ENVIRONMENTAL-RISK (E-RISK) LONGITUDINAL TWIN STUDY
CONCEPT PAPER FORM

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Provisional Paper Title: The developmental course of loneliness from childhood to young adulthood

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Objective of the study and its significance:

Many individuals will experience loneliness at some stage of life, and in most cases it is a temporary feeling that emerges and subsides due to changes in circumstances. In these cases, loneliness, though distressing at the time, is unlikely to have long-term implications for health. However, a minority of lonely individuals become trapped in a feedback loop, in which maladaptive cognitions and behavioural styles impair social interactions and inhibit the formation of close bonds with others (Qualter et al, 2015). Under these circumstances, loneliness can become a self-perpetuating problem that persists for months or even years. This chronic loneliness is a greater concern with regard to health, as it acts as a cumulative stressor that exerts a wear-and-tear effect on health (Holt-Lunstad et al, 2015).

Research on the long-term effects of chronic loneliness have focused primarily on illness and mortality in the later years of life. However, it is now well-established that loneliness is particularly common among adolescents and young adults (Victor & Yang, 2012). Loneliness in this age group is known to correlate with impairments in diverse domains of life, including mental health, employment and lifestyle behaviours (Matthews et al, 2019). While there is some existing longitudinal research on loneliness in young people, few such studies have attempted to disentangle transient versus chronic forms of loneliness. It would be expected that transient loneliness is common at this age, due to life changes such as leaving school and moving out of the family home. This could be argued to be a normal part of growing up, and not pathological in its own right. The higher prevalence of mental health problems among lonely young adults could therefore be driven by those suffering from more chronic forms of loneliness.

In the present study, I will examine the persistence of loneliness from ages 12 to 18, and how chronic versus transient forms of loneliness are associated with health and lifestyle outcomes. It is anticipated that lonely young adults in general will be at greater risk of mental health problems, but those who have been persistently lonely in childhood will show the greatest risk. Meanwhile, children whose loneliness subsided before adulthood may be spared such long-term mental health outcomes, but could show deficits in other areas, such as finishing school with low qualifications. I will look at a total of 10 outcomes across two domains: (1) mental health (depression, anxiety, conduct disorder, self-harm, and service use), and (2) lifestyle (NEET, qualifications, smoking, criminal offending, early parenthood).

Loneliness is also known to be heritable, and the relative contribution of genetic and environmental influences has been shown to vary across childhood, with the effect of genes becoming smaller around the onset of puberty (Bartels et al, 2008). However, no behavioural genetic research has examined the period from preadolescence to young adulthood, or examined the extent to which the persistence of loneliness is

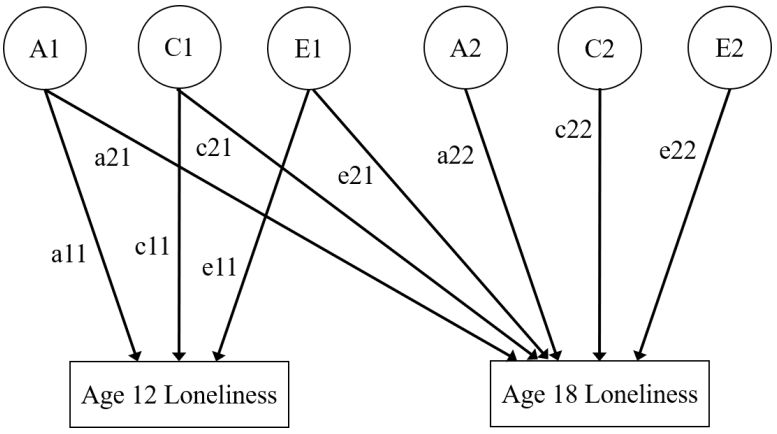
explained by genetic and environmental factors. Therefore, in the second part of this study I will fit a bivariate twin model to loneliness measured at ages 12 and 18, which will reveal the genetic contributions to the persistence of (and change in) loneliness over time.

Statistical analyses:

I will identify groups of lonely individuals by taking the top decile of loneliness at ages 12 and 18. This is consistent with the percentage of young individuals who report feeling lonely "often" in surveys (Office for National Statistics, 2018). I will then create groups based on the continuity of loneliness between these two ages:
0 "Never lonely"
1 "Remittted" (lonely at 12 but not 18)
2 "New onset" (lonely at 18 but not at 12)
3 "Chronic" (lonely at both 12 and 18)

Using "never lonely" as the reference, I will enter these dummy-coded groups as the independent variable in a series of logistic regression models, testing their association with each outcome described above.

For the behavioural genetic analyses, I will apply a bivariate Cholesky decomposition to ages 12 and 18 loneliness, in order to decompose their variances and covariance into additive genetic, common environment and unique environment effects. This will establish both the heritability of loneliness at each age, and the extent to which the genetic/environmental influences on loneliness at age 12 and 18 are the same.



The Cholesky approach allows genetic and environmental effects on loneliness at age 12 (A1, C1, E1) to also explain variance in loneliness at age 18 (but not vice versa). Variance not explained by these age-12 effects is explained by 'new' genetic/environmental effects at age 18 (A2, C2, E2).

The relative contribution of genetic/environmental effects to **stability** in loneliness at ages 12 and 18 is calculated by multiplying the paths connecting them via each of the factors and dividing by the phenotypic correlation, e.g. for the additive genetic factor: (a11 * a21) / rPh.

Change in loneliness is reflected in the 'new' effects at age 18 (A2, C2, E2). The contribution of (for example) genetic effects to change in loneliness is calculated as: a22 / (a22 + c22 + e22). By calculating these relative contributions of genetic/environmental factors, I will be able to establish (1) why some children escape loneliness (or become lonely when they previously were not), and (2) why some children become chronically lonely.

Variables Needed at Which Ages (names and labels):

E-RISK

Age 12:

lonelye12 Loneliness age 12

Age 18:

Derived variables:
Lonelye18 Loneliness
dxmdee18 MDE diagnosis
dxgade18 GAD diagnosis
cdmode18 CD diagnosis
sharme18 Self harm
suicate18 Suicide attempt
ser1e18 GP
ser2e18 Psychiatrist
ser4e18 Counsellor
neete18 NEET
educachve18 Highest qualification
smkcure18 Current smoking
anycrime18 Criminal offending
parente18 Early parenthood

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Data Security Agreement

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Proposing Author	Timothy Matthews
Today's Date	7th April 2020

Please keep one copy for your records
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TM I am familiar with the King's College London research ethics guidelines (https://www.kcl.ac.uk/innovation/research/support/ethics/about/index.aspx) and the MRC good research practice guidelines (https://www.mrc.ac.uk/research/policies-and-guidance-for-researchers/good-research-practice/).

TM My project has ethical approval from my institution.

TM I am familiar with the EU General Data Protection Regulation (https://mrc.ukri.org/documents/pdf/gdpr-guidance-note-3-consent-in-research-and-confidentiality/), and will use the data in a manner compliant with its requirements.

TM My computer is (a) encrypted at the hard drive level, (b) password-protected, (c) configured to lock after 15 minutes of inactivity, AND (d) has an antivirus client which is updated regularly.

TM I will treat all data as "restricted" and store in a secure fashion.

TM I will not share the data with anyone, including students or other collaborators not specifically listed on this concept paper.

TM I will not merge data from different files or sources, except where approval has been given by the PI.

TM 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 E-Risk Study cannot be shared because the Study Members have not given informed consent for unrestricted open access. Speak to the study PI for strategies for dealing with data sharing requests from Journals.

TM Before submitting my paper to a journal, I will submit my draft manuscript and scripts for data checking, and my draft manuscript for co-author mock review, allowing three weeks.

TM I will submit analysis scripts and new variable documentation to project data manager after the manuscript gets accepted for publication.

TM I will delete the data after the project is complete.

TM **For projects using location data:** I will ensure geographical location information, including postcodes or geographical coordinates for the E-Risk study member's homes or schools, is never combined or stored with any other E-Risk data (family or twin-level data)

TM **For projects using genomic data:** I will only use the SNP and/or 450K data in conjunction with the phenotypes that have been approved for use in this project at the concept paper stage.

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