minimal number of observations in a leaf node*, which defines the number of observations that one leaf node should at least contain, was tested for seven values.

Analyses were run using the Mathworks MATLAB® software package version R2018a.

2.3.2. Prediction

Using only the per-method selected variables, two predictive models (one with logistic regression, one with random forest) were trained in each cohort separately (Fig. 1-2A), resulting in 4 final models using only the selected variables. After that, the predictive models were tested on the other, unseen cohort (Fig. 1-2B). The performance of the predictive models was evaluated using receiver operating characteristic (ROC) curves and their area under the curves (AUC) for the binary outcome of ABPC. The AUC is a number between 0-100 and can be roughly interpreted as 50-60: fail; 60-70: poor; 70-80 fair; 80-90: good; and 90-100: excellent (Safari et al., 2016).

2.3.3. Stability selection

The variable selection results may not be uniquely informative if they are sensitive to small changes in the sample. To avoid implicating one specific risk factor when any one in a correlated variable group would perform similarly, we verified the stability of results using the sample splitting procedure outlined in (Meinshausen and Bühlmann, 2010), which consists of splitting each cohort into half to test whether the variable selection is sensitive to changes in the sample size and characteristics (Fig. 1-3A). In both cohorts, the splitting

procedure was performed 100 times for both elastic net logistic regression and random forest.

2.3.4. Mediation analysis

Mediation analysis was performed using Bayesian Constraint-based Causal Discovery (BCCD; (Claassen and Heskes, 2012)). BCCD can help identify whether the effects of predictors on ABPC are direct or indirect (i.e. a shared effect) and was used to determine the relationship structure between the selected predictors and ABPC.

Causal discovery benefits from the inclusion of peripheral information. This means that mediation effects in the data can better be detected if information is included that does not directly relate to our outcome. Thus, to facilitate mediation analysis, all available sum scores from questionnaires were included in the mediation model (Fig. 1-4A). This approach maximises the included peripheral information, while still limiting the total number of variables in the model (reducing computational complexity).

For BCCD mediation analysis, the two separate cohorts were pooled (Fig. 1-4C) and a cohort indicator was included (Mooij et al., 2016). A correlation matrix of all 21 variables was also computed.

3. Results

3.1. Sample

After pre-processing and imputation (Fig. 1-1A-C), the final data sets consisted of $n=412$ individuals (younger cohort) and $n=460$ individuals (elder cohort), with $d=555$ remaining overlapping variables including the ABPC outcome (Fig. 1-1D). Table S1 shows the distribution of age, gender, and ABPC across the two cohorts. The outcome variable of ABPC was nominal significantly different in the cohorts ($p=0.045$), with the younger cohort having a higher incidence (25%) compared to the elder cohort (20%). Overall, 257 out of 555 variables had nominal significantly ($p<0.05$) different distributions. The distribution of p -values for the differences between variables in the two cohorts is shown in Fig. S1.

3.2. Prediction results

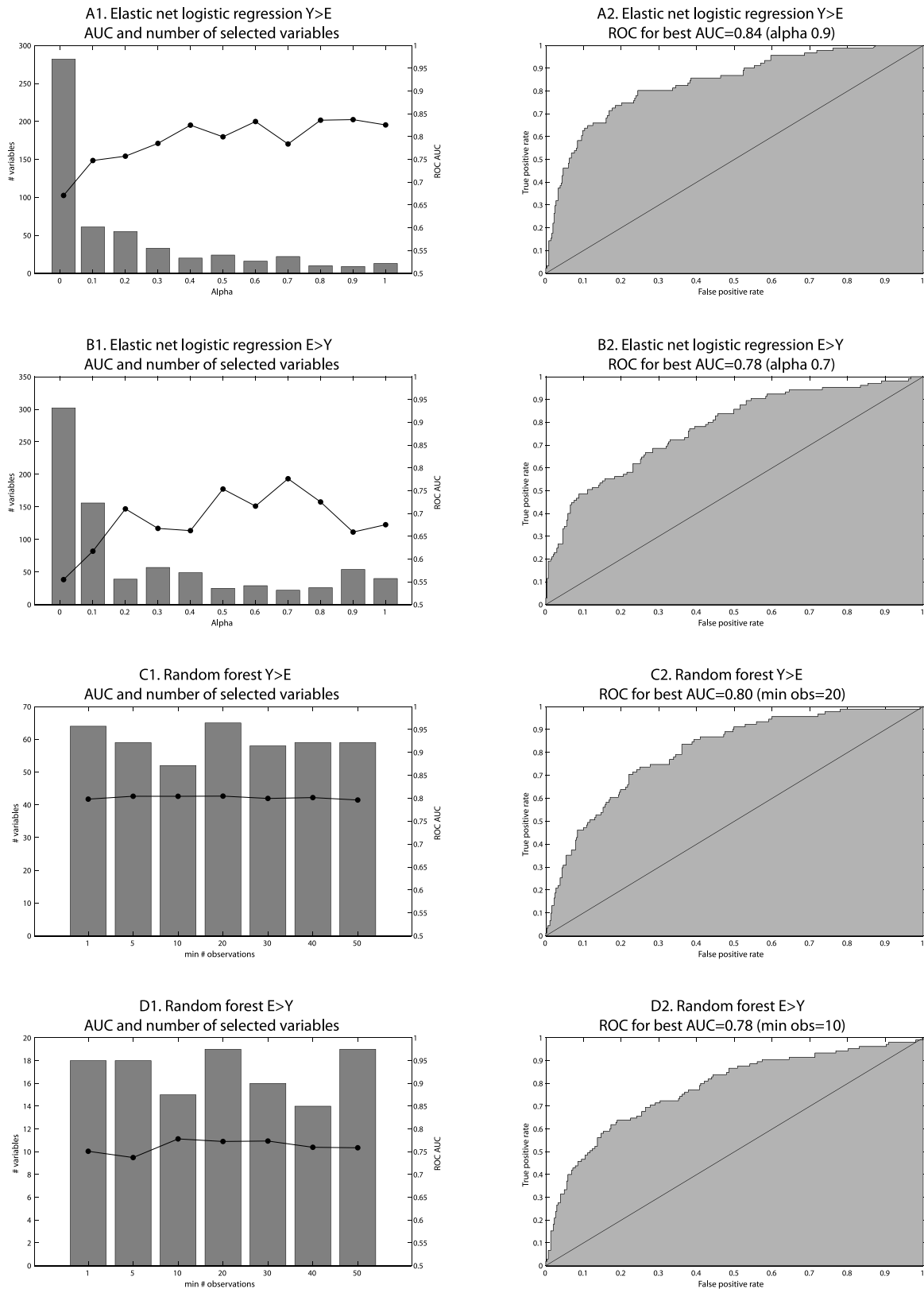
The main results are shown in Fig. 2. Information on the parameter-dependent performance of the models for the two variable selection methods is shown in panels A1, B1, C1, and D1. Information on the prediction accuracy ROC using the optimal parameter is shown in panels A2, B2, C2, and D2.

For elastic net logistic regression, the best prediction result of $AUC=0.84$ was obtained with a model consisting of 9 variables (see Section 3.3). Overall, models with fewer variables tend to perform better using logistic regression prediction in the unseen cohort.

For random forest, the best result of $AUC=0.80$ was obtained with a model consisting of 52 variables. The *minimum number of observations per leaf* parameter (see 2.3.2) shows little effect on the total number of variables selected, which is consistently higher in the younger-to-elder selection (52-75 selected variables) than in the elder-to-younger selection (14-19), or the prediction accuracy. Again, models with fewer variables tend to perform slightly better.

3.3. Selected variables

In total, 70 unique variables were selected by the four models. Of those, 53 variables were selected only by a single model, eight variables were selected by two models, four variables by three models, and five variables were selected by all models. The five variables selected by all models were: *gender*, *past substance use disorder*, *the APQ aggressive mode of action*, *teacher-rated concentration difficulties at age 15*, and *the UIBS item 9 as answered by peers: physical fighting*. The four variables selected by three models were *excessive drinking at age 25*, *education level at age*



(caption on next page)

25, maternal education at age 15, and teacher-rated motor restlessness at age 15.

Fig. 3 shows the 9 selected variables with their relative importance for the younger-to-elder logistic regression prediction in panel A1 from Fig. 2. In supplemental Figs. S2, S3, and S4, the selected variables for

the other three models are shown.

3.4. Stability selection results

We tested the stability (with the elastic net logistic regression and

Fig. 2. This figure shows in the left column the results for the number of variables selected and the resulting area under the curve (AUC) for the receiver operating characteristic (ROC) with varying hyperparameters. In the right column the ROC curve belonging to the best AUC from the left is shown.

The top two panels (A1 and A2) show results using the younger cohort to build the model, and the elder cohort to test the model. The topmost left panel A1 shows the AUC results for different values of elastic net parameter alpha (see 2.3.2), as well as the number of selected variables per AUC result. Panel A2 shows the ROC curve for the best AUC value from Fig. 2-A1, which is AUC=0.84 for alpha=0.9. This AUC of 0.84 suggests that the prediction for ABPC from the younger to the elder model was good. In total, 9 variables were selected for this model.

Similarly, the Fig. 2 panels B1 and B2 show the results for elastic net logistic regression using the elder cohort to build the model, and the younger cohort to test. The best prediction was made using alpha=0.7, with 22 variables selected and an AUC of 0.78.

The bottom four panels in Fig. 2 show the results for random forest. Panels C1 and D1 show the AUC and variable selection results for different values of the minimum number of observations per leaf parameter (see 2.3.2) for training in the younger and testing in the elder cohort, and vice versa respectively. The best results of AUC=0.80 with 52 variables and AUC=0.78 with 18 variables indicate fair to good predictions for ABPC.

random forest methods) of the 9 variables selected by at least three models by splitting each cohort into two halves. The results are shown in Fig. 4.

For elastic net logistic regression, the most stable predictors for ABPC (selected >60% in both splits) were *past substance use disorder*, *gender*, and *education level at age 25*. For random forest, the most stable predictors were *past substance use disorder* and *UIBS item 9: physical fighting*. Less stable variables (selected between 40%–60% in both splits) for elastic net logistic regression were *teacher-rated concentration difficulties at age 15*, *the APQ aggressive mode of action*, *UIBS item 9 physical fighting*, *maternal education*, and *excessive drinking at age 25*. For random forest, these were the *APQ aggressive mode of action*, *teacher-rated concentration difficulties*, *teacher-rated motor restlessness*, *education level*, and *gender*. These were selected in both splits around 50% of the time, suggesting that these effects were driven by a subset of our sample or that the information they provided could also be provided by other (correlated) variables. The least stable variables (selected <40% in both splits) were for elastic net logistic regression *teacher-rated motor restlessness at age 15*, and for random forest *excessive drinking* and *maternal education*. These variables likely did not provide unique information but rather correlated with other variables.

3.5. Mediation analysis

In total, 21 variables were included in the mediation analysis: (a) the nine variables that were selected by at least three out of four models, (b) ten sum total scores from available questionnaires to provide peripheral information, (c) a binary dummy variable to represent the age cohorts, and (d) the outcome variable ABPC. The full

correlation matrix and mediation model are included as Figs. S5 and S6 in the supplement.

Out of the included variables, four were found to have an unmediated (i.e. direct) effect on ABPC. These were *past substance use disorder*, *the APQ aggressive mode of action*, *education level at age 25*, and *the UIBS item 9 physical fighting*. The effects on ABPC of all other variables in the model were mediated through these four. Notably, *gender* did not have a direct effect on our outcome, but instead indirectly affected ABPC through the substance use and aggression/bullying measures (see Fig. S5). Highly correlated variables, such as *teacher-rated concentration difficulties* and *motor restlessness*, group together.

4. Discussion

We aimed to identify and validate robust predictors for ABPC by going beyond traditional correlation studies. Our approach was to apply two different selection methods and identify the best predictors in one cohort followed by their use for prediction of the same outcome in a second *independent* cohort. The best prediction (AUC=0.84) was obtained using 9 out of 554 possible predictors selected in the younger cohort and tested in the elder. Vice versa, the best prediction from the elder to the younger cohort (AUC=0.78) was obtained using 22 variables. Because the predictive power was tested in an unseen, independent cohort, the identified predictors are robust to overfitting and are likely to generalise well to the population level.

Five predictors were selected by all models. *Past substance use disorder* at age 25 was the most influential and stable predictor for ABPC in all models. The association between antisocial behaviour and substance use is well documented (Robins, 1998; Westermeyer and Thuras, 2005).

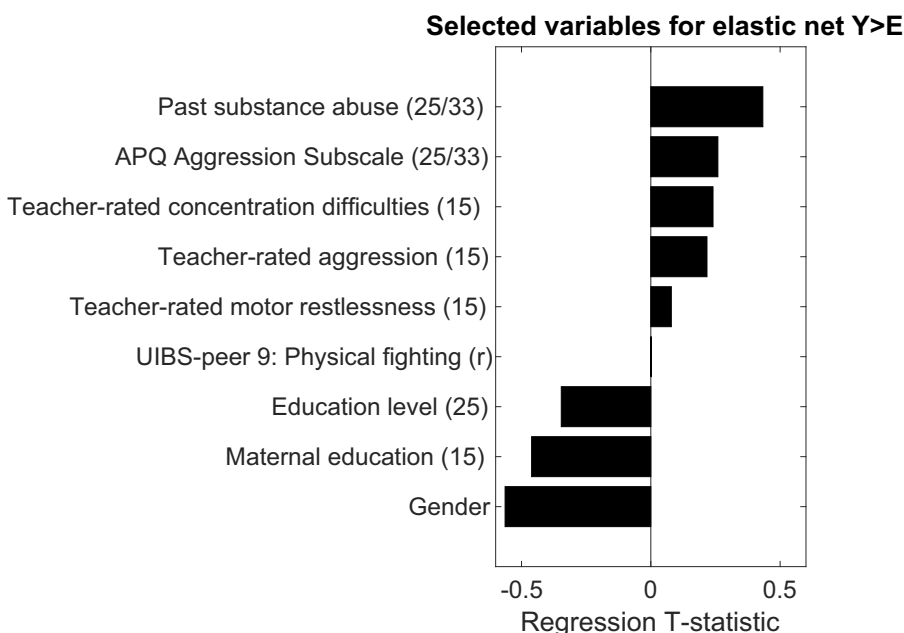


Fig. 3. The 9 selected variables from elastic net logistic regression in the younger cohort predicting the elder (“Y>E”), which corresponds to the first row from Fig. 2. The within-sample regression T-statistic is shown on the x-axis. A variable with a positive T-statistic indicates an increased risk for ABPC, corrected for the other variables in the model. Gender here represents female gender. The values in parentheses at the end of variable names (e.g. “25/33”) show the age at which the measurement was taken for the younger and elder cohort respectively, with “r” meaning retrospective. Similar figures for the other three predictive models are included in the supplemental material (Figs. S2-4).

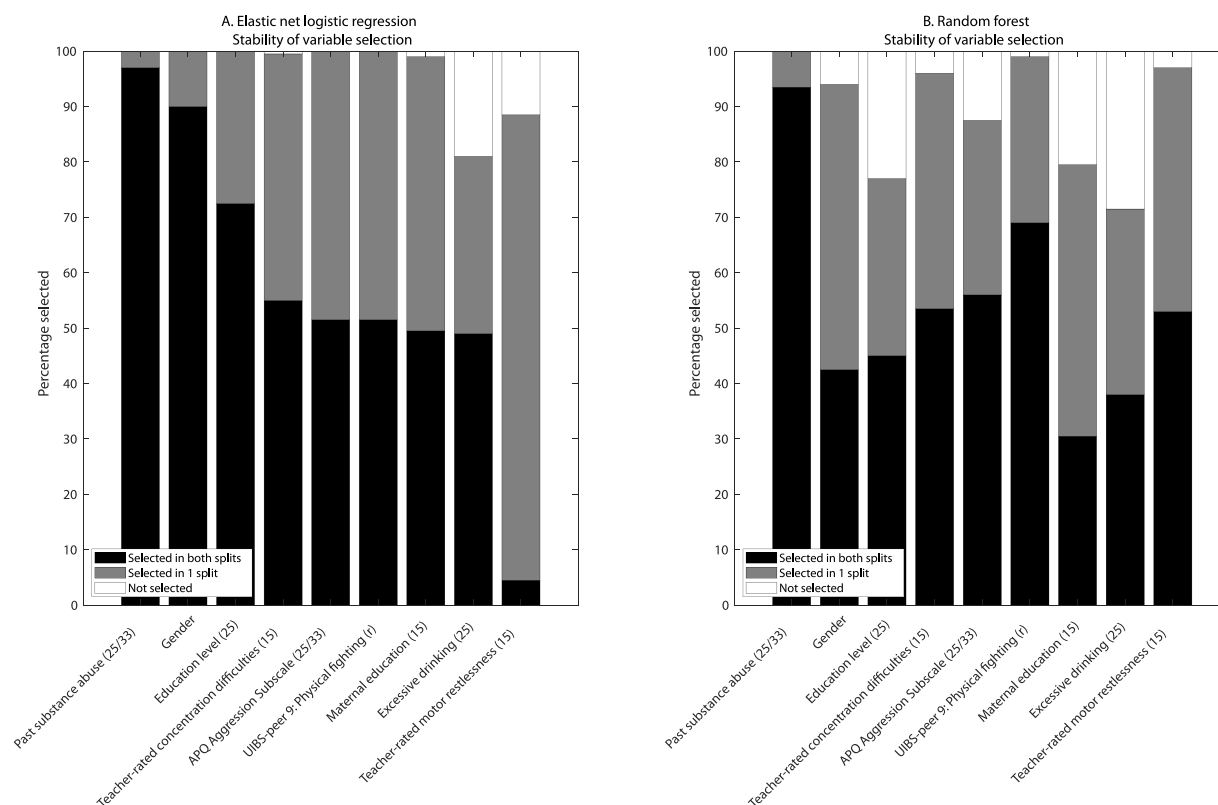


Fig. 4. Stability analysis for the 9 variables that were selected by at least three out of four models. In the top graph (A) the results from elastic net logistic regression are shown. Below that (B) the results from random forest are shown. The y-axis shows how often, percentage-wise, variables are selected. A higher black bar indicates a more stable variable. The values in parentheses at the end of variable names (e.g. “25/33”) show the age at which the measurement was taken for the younger and elder cohort respectively, with “r” meaning retrospective.

While it is not surprising that past substance use disorder was found to be a good predictor for ABPC, this finding increases the confidence that our approach does indeed identify relevant predictors. Adding to what was previously known, we have found that effects of stress and excessive drinking are mediated by past substance use disorder, and that it can be used to predict ABPC in an independent sample.

Gender was identified as the second-most stable predictor. While boys and girls experience similar trajectories and outcomes for antisocial behaviour (Odgers et al., 2008), evidence for differential gender pathways have also been found (e.g. (Lewin et al., 1999; McEachern and Snyder, 2012; Raine et al., 2011)). In this study, especially the linear logistic regression model found gender to be both influential and stable for ABPC, whereas the non-linear random forest model showed less stability in selecting gender as a predictor. This result can be explained by the mediation analysis: the effects of gender on ABPC are fully mediated by substance use, aggression, and bullying behaviour, each of which has known gender effects (Menesini and Salmivalli, 2017; Stone et al., 2012; Tremblay and Côté, 2019). This shows that gender does not provide additional information when substance use and aggression data are available.

The *APQ aggressive mode of action* was also selected by all models as a predictor for ABPC, albeit with lower stability. This lower stability may be explained by the high correlation between the APQ aggression subscale and other aggression questionnaires: the DAS and B-P. Even so, our research shows that among these three instruments, the APQ aggressive mode of action best predicts ABPC. Importantly, the DAS, B-P, and instruments that measure ADHD-like symptoms do not provide additional information.

Teacher-rated concentration difficulties at age 15 were a predictor for ABPC measured before adulthood. In previous work, concentration difficulties in childhood and adolescence have been associated with antisocial behaviour (Farrington, 2005; af Klinteberg et al., 1993); we

additionally show that this correlation can be exploited for prediction.

The final predictor selected by all models was *UIBS item 9: physical fighting* as reported by peers. The UIBS was taken at age 25 (younger) or 33 years (elder cohort) and assessed the middle school period (ages 11–16), retrospectively. Bullying behaviour has already been suggested as a strong predictor for antisocial behaviour (Ttofi et al., 2012). However, our models selected this specific item over the subscale that it belongs to. This novel result suggests that this physical fighting behaviour is particularly indicative of later ABPC. The mediation model shows *physical fighting* has a direct effect on ABPC, distinct from the effects of other aggression measures. This shows that physical fighting in school is a unique and specific risk factor for later antisocial behaviour.

Because most aggression measures in our sample were taken later in life (ages 25/33 years), their usefulness for intervention before adulthood should be validated. However, two of the five best predictors may be particularly interesting for early intervention: concentration difficulties and physical fighting in school. Together, these two explain roughly 20% of observed variance for later ABPC in our sample with a Nagelkerke pseudo-R² of 0.19 (data not shown). Other candidates for early identification include *motor restlessness* at age 15 as a risk factor and *maternal education* at age 15 as a protective factor.

We have applied both linear (logistic regression) and non-linear (random forest) prediction methods. The linear models never performed worse than the non-linear models. This suggests either that there are no significant non-linear interactions in our measures that are predictive of ABPC, or alternatively that a larger sample is needed to leverage them.

Our results enable prediction at an individual level at a chosen level of sensitivity/specificity. Because false positives in ABPC risk stigmatisation as well as unnecessary treatment, individual predictions ideally have a high level of specificity. While our prediction with an AUC of 0.74–0.84 by itself may not be enough to provide this level of

discriminate power, the aim of this research was not to diagnose, but to identify risk factors that may be used to refer potentially at-risk individuals to proper care as early as possible.

Our results can aid both education professionals and clinicians. Because we show that early ratings by teachers are predictive of ABPC, it may help to extend the early prevention aspect in this direction. Our results can help education professionals be more proactive when observing early predictors as described in this paper. For clinicians, who generally face patients who already have developed a disorder, it is beneficial to know which (combinations of) problematic behaviours are indicative of future ABPC, especially in cases where the primary referral is not for antisocial behaviour.

Actionable suggestions for education professionals, clinicians, and practitioners based on our results include the following. Firstly, while gender is a risk factor for ABPC, it is not informative when aggression and substance use information is already considered. Secondly, physical fighting specifically is a risk factor; other types of bullying behaviour much less so. Thirdly, stress and stressful life events are not indicative of later ABPC, unless accompanied by substance abuse. Fourthly and lastly, symptoms relating to inattention and hyperactivity are not direct risk factors for later ABPC, but may be among the earliest to be noticed. If accompanied by any aggressive behaviour, they become risk factors.

The results of this study should be considered in light of some strengths and limitations. Our results show that it is possible to identify robust predictors for complex behaviours by leveraging large-scale data collection as well as current data processing techniques. These techniques make it possible to analyse large quantities of data in a hypothesis-free framework without compromising on reproducibility. In terms of limitations, we would like to emphasise that the causal mediation analysis that identified predictors should not be considered causative for ABPC. Instead, they should be treated as (mediated or unmediated) risk factors. Secondly, while the variable selection and prediction steps were performed in independent cohorts, these cohorts both were drawn from a specific geographic population and age range. This means that even though our risk factors generalise well within this population, it is to be determined whether they predict equally well in different populations. Promisingly, our risk factors partially overlap with findings in other populations. In addition, other results from the same two cohorts have been observed in different populations, such as a genetic/environment interaction in disordered eating in a Caucasian-American population (Akkermann et al., 2012; Rozenblat et al., 2017; Stoltenberg et al., 2012), physical activity and sleep related findings in a Swedish population (Ortega et al., 2011), and a genetic/ADHD association in a Croatian population (Nikolic Perkovic et al., 2013). This suggests that our risk factors might generalise beyond Estonia, but further research remains needed. Thirdly, because the UIBS was administered retrospectively, it may have been vulnerable to distortion by later experiences. Prospective data collections could therefore be even more informative for prediction studies.

In conclusion, by combining a data-driven approach in separate cohorts with stability testing and a causal mediation analysis, our work fills a hole in existing literature by moving away from testing specific hypotheses with a focus on robust, reproducible results. This approach of using independent cohorts combined with variable selection and prediction techniques allows large scale analyses while improving scientific reproducibility over traditional correlation studies. We confirmed known risk factors for ABPC in a population sample and identified the novel specific risk factor of physical fighting in school which together have good predictive power in an unseen cohort. These predictors may be suitable as indicators for the start of early intervention treatments.

Disclosures

G. Schoenmacker reported no potential conflicts of interest.
K. Sakala reported no potential conflicts of interest.

B. Franke reported no potential conflicts of interest.
J. Buitelaar reported no potential conflicts of interest.
T. Veidebaum reported no potential conflicts of interest.
J. Harro reported no potential conflicts of interest.
T. Heskes reported no potential conflicts of interest.
T. Claassen reported no potential conflicts of interest.
A. Arias Vasquez reported no potential conflicts of interest.

CRediT authorship contribution statement

Gido H. Schoenmacker: Methodology, Software, Validation, Formal analysis, Investigation, Writing - original draft, Writing - review & editing, Visualization. **Katre Sakala:** Validation, Investigation, Resources, Data curation, Writing - review & editing. **Barbara Franke:** Conceptualization, Resources, Writing - review & editing, Project administration, Funding acquisition. **Jan K. Buitelaar:** Conceptualization, Writing - review & editing, Supervision, Project administration, Funding acquisition. **Toomas Veidebaum:** Resources, Data curation, Writing - review & editing. **Jaanus Harro:** Conceptualization, Resources, Data curation, Writing - review & editing, Supervision, Project administration, Funding acquisition. **Tom Heskes:** Methodology, Formal analysis, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition. **Tom Claassen:** Methodology, Formal analysis, Writing - review & editing, Supervision. **Arias Vásquez Alejandro:** Conceptualization, Methodology, Resources, Writing - review & editing, Supervision, Project administration, Funding acquisition.

Declaration of Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

This project has received funding from the European Union's Seventh Framework Programme [FP7/2007-2013] for research, technological development and demonstration under grant agreement no 602805 - AGGRESSOTYPE. This paper reflects only the author's views and the European Union is not liable for any use that may be made of the information contained therein. Additional support is received from the Dutch National Science Agenda for the NWANeurolabNL project (grant 400 17 602), as well as the Estonian Research Council Grant IUT20-40. Thanks to Masha Pikulina, who designed the schematic overview in Fig. 1.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.psychres.2020.113208](https://doi.org/10.1016/j.psychres.2020.113208).

References

- af Klinteberg, B., 1988. *Studies on Sex-Related Psychological and Biological Indicators of Psychosocial Vulnerability: A Developmental Perspective*. Department of Psychology, University of Stockholm.
- af Klinteberg, B., Andersson, T., Magnusson, D., Stattin, H., 1993. Hyperactive behavior in childhood as related to subsequent alcohol problems and violent offending: a longitudinal study of male subjects. *Pers. Individ. Differ.* 15, 381–388. [https://doi.org/10.1016/0191-8869\(93\)90065-B](https://doi.org/10.1016/0191-8869(93)90065-B).
- Akkermann, K., Kaasik, K., Kiive, E., Nordquist, N., Orelund, L., Harro, J., 2012. The impact of adverse life events and the serotonin transporter gene promoter polymorphism on the development of eating disorder symptoms. *J. Psychiatr. Res.* 46, 38–43. <https://doi.org/10.1016/j.jpsychires.2011.09.013>.
- Black, D.W., Gunter, T., Loveless, P., Allen, J., Sieleni, B., 2010. Antisocial personality disorder in incarcerated offenders: psychiatric comorbidity and quality of life. *Ann. Clin. Psychiatry* 22, 113–120 <https://doi.org/acp.2202e> [pii].
- Boulesteix, A.-L., Janitza, S., Kruppa, J., König, I.R., 2012. Overview of random forest

- methodology and practical guidance with emphasis on computational biology and bioinformatics. Wiley Interdiscip. Rev. Data Min. Knowl. Discov. 2, 493–507. <https://doi.org/10.1002/widm.1072>.
- Breiman, L., 2001. Random forests. *Mach. Learn.* 45, 5–32. <https://doi.org/10.1023/A:1010933404324>.
- Buss, A.H., Perry, M., 1992. The aggression questionnaire. *J. Pers. Soc. Psychol.* 63, 452–459.
- Calkins, S.D., Keane, S.P., 2009. Developmental origins of early antisocial behavior. *Dev. Psychopathol.* 21, 1095. <https://doi.org/10.1017/S095457940999006X>.
- Claassen, T., Heskes, T., 2012. A Bayesian approach to constraint based causal inference. In: *UAI 2012, Proceeding 28th Conference on Uncertainty in Artificial Intelligence*, pp. 207–216.
- Coccaro, E.F., Berman, M.E., Kavoussi, R.J., 1997. Assessment of life history of aggression: development and psychometric characteristics. *Psychiatry Res.* 73, 147–157. [https://doi.org/10.1016/S0165-1781\(97\)00119-4](https://doi.org/10.1016/S0165-1781(97)00119-4).
- Criminal Policy Department of the Estonian Ministry of Justice, 2019. Kuritegevuse ülevaade [WWW Document]. <https://www.kriminaalpolitika.ee/>. URL <https://www.kriminaalpolitika.ee/kuritegevuse-statistika/> (accessed 2020-06-02).
- Espelage, D.L., Holt, M.K., 2001. Bullying and Victimization During Early Adolescence. *J. Emot. Abus.* 2, 123–142. https://doi.org/10.1300/J135v02n02_08.
- Fairchild, G., Van Goozen, S.H.M., Calder, A.J., Goodyer, I.M., 2013. Research review: evaluating and reformulating the developmental taxonomic theory of antisocial behaviour. *J. Child Psychol. Psychiatry Allied Discip.* 54, 924–940. <https://doi.org/10.1111/jcpp.12102>.
- Farrington, D.P., 2005. Childhood origins of antisocial behavior. *Clin. Psychol. Psychother.* <https://doi.org/10.1002/cpp.448>.
- Farrington, D.P., 1993. Childhood origins of teenage antisocial behaviour and adult social dysfunction. *J. R. Soc. Med.* 86, 13–17.
- Foster, E.M., Jones, D., Bierman, K.L., Coie, J.D., Dodge, K.A., Greenberg, M.T., Lochman, J.E., McMahon, R.J., Pinderhughes, E.E., 2006. Can a costly intervention be cost-effective? An analysis of violence prevention. *Arch. Gen. Psychiatry* 63, 1284–1291. <https://doi.org/10.1001/archpsyc.63.11.1284>.
- Foster, E.M., Jones, D.E., Group, and T.C.P.P.R., 2005. The high costs of aggression: public expenditures resulting from conduct disorder. *Am. J. Public Health* 95, 1767–1772. <https://doi.org/10.2105/AJPH.2004.061424>.
- Gibbon, S., Duggan, C., Stoffers, J., Huband, N., Völlm, B.A., Ferriter, M., Lieb, K., 2010. Psychological interventions for antisocial personality disorder. *Cochrane Database Syst. Rev.* <https://doi.org/10.1002/14651858.CD007668.pub2>.
- Harro, M., Eensoo, D., Kiive, E., Merenäkk, L., Alep, J., Orelund, L., Harro, J., 2001. Platelet monoamine oxidase in healthy 9- and 15-years old children: The effect of gender, smoking and puberty. *Prog. Neuro-Psychopharmacol. Biol. Psychiatry* 25, 1497–1511. [https://doi.org/10.1016/S0278-5846\(01\)00212-3](https://doi.org/10.1016/S0278-5846(01)00212-3).
- Institute for Crime & Justice Policy Research, 2020. World prison brief [WWW Document]. <https://www.prisonstudies.org>. URL <https://www.prisonstudies.org/country/estonia> (accessed 2020-06-02).
- Jackson, J., Hough, M., Bradford, B., Pooler, T., Hohl, K., Kuha, J., 2011. Trust in justice: topline results from the round 5 of the European social survey. *ESS Topline Results Ser.*
- Kessler, R.C., Adler, L., Ames, M., Demler, O., Faraone, S., Hiripi, E., Howes, M.J., Jin, R., Secnik, K., Spencer, T., Ustun, T.B., Walters, E.E., 2005. The World Health Organization adult ADHD self-report scale (ASRS): a short screening scale for use in the general population. *Psychol. Med.* 35, 245–256. <https://doi.org/10.1017/S0033291704002892>.
- Khalifa, N., Duggan, C., Stoffers, J., Huband, N., Völlm, B.A., Ferriter, M., Lieb, K., 2010. Pharmacological interventions for antisocial personality disorder. *Cochrane Database Syst. Rev.* <https://doi.org/10.1002/14651858.CD007667.pub2>.
- Kivirähk, J., 2018. Avalik arvamus ja riigikaitse.
- Laas, K., Reif, A., Herterich, S., Eensoo, D., Lesch, K.-P., Harro, J., 2010. The effect of a functional NOS1 promoter polymorphism on impulsivity is moderated by platelet MAO activity. *Psychopharmacology (Berl)* 209, 255–261. <https://doi.org/10.1007/s00213-010-1793-z>.
- Lajunen, T., Parker, D., Stradling, S.G., 1998. Dimensions of driver anger, aggressive and highway code violations and their mediation by safety orientation in UK drivers. *Transp. Res. Part F Traffic Psychol. Behav.* 1, 107–121. [https://doi.org/10.1016/S1369-8478\(98\)00009-6](https://doi.org/10.1016/S1369-8478(98)00009-6).
- Lewin, L.M., Davis, B., Hops, H., 1999. Childhood social predictors of adolescent antisocial behavior: gender differences in predictive accuracy and efficacy. *J. Abnorm. Child Psychol.* 27, 277–292. <https://doi.org/10.1023/A:1022606608840>.
- McEachern, A.D., Snyder, J., 2012. Gender differences in predicting antisocial behaviors: developmental consequences of physical and relational aggression. *J. Abnorm. Child Psychol.* 40, 501–512. <https://doi.org/10.1007/s10802-011-9589-0>.
- Meinshausen, N., Bühlmann, P., 2010. Stability selection. *J. R. Stat. Soc. Ser. B Stat. Methodol.* 72, 417–473. <https://doi.org/10.1111/j.1467-9868.2010.00740.x>.
- Menesini, E., Salmivalli, C., 2017. Bullying in schools: the state of knowledge and effective interventions. *Psychol. Heal. Med.* 22, 240–253. <https://doi.org/10.1080/13548506.2017.1279740>.
- Mooij, J.M., Magliacane, S., Claassen, T., 2016. Joint causal inference from multiple contexts.
- Nikolac Perkovic, M., Kiive, E., Nedec Erjavec, G., Veidebaum, T., Curkovic, M., Dodig-Curkovic, K., Muck-Seler, D., Harro, J., Pivac, N., 2013. The association between the catechol-O-methyltransferase Val108/158Met polymorphism and hyperactive-impulsive and inattentive symptoms in youth. *Psychopharmacology (Berl)* 230, 69–76. <https://doi.org/10.1007/s00213-013-3138-1>.
- O'Connor, D.B., Archer, J., Frederick, W.c. W., 2001. Measuring aggression: self-reports, partner reports, and responses to provoking scenarios. *Aggress. Behav.* 27, 79–101. <https://doi.org/10.1002/ab.2>.
- Ogders, C.L., Moffitt, T.E., Broadbent, J.M., Dickson, N., Hancox, R.J., Harrington, H., Poulton, R., Sears, M.R., Thomson, W.M., Caspi, A., 2008. Female and male antisocial trajectories: from childhood origins to adult outcomes. *Dev. Psychopathol.* 20, 673–716. <https://doi.org/10.1017/S0954579408000333>.
- Ortega, F.B., Ruiz, J.R., Labayan, I., Kwak, L., Harro, J., Oja, L., Veidebaum, T., Sjöström, M., 2011. Sleep duration and activity levels in Estonian and Swedish children and adolescents. *Eur. J. Appl. Physiol.* 111, 2615–2623. <https://doi.org/10.1007/s00421-011-1883-6>.
- Paaver, M., Kurrikoff, T., Nordquist, N., Orelund, L., Harro, J., 2008. The effect of 5-HTT gene promoter polymorphism on impulsivity depends on family relations in girls. *Prog. Neuro-Psychopharmacol. Biol. Psychiatry* 32, 1263–1268. <https://doi.org/10.1016/j.pnpbp.2008.03.021>.
- Raine, A., Yang, Y., Narr, K.L., Toga, A.W., 2011. Sex differences in orbitofrontal gray as a partial explanation for sex differences in antisocial personality. *Mol. Psychiatry* 16, 227–236. <https://doi.org/10.1038/mp.2009.136>.
- Raven, J., Raven, J.C., Court, J., 1998. Manual for Raven's progressive matrices and vocabulary scales. Raven Man. <https://doi.org/10.1006/cogp.1999.0735>.
- Reunanan, J., 2003. Overfitting in making comparisons between variable selection methods. *J. Mach. Learn. Res.* 3, 1371–1382.
- Robins, L.N., 1998. The intimate connection between antisocial personality and substance abuse. *Soc. Psychiatry Psychiatr. Epidemiol.* 33, 393–399.
- Romeo, R., Knapp, M., Scott, S., 2006. Economic cost of severe antisocial behaviour in children - and who pays it. *Br. J. Psychiatry* 188, 547–553. <https://doi.org/10.1192/bjp.bp.104.007625>.
- Rozenblat, V., Ong, D., Fuller-Tyszkiewicz, M., Akkermann, K., Collier, D., Engels, R.C.M.E., Fernandez-Aranda, F., Harro, J., Homberg, J.R., Karwautz, A., Kiive, E., Klump, K.L., Larson, C.L., Racine, S.E., Richardson, J., Steiger, H., Stoltenberg, S.F., van Strien, T., Wagner, G., Treasure, J., Krug, I., 2017. A systematic review and secondary data analysis of the interactions between the serotonin transporter 5-HTTLPR polymorphism and environmental and psychological factors in eating disorders. *J. Psychiatr. Res.* <https://doi.org/10.1016/j.jpsychires.2016.09.023>.
- Safari, S., Baratloo, A., Elfil, M., Negida, A., 2016. Evidence based emergency medicine; part 5 receiver operating curve and area under the curve. *Emerg. (Tehran, Iran)* 4, 111–113.
- Scott, S., Knapp, M., Henderson, J., Maughan, B., 2001. Financial cost of social exclusion: follow up study of antisocial children into adulthood. *BMJ* 323, 191. <https://doi.org/10.1136/BMJ.323.7306.191>.
- Scott, S., Sylva, K., Doolan, M., Price, J., Jacobs, B., Crook, C., Landau, S., 2010. Randomised controlled trial of parent groups for child antisocial behaviour targeting multiple risk factors: the SPOKES project. *J. Child Psychol. Psychiatry* 51, 48–57. <https://doi.org/10.1111/j.1469-7610.2009.02127.x>.
- Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The mini-international neuropsychiatric interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J. Clin. Psychiatry* 59 (Suppl 20), 22–33 quiz 34–57.
- Simonoff, E., Elander, J., Holmshaw, J., Pickles, A., Murray, R., Rutter, M., 2004. Predictors of antisocial personality: Continuities from childhood to adult life. *Br. J. Psychiatry.* <https://doi.org/10.1192/bjp.184.2.118>.
- Sööt, M.-L., Salla, J., Ginter, J., 2014. Karistushinnangud. Kokkuvõtte Eesti elanike, politseinike, prokuröride ja kohtunike karistushinnangutest.
- Stekhoven, D.J., Bühlmann, P., 2012. MissForest—non-parametric missing value imputation for mixed-type data. *Bioinformatics* 28, 112–118. <https://doi.org/10.1093/bioinformatics/btr597>.
- Stoltenberg, S.F., Anderson, C., Nag, P., Anagnopoulos, C., 2012. Association between the serotonin transporter triallelic genotype and eating problems is moderated by the experience of childhood trauma in women. *Int. J. Eat. Disord.* 45, 492–500. <https://doi.org/10.1002/eat.20976>.
- Stone, A.L., Becker, L.G., Huber, A.M., Catalano, R.F., 2012. Review of risk and protective factors of substance use and problem use in emerging adulthood. *Addict. Behav.* <https://doi.org/10.1016/j.addbeh.2012.02.014>.
- Swanson, J.M., 1981. The SNAP rating scale for the diagnosis of the attention deficit disorder.
- Tabur, L., Sepp, R., 2020. Õiguskaitse-ja justiitsreformid Eestis 1991–2019. *Sisekaitseakadeemia*.
- Tomson, K., Merenäkk, L., Loit, H.M., Mäestu, J., Harro, J., 2011. The relationship between serotonin transporter gene promoter polymorphism and serum lipid levels at young age in a longitudinal population-representative study. *Prog. Neuro-Psychopharmacol. Biol. Psychiatry* 35, 1857–1862. <https://doi.org/10.1016/j.pnpbp.2011.08.004>.
- Tremblay, R.E., Côté, S.M., 2019. Sex differences in the development of physical aggression: an intergenerational perspective and implications for preventive interventions. *Infant Ment. Health J.* 40, 129–140. <https://doi.org/10.1002/imhj.21760>.
- Ttofi, M.M., Farrington, D.P., Lösel, F., 2012. School bullying as a predictor of violence later in life: a systematic review and meta-analysis of prospective longitudinal studies. *Aggress. Violent Behav.* <https://doi.org/10.1016/j.avb.2012.05.002>.
- Ttofi, M.M., Farrington, D.P., Lösel, F., Loeber, R., 2011. Do the victims of school bullies tend to become depressed later in life? A systematic review and meta-analysis of longitudinal studies. *J. Aggress. Confl. Peace Res.* <https://doi.org/10.1108/17596591111132873>.
- Westermeyer, J., Thuras, P., 2005. Association of antisocial personality disorder and substance disorder morbidity in a clinical sample. *Am. J. Drug Alcohol Abuse* 31, 93–110.
- White, Jennifer L., Moffitt, Earls, Terrie E., Robins, Felton, Lee Silva, P.A., 1990. How early can we tell? predictors of childhood conduct disorder and adolescent delinquency. *Criminology* 28, 507–535. <https://doi.org/10.1111/j.1745-9125.1990.tb01337.x>.
- Zou, H., Hastie, T., 2005. Regression and variable selection via the elastic net. *J. R. Stat. Soc. Ser. B* 67, 301–320. <https://doi.org/10.1111/j.1467-9868.2005.00503.x>.