Appendix Section B(2): CONCEPT PAPER TEMPLATE

DUNEDIN MULTIDISCIPLINARY HEALTH AND DEVELOPMENT STUDY

(The Dunedin Study)

CONCEPT PAPER TEMPLATE

(July 2024)

DUNEDIN STUDY CONCEPT PAPER

Provisional Paper Title: Do Positive Childhood Environments Compensate for Early Risk for Life-Course-Persistent Antisocial Behavior?

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Objective of the study:

Within any population there is a small group of individuals who display chronic and persistent antisocial behavior. This group is labeled life-course-persistent (LCP) to reflect their continuity in acting antisocially at every stage of life.[1] Their antisocial behavior develops over time; it begins in early childhood, persists into adulthood, and imposes high costs on society.[2] Naturally, these individuals are at an increased risk of coming into contact with the justice system.[3-7]

The wide-ranging consequences—and the developmental nature—of LCP antisocial behavior highlights the need for early prevention and intervention (e.g., during the first decade of the life course). If effective, such efforts could benefit society by saving tax-payer money and by reducing harm in communities. Yet, to best implement prevention and intervention programs, an understanding of the mechanisms underlying antisocial development is needed. Moffitt noted that, "For life-course-persistent antisocial individuals, deviant behavior patterns later in life may…reflect early individual differences that are perpetuated or exacerbated by interactions with the social environments: first at home, and later at school" (p. 682).[1] In other words, whether or not a person's early risk for antisocial behavior will ever be expressed as antisocial actions depends on input from the environment. The development of LCP behavior could be the product of individual differences in early risk for antisocial development plus the environments that those differences are associated with (see figure below).

As shown in the figure, the process of LCP antisocial development may begin with a heightened risk in childhood. From there, an individual's risk may shape their environments through person-environment transactions (early risk for antisocial development → early environmental experiences). When problematic environments perpetuate or exacerbate early risk for antisocial development, an individual is expected to have an increased probability of following an LCP pattern of antisocial behavior (early environmental experiences → LCP probability). Antisocial development is, therefore, a product of the early individual differences along with the subsequent accumulation of consequences and risk factors from the environment.

Any hope to prevent the development of LCP antisocial behavior depends on counteracting or compensating for the early risk factors and enhancing the early protective factors. Prevention becomes more difficult as the bonds of contemporary and cumulative continuity grow over time.

In this project, we propose to explore the nature of person-environment transactions that may precede LCP antisocial behavior patterns. In doing so, we seek to estimate the extent to which intervening upon certain early-in-life environments could reduce the likelihood that someone at risk of developing LCP antisocial behavior will realize that risk. Although there is much research that has looked into the risk, promotive, and protective factors that are associated with antisocial behavior[8-13], what makes this project unique to criminology is the inclusion of a novel measure that is capable of capturing early individual differences in risk for antisocial development. By leveraging this novel measure, we can glean some of the most robust and compelling evidence regarding the person-environment transactions that lead to antisocial and criminal behavior.[14-17]

We will use a genome-wide polygenic score to capture early individual differences in the risk of externalizing behavior. Genome-wide polygenic scores are high-powered and free from reverse-causation because they are established and fixed at conception.

We seek to answer the following research questions using data from the Dunedin Longitudinal Study: (RQ1) Can positive childhood environments compensate for early risk for life-course-persistent antisocial behavior? (RQ2) If so, by how much?

Through the course of this study, two objectives will be addressed:

- *Objective #1: Demonstrate the utility of a polygenic score to measure individual differences in early risk for antisocial development.*

- *Objective #2: Assess whether childhood environments compensate for early risk for antisocial development (as measured by the externalizing polygenic score).*

Data analysis methods[1]:

We will analyze data from the Dunedin Longitudinal Study using *Stata* version 16.1.[18] The predictor variable will be a polygenic score computed from the summary statistics of a recent GWAS of externalizing problems.[19] The externalizing polygenic score—which was recently shown to explain ~10% of the variance in externalizing behavior—is the most powerful and theoretically relevant polygenic score currently available.

Objective #1: Demonstrate the utility of a polygenic score to measure individual differences in early risk for antisocial development.

The first objective is descriptive in nature. Here, **we hypothesize that a polygenic score for externalizing behavior can be used as a measure of individual differences in early risk for antisocial development**. To test this hypothesis, regression analysis will be used to observe associations between the polygenic score for externalizing behavior and a variety of antisocial

[1] A key concern for the Dunedin Study is superficial analyses of data that simply identify differences or deficits between ethnic groups or other communities where inequities exist (e.g. persons with disabilities, Pasifika peoples, members of migrant and SOGIESC (Sexual Orientation, Gender Identify and Expression and Sexual Characteristics) communities). The cumulative effect of these types of studies is stigmatising and not of benefit. Any research that identifies differences must (a) incorporate information on the broader context (e.g. historical or political factors); (b) where possible undertake additional analyses to examine the source of the difference/s, and (c) include policy recommendations for its resolution.

outcomes. All regression analyses will adjust for participant sex and the model type will depend on the level of measurement of the outcome variable of focus.

Table 1 outlines the research questions, hypotheses, proposed measures, and analytical strategies, that will be used to satisfy this objective.

Table 1: Objective #1 – Main Analyses

	Analysis 1:	Analysis 2:	Analysis 3:	Analysis 4:	Analysis 5:
Research Question	How well does the polygenic score predict what it was constructed to predict?	How well does the polygenic score predict any contact with the justice system?	How well does the polygenic score predict repeated contact with the justice system?	How well does the polygenic score predict timing to first contact with the justice system?	Does the polygenic score help differentiate between different trajectories of antisocial behavior?
Hypothesis	The polygenic score with be positively associated with externalizing psychopathology factor.	The polygenic score will be positively associated with a greater risk of justice system contact.	The polygenic score will be positively associated with a greater rate of justice system contact.	The polygenic score will be positively associated with an earlier onset of offending.	The average polygenic score will differ across trajectory groups, with LCPs having the highest polygenic scores, followed by AL, Childhood-limited, and Low.
DV	Externalizing Psychopathology Factor, age 18-45	Any Criminal Conviction	Number of Convictions	Age at First Conviction	Trajectories of Antisocial Behavior
Key IV	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior
Covariate(s)	Sex	Sex	Sex	Sex	Sex
Model Type	OLS Regression	Logistic Regression	Poisson or Negative Binomial Regression	Cox/Hazard Models	Multinomial Logistic Regression

Following the main regression analyses, subsequent analyses will be performed to further assess the PGS-outcome relationships. In all, the purpose of these subsequent analyses is to provide additional context regarding the utility and limitations of the externalizing polygenic score to a criminological audience.

The first round of subsequent analyses will compare the prediction accuracy of the externalizing polygenic score to the prediction accuracy of other well-known early-life risk factors. Comparison variables will include: difficult temperament at age 3,[20] brain health at age 3,[21] parent's antisocial behavior,[22] and childhood SES.

The prediction accuracy of each variable will be identified by its "incremental R^2".[23] Incremental R^2 is the observed change in R^2 value when the predictor variable is added as a covariate to a baseline model of the outcome regressed on participant sex. Outcomes for such analyses will include externalizing psychopathology in adulthood, any criminal convictions, and LCP-type developmental trajectory of antisocial behavior. Given the binary nature of the latter two variables, McFadden's pseudo R^2 will be assessed.

Table 2 outlines the process of the incremental R^2 analysis and highlights the measures and analyses that will be involved

Table 2: Objective #1 – Incremental R^2 Analyses

	Baseline Model	Polygenic Score Model	Difficult Temperament at Age 3 Model	Brain Health at Age 3 Model	Childhood SES Model	Parental Antisocial Behavior Model
DV	Model 1: Externalizing Psychopathology Factor, age 18-45 Model 2: Any Criminal Conviction Model 3: LCP-Type Antisocial Trajectory	Model 1: Externalizing Psychopathology Factor, age 18-45 Model 2: Any Criminal Conviction Model 3: LCP-Type Antisocial Trajectory	Model 1: Externalizing Psychopathology Factor, age 18-45 Model 2: Any Criminal Conviction Model 3: LCP-Type Antisocial Trajectory	Model 1: Externalizing Psychopathology Factor, age 18-45 Model 2: Any Criminal Conviction Model 3: LCP-Type Antisocial Trajectory	Model 1: Externalizing Psychopathology Factor, age 18-45 Model 2: Any Criminal Conviction Model 3: LCP-Type Antisocial Trajectory	Model 1: Externalizing Psychopathology Factor, age 18-45 Model 2: Any Criminal Conviction Model 3: LCP-Type Antisocial Trajectory
Key IV	—	Residualized Standardized PGS for Externalizing Behavior	Age-3 Temperament: Lack of Control	Age-3 Brain Health Factor	Household SES through Childhood	Parent's History of Antisocial Behavior
Covariate(s)	Sex	Sex	Sex	Sex	Sex	Sex
Model Type	A1: OLS Regression A2/A3: Logistic Regression	A1: OLS Regression A2/A3: Logistic Regression	A1: OLS Regression A2/A3: Logistic Regression	A1: OLS Regression A2/A3: Logistic Regression	A1: OLS Regression A2/A3: Logistic Regression	A1: OLS Regression A2/A3: Logistic Regression
Metric	A1: R^2 A2/A3: McFadden's pseudo-R^2	A1: ΔR^2 A2/A3: Δ McFadden's pseudo-R^2	A1: ΔR^2 A2/A3: Δ McFadden's pseudo-R^2	A1: ΔR^2 A2/A3: Δ McFadden's pseudo-R^2	A1: ΔR^2 A2/A3: Δ McFadden's pseudo-R^2	A1: ΔR^2 A2/A3: Δ McFadden's pseudo-R^2

For the second round of subsequent analyses, we will perform classification analyses (ROC curve and AUC analysis). Classification analysis will allow us to evaluate whether the externalizing polygenic score is capable of predicting whether a participant has experienced a conviction or whether a participant has been identified as following an LCP-type developmental trajectory of antisocial behavior. **We hypothesize that the externalizing polygenic score will have a prediction accuracy that is similar to other early-life risk factors, but it will perform poorly as a classifier of individual-level prediction.**

Objective #2: Assess whether childhood environments compensate for early risk for antisocial development (as measured by the externalizing polygenic score).

The second objective is inferential. Statistical mediation analysis will be used to assess whether childhood environments compensate for early risk for antisocial development (as measured by the externalizing polygenic score). This part of the analysis will unfold in three steps.

1. Establish the relationship between the externalizing polygenic score and childhood environments through OLS regression.
2. Establish the relationship between the externalizing polygenic score and LCP antisocial behavior through logistic regression.
3. Estimate the effect of the externalizing polygenic score on LCP antisocial behavior with the childhood environment measure included in the model as a statistical mediator.

Separate analyses will be conducted for positive-experienced parenting and peer inclusion as the indicators of childhood environments. Sex will be included as a covariate for all analyses.

Table 3 outlines the measures and analytical strategies that will be involved in the steps for these analyses.

Table 3: Objective #2 – Main Mediation Analyses

	Positive-Experienced Parenting Analyses			Childhood Inclusion Analyses		
	Model 1A	**Model 2A**	**Model 3A**	**Model 1B**	**Model 2B**	**Model 3B**
Purpose	Reveals the total effect of the polygenic score on LCP-type antisocial behavior.	Reveals the extent to which the polygenic score is associated with the mediator (positive-experienced parenting).	Reveals the indirect effect of the polygenic score on LCP-type antisocial behavior that works through positive-experienced parenting.	Reveals to what extent the polygenic score is associated with peer inclusion in childhood.	Reveals the extent to which the polygenic score is associated with the mediator (peer inclusion in childhood).	Reveals the indirect effect of the polygenic score on LCP-type antisocial behavior that works through peer inclusion in childhood.
DV	LCP-Type Antisocial Trajectory	Positive-Experienced Parenting	LCP-Type Antisocial Trajectory	LCP-Type Antisocial Trajectory	Peer Inclusion (reversely-coded peer isolation)	LCP-Type Antisocial Trajectory
Key IV	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior
Mediator	—	—	Positive-Experienced Parenting	—	—	Peer Inclusion (reversely-coded peer isolation)
Covariate(s)	Sex	Sex	Sex	Sex	Sex	Sex
Model Type	Logistic Regression	OLS Regression	Logistic Regression	Logistic Regression	OLS Regression	Logistic Regression

To the extent that this analysis finds support for statistical mediation, we will also produce an estimate for the proportion mediated, which will provide an estimate of the degree to which positive childhood environments may compensate for early risk for antisocial development (as measured by the externalizing polygenic score).[24] Even without evidence for mediation, the model produced in the 3rd step will provide meaningful results on the relationship between the social environment measures and LCP development after accounting for the influence of individual differences in early risk for antisocial development (as measured by the externalizing polygenic score).

Sensitivity Analyses:

Subsequent analyses will be performed to test whether the sensitivity of the results to the inclusion of different theoretically relevant early-life covariates.

Table 4 displays the proposed research questions and the covariates that will be included in each of the proposed sensitivity analyses.

Table 4: Objective #2 – Sensitivity Analyses for Mediation Models

	Supplemental Analysis 1:	**Supplemental Analysis 2:**	**Supplemental Analysis 3:**
Research Question	Are the observed relationships independent of household SES through childhood?	Are the observed relationships independent of a criminogenic family environment and passive gene-environment correlation?	Are the observed relationships independent of experiencing childhood maltreatment?
DV	LCP-Type Antisocial Trajectory	LCP-Type Antisocial Trajectory	LCP-Type Antisocial Trajectory
Key IV	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior	Residualized Standardized PGS for Externalizing Behavior
Mediator	A1: Positive-Experienced Parenting A2: Peer Inclusion (reversely-coded peer isolation)	A1: Positive-Experienced Parenting A2: Peer Inclusion (reversely-coded peer isolation)	A1: Positive-Experienced Parenting A2: Peer Inclusion (reversely-coded peer isolation)
Covariate(s)	Sex Household SES though childhood	Sex Household SES through Childhood Parent's History of Antisocial Behavior	Sex Childhood Maltreatment
Justification	Included covariates will assess whether the results are sensitive to socioeconomic status in childhood.	Included covariates will assess whether the results are sensitive to being raised in criminogenic environment.	Included covariates will assess whether the results are sensitive to extremely negative parenting experiences (i.e., childhood maltreatment).

Described above are the primary, pre-planned analyses. Secondary analyses may be added as suggested through internal review and will be identified as secondary in the manuscript.

Variables needed at which ages:

Concept	Variable	Appears in Which Analysis?
Key Independent Variable: Polygenic Score for Externalizing Behavior (Karlsson Linnér, Mallard et al., 2021)	Residualized standardized polygenic score for externalizing behavior	Objective #1 - Main Analyses (Table 1) - Incremental R^2 analysis (Table 2) - Classification Analyses Objective #2 - Mediation Analysis (Table 3) - Supplemental Mediation Analyses (Table 4)
Outcome Variables: Antisocial/Criminal Behavior	Criminal Records/Dated Convictions Data - Age at first conviction - Any conviction - Number of convictions	Objective #1 - Main Analyses (Table 1) - Incremental R^2 analysis (Table 2) - Classification Analyses
	Trajectories of Antisocial behavior between ages 7-26 from Odgers et al., 2008 (CDTraj7_26)	Objective #1 - Main Analyses (Table 1) - Incremental R^2 analysis (Table 2) - Classification Analyses Objective #2 - Mediation Analysis (Table 3) - Supplemental Mediation Analyses (Table 4)
	Externalizing Psychopathology Factor, age 18-45	Objective #1 - Main Analyses (Table 1) - Incremental R^2 analysis (Table 2)
Mediator Variables: Positive-experienced Parenting in Childhood & Childhood Isolation	Overall measure of positive-experienced parenting in childhood from Wertz et al., 2019 (G1G2pospar)	Objective #2 - Mediation Analysis (Table 3) - Supplemental Mediation Analyses (Table 4)
	Childhood Isolation 5-11 (Zisolkid)	Objective #2: - Mediation Analysis (Table 3) - Supplemental Mediation Analyses (Table 4)

Covariates and Comparison Variables	Age-3 Temperament: Lack of Control (DIFF3)	Objective #1: - Incremental R^2 analysis (Table 2)
	Age-3 Brain Health Factor z-score	Objective #1: - Incremental R^2 analysis (Table 2)
	Sex	Objective #1 - Main Analyses (Table 1) - Incremental R^2 analysis (Table 2) Objective #2 - Mediation Analysis (Table 3) - Supplemental Mediation Analyses (Table 4)
	Household SES through childhood (birth-15)	Objective #1: - Incremental R^2 analysis (Table 2) Objective #2: - Supplemental Mediation Analyses (Table 4)
	Parent's History of Antisocial Behavior from the Diagnostic Interview Schedule (Used in Wertz et al. 2018 – Genetics and Crime)	Objective #1: - Incremental R^2 analysis (Table 2) Objective #2: - Supplemental Mediation Analyses (Table 4)
	Childhood maltreatment 3-11	Objective #2: - Supplemental Mediation Analyses (Table 4)

Significance of the Study (for theory, research methods or clinical practice):

This project is important to the field of criminology for reasons related to both theory and methods. When it comes to theory, we seek to further our understanding of LCP development by assessing the potential person-environment transactions underlying the development of LCP antisocial behavior. Such findings could provide strong evidence in favor of early-years intervention to improve childhood environments and decrease the probability of LCP development.

When it comes to methods, we propose to integrate polygenic scores into criminological research. While polygenic scores have been used by scholars writing in criminology journals,[25,26] they have yet to be fully introduced as a way to measure initial risk for antisocial development. Individual differences in antisocial behavior are highlighted as playing a critical role in the development of chronic and persistent antisocial behavior in all major theories. When it comes to testing research questions related to these theories, however, such individual differences are either ignored or

measured at stages that are too late in the life course to make sense developmentally. As such, this project will fully introduce polygenic scores (their benefits and limitations), demonstrate how the use of polygenic scores can further aid our understanding of the developmental nature of LCP antisocial behavior, and produce robust estimates for the compensating and independent influences of positive-experienced parenting and peer inclusion on LCP development.

How the paper will contribute to Māori health advancement and/or equitable health outcomes[2]

This research will not include separate analysis of specific ethnic groups. Yet, we believe the findings from this study will be generalizable to the Māori community. Indeed, the importance of the findings may be particularly important for the advancement of Māori health.

Disparities exist at every stage of the New Zealand justice system. For example, while Māori are approximately 18% of Aotearoa New Zealand's general population, approximately 44% of convictions in 2023 were Māori.[27] Furthermore, when it comes to youth involvement in the justice system, the majority of child and youth offenses proceeded against by Police were of Māori descent (54%), despite comprising only 25% of the youth population.[28] The disparities widen when it comes to young people with serious and persistent offending behavior, as 68% of such individuals in 2023 were Māori.[28] Yet, research finds the self-reported delinquency behavior of Māori youth is no different from non-Māori and that Māori experience harsher responses from the justice system for the same crimes compared to non-Māori.[29-31] As such, disparities in justice system contact are at least partially a function of structural discrimination and bias.[32]

The detrimental burden of persistent antisocial behavior exists even in the absence of ethnic disparities. Children who have been identified as following the LCP developmental path are at an elevated risk for myriad health problems in young adulthood.[2] Such consequences highlight need for early-years prevention and intervention to break the chain of LCP antisocial development. But what size of effect can we expect such effort to have? Nearly all children (87%) and the vast majority of adolescents (87%) whose offending behavior led to justice system proceedings had a previous child-welfare notification about their care and protection.[28] As such, the present study will produce estimates of the potential impact that parenting and peer inclusion intervention may have on breaking the chain of LCP development, after taking into consideration the existence of individual differences in early risk for externalizing behavior. And we believe the results will benefit both Māori and non-Māori communities.

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[2] Helpful information can be found here: https://www.hrc.govt.nz/sites/default/files/2020-01/NZ%20Prioritisation-Framework-FA-web_0.pdf

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Data Security Agreement

Provisional Paper Title	Do Positive Childhood Environments Compensate for Early Risk for Life-Course-Persistent Antisocial Behavior?
Proposing Author	Ryan Motz
Today's Date	19 August 2024

Please keep one copy for your records and return one to the PI Sponsor and the Study's Research Manager, Dr Sandhya Ramrakha

Please initial your agreement: (customize as necessary)

x	I am current on Human Subjects Training [CITI www.citigrogram.org] or equivalent.
x	My project is covered by the Dunedin Study's ethics approval OR I have /will obtain ethical approval from my home institution (please specify).
x	I will treat all data as "restricted" and store in a secure fashion. My computer or laptop is: • encrypted (recommended programs are FileVault2 for Macs, and Bitlocker for Windows machines) • password-protected • configured to lock-out after 15 minutes of inactivity AND • has an antivirus client installed as well as being patched regularly.
x	I will not "sync" the data to a mobile device.
x	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact my PI Sponsor and Director, Professor Reremoana (Moana) Theodore (director.dunedinstudy@otago.ac.nz).
x	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
x	I will not post data online or submit the data file to a journal for them to post. *Some journals are now requesting the data file as part of the manuscript submission process. The Dunedin Study Members have not given informed consent for unrestricted open access, so we have a managed-access process. Speak to your PI Sponsor or Reremoana (Moana) Theodore for strategies for achieving compliance with data-sharing policies of journals.*
x	I will delete all data files from my computer after the project is complete. Collaborators and trainees may not take a data file away from the office. The data remains the property of the Study and cannot be used for further analyses without an approved concept paper for new analyses.
x	I will provide a copy of all newly created variables to the Dunedin Study unit through the Research manager (sandhya.ramrakha@otago.ac.nz) and Data manager (antony.ambler@otago.ac.nz), copying in the Director.

Signature:  _____

CONCEPT PAPER RESPONSE FORM

A To be completed by the proposing author:

Provisional Paper Title	Do Positive Childhood Environments Compensate for Early Risk for Life-Course-Persistent Antisocial Behavior?
Proposing Author	Ryan Motz
Other Contributors	JC Barnes, Terrie Moffitt, Avshalom Caspi, Reremoana Theodore
Potential Journals	
Today's Date	19 August 2024
Intended Submission Date	2025

Please keep one copy for your records and return one to the proposing author

B. To be completed by potential co-authors:

☐ Approved ☐ Not Approved ☐ Let's discuss, I have concerns

Comments: _____

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Please check your contribution(s) for authorship:

	Conceptualizing and designing the longitudinal study
	Providing funds for the study
	Conceptualizing data collection protocols and creating variables
	Data collection
	Conceptualizing and designing this specific paper project
	Statistical analyses and interpretation (or reproducibility check)
	Writing
	Reviewing manuscript drafts
	Final approval before submission for publication
	Agreement to be accountable for the work
	Acknowledgment only, I will not be a co-author

Signature: _____