Thoughts of self-harm in late adolescence as a risk indicator for mental disorders in early adulthood

Authors: David Mongan[1,2]*, PhD; Colm Healy[2,3], PhD; Emmet Power[2], MRCPsych; Jonah F. Byrne[2,4], BSc; Stan Zammit[5,6,], PhD; Ian Kelleher, PhD[7,8,9]; Mary Cannon[2], PhD; David R. Cotter[2,4], PhD.

1. Centre for Public Health, Queen's University Belfast, Northern Ireland
2. Department of Psychiatry, Royal College of Surgeons in Ireland, Dublin, Ireland
3. Department of Health Psychology, School of Population Health, Royal College of Surgeons in Ireland, Dublin, Ireland.
4. SFI FutureNeuro Research Centre, Royal College of Surgeons in Ireland, Dublin, Ireland
5. Centre for Academic Mental Health, Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom
6. Division of Psychological Medicine and Clinical Neurosciences, MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, United Kingdom
7. Centre for Clinical Brain Sciences, Division of Psychiatry, University of Edinburgh, Edinburgh, United Kingdom
8. School of Medicine, University College Dublin, Dublin, Ireland
9. St John of God Research Foundation, Stillorgan, Co. Dublin, Ireland

***Corresponding author:** Dr David Mongan, Centre for Public Health, Queen's University Belfast, Royal Victoria Hospital, Belfast, Northern Ireland.

E-mail: davidmongan@rcsi.ie

Keywords: self-harm, psychotic disorder, depressive disorder, generalised anxiety disorder, ALSPAC
Word count: 1238
Supplemental information: Tables 1 – 3; Figure 1

Early intervention for youth mental disorders has received increasing attention in recent decades. For psychosis, this is exemplified by the clinical high-risk (CHR) paradigm, which has been highly successful in defining a subpopulation at enhanced risk. However, criticisms include that the subpopulation captured by CHR services represents a small proportion of all psychosis cases,[1] highlighting the need for additional approaches to early detection of at-risk individuals.

Thoughts of self-harm are common in youth populations and are associated with several psychiatric outcomes. A recent Finnish registry study found that 18% of young people in Finland who presented to hospital with self-harm were diagnosed with a psychotic disorder by age 28,[2] suggesting that hospital presentation with self-harm may be a systems-based risk marker for psychosis. However, most individuals with self-injurious thoughts or behaviours do not present to hospital, and only a small proportion (4%) of future psychosis cases were captured.

Expanding on this approach, we examined whether having thoughts of self-harm in late adolescence (irrespective of hospital presentation) was a risk indicator for development of psychotic disorder, as well as depressive disorder and generalised anxiety disorder (GAD), in early adulthood. In exploratory secondary analyses, we also examined whether telling a General Practitioner (GP) about thoughts of self-harm was a risk marker for these disorders.

The sample was drawn from the Avon Longitudinal Study of Parents and Children (ALSPAC)[3-5] (http://www.bristol.ac.uk/alspac/researchers/access). Pregnant women in Avon, UK with expected delivery dates between 1st April 1991-31st December 1992 were invited to participate. 14,541 pregnancies were enrolled (13,988 children alive at 1 year of age). When the oldest children were approximately 7, an attempt was made to bolster the initial sample with eligible cases who did not join originally. The total sample size for analyses using data collected after age 7 is 15,447 pregnancies (14,901 children were alive at 1 year of age). Data were collected and managed using REDCap.[6,7] Ethical approval was obtained from ALSPAC Ethics and Law Committee and local research ethics committees. Informed consent for use of questionnaire and clinic data was obtained following recommendations of the ALSPAC Ethics and Law Committee at the time.

At the age 17 clinic, participants completed the Clinical Interview Schedule Revised (CIS-R).[8] This included a question asking whether the participant had thoughts of self-harm in the week prior to assessment. This was coded as a binary exposure variable indicating presence of thoughts of self-harm in the preceding week at age 17 (yes/no).

At the age 24 clinic, participants completed the semi-structured Psychosis-Like Symptoms Interview (PLIKSi) to assess for psychotic experiences.[9] Psychotic disorder was defined as having at least one definite psychotic experience (not attributable to sleep or fever) which recurred at least once per month over the previous six months, and was associated with severe distress, marked impairment of the participant's social or occupational functioning, or led them to seek professional help. We also examined outcomes of moderate/severe depressive disorder and GAD, defined according to ICD-10 criteria, based on responses to the CIS-R completed at the age 24 clinic.

Secondary analyses examined associations between telling a GP about thoughts of self-harm at age 17 in relation to the same outcomes at age 24. At age 17, where participants reported thoughts of self-harm, they were also asked if they had spoken to their GP about their thoughts (no; no, but has spoken to others; yes). This variable was recoded with four categories: no thoughts of self-harm; told no-one; told someone other than their GP; told their GP.

Primary analyses used logistic regression to evaluate associations between thoughts of self-harm at age 17 and psychotic disorder, depressive disorder and GAD at age 24. Secondary analyses used logistic regression to evaluate associations between telling someone about thoughts of self-harm at age 17 and the same outcomes at age 24. For all analyses, 'no thoughts of self-harm' was the reference category. For each analysis, participants who already met criteria for the relevant outcome at age 17 were excluded. In keeping with the predictive nature of this study, models were not adjusted for potential confounders. Analyses were performed using Stata 17 (StataCorp).

4563 participants attended the age 17 clinic and had data available on thoughts of self-harm (see supplemental information for sample characteristics). Following exclusion of participants who met outcomes criteria at age 17, the numbers of participants in each analytical sample were: 2591 for

psychotic disorder; 2622 for depressive disorder; and 2628 for GAD. The numbers of participants who reported thoughts of self-harm at age 17 in each analytical sample were: 267 (10.3%); 234 (8.9%); and 247 (9.4%) respectively.

Of 18 participants who met criteria for psychotic disorder at age 24, 8 (44.4%) had previously reported thoughts of self-harm at age 17. This compares to 34 of 157 (21.7%) among those with depressive disorder and 50 of 205 (24.4%) among those with GAD at age 24. Conversely, the absolute risk of psychotic disorder by age 24 among those with thoughts of self-harm at age 17 was 3.0% (odds ratio [OR] 7.15, 95% confidence interval [CI] 2.80–18.27), compared to 14.5% for depressive disorder (OR 3.19, 95% CI 2.12–4.78); and 20.2% for GAD (OR 3.64, 95% CI 2.57–5.17).

Secondary analyses provided evidence of associations between telling a GP about thoughts of self-harm at age 17 years and psychotic disorder (OR 19.34, 95% CI 5.11–73.24), depressive disorder (OR 14.42, 95% CI 6.20–33.53) and generalised anxiety disorder (OR 5.00, 95% CI 2.20–11.35) at age 24 (see supplemental information).

This study investigated whether endorsing thoughts of self-harm in late adolescence was a risk indicator for psychotic disorder, depressive disorder and GAD in early adulthood. The results suggest that a large proportion of those who develop these disorders, particularly psychotic disorder (44.4%), may be captured through screening for thoughts of self-harm in late adolescence. Conversely, of all those endorsing thoughts of self-harm at age 17, only 3% developed a psychotic disorder at age 24; 14.5% developed depressive disorder; and 20.2% developed generalised anxiety disorder. The simplicity of this approach is that it is based on a single reported symptom. However, in isolation, utility for defining an at-risk subgroup may be limited based on low positive predictive values. Nonetheless, the findings underscore the importance of appropriate long-term follow-up for young people with thoughts of self-harm in relation to distal mental health outcomes.

Secondary analyses indicated that presenting to a GP with thoughts of self-harm may be a particular indicator of risk for psychotic disorder in early adulthood, as well as depressive disorder and generalised anxiety disorder. This suggests a possible system-based approach for early detection in

primary care. However, these results should be viewed as preliminary and interpreted with caution given the small numbers of participants in the exposure category.

It is notable that effect estimates were highest for psychotic disorder compared to depressive disorder or GAD. However, confidence intervals overlapped, in keeping with the view that thoughts of self-harm in late adolescence may be a transdiagnostic risk marker. One possible explanation is that endorsement of thoughts of self-harm in late adolescence captures young people exposed to known transdiagnostic risk factors for future mental disorders, such as bullying and other forms of childhood adversity, socio-economic disadvantage and substance use problems. However, the aims of this study were predictive rather than explanatory, and causal inferences cannot be drawn. If confirmed in further populations, these findings suggest novel opportunities for early detection of young people at risk of mental disorders in early adulthood.

ACKNOWLEDGEMENTS

We are extremely grateful to all the families who took part in ALSPAC, the midwives for their help in recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses. The UK Medical Research Council and Wellcome Trust (Grant ref: 217065/Z/19/Z) and the University of Bristol provide core support for ALSPAC. This publication is the work of the authors and David Mongan will serve as guarantor for the contents of this paper. A comprehensive list of grants funding is available on the ALSPAC website (http://www.bristol.ac.uk/alspac/external/documents/grant-acknowledgements.pdf). Data collection for primary outcomes and exposures data used in this research was funded by the Medical Research Council (MR/M006727/1, MR/L022206/1 and G0701503/85179) and Wellcome Trust (08426812/Z/07/Z).

DM is a Fellow on the Irish Clinical Academic Training (ICAT) Programme which is supported by the Wellcome Trust and the Health Research Board (Grant Number 203930/B/16/Z), the Health Service Executive National Doctors Training and Planning and the Health and Social Care, Research and Development Division, Northern Ireland. MC is supported by a European Research Council Consolidator Award (iHEAR 724809). CH is supported by the Health Research Board (HRB ILP-PHR-2019-009). MC is supported by a European Research Council Consolidator Award (iHEAR 724809). DC is supported by the Wellcome Trust Flagship Innovations Program (IMPETUS - 220438Z/20/Z) and Health Research Board (HRB POR 2019-0005 and HRB ILP-2017-039). This publication has emanated from research supported in part by a research grant from Science Foundation Ireland (SFI) under Grant Number 16/RC/3948. SZ is supported by the NIHR Biomedical Research Centre at University Hospitals Bristol and Weston NHS Foundation Trust and the University of Bristol. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

CONFLICTS OF INTEREST

DM, MC and DRC report a patent pending (UK Patent Application No. 1919155.0, “Biomarkers to predict psychosis”). CH, EP, IK and SZ report no financial relationships with commercial interests.

SUPPLEMENTAL INFORMATION

Table 1: Sample characteristics

		Psychotic disorder sample, *n*=2591		Depressive disorder sample, *n*=2662		Generalised anxiety disorder sample, *n*=2628	
		Summary statistics	**Missing data, n (%)**	**Summary statistics**	**Missing data, n (%)**	**Summary statistics**	**Missing data, n (%)**
Age in years, mean (SD)		17.7 (0.3)	0 (0%)	17.7 (0.4)	0 (0%)	17.7 (0.4)	0 (0%)
Sex, n (%)	Female	1602 (61.8%)	0 (0%)	1628 (61.2%)	0 (0%)	1602 (61.0%)	0 (0%)
	Male	989 (38.1%)		1034 (38.8%)		1026 (39.0%)	
Ethnicity, n (%)	White	2286 (96.4%)	219 (8.5%)	2350 (96.4%)	224 (8.4%)	2311 (96.2%)	225 (8.6%)
	Non-white	86 (3.6%)		88 (3.6%)		92 (3.8%)	
BMI in kg/m^2 at age 17 years, mean (SD)		22.6 (4.1)	34 (1.3%)	22.6 (4.0)	46 (1.7%)	22.6 (4.1)	45 (1.7%)
Daily smoker at age 17 years, n (%)	No	2115 (90.1%)	243 (9.4%)	2172 (90.5%)	261 (9.8%)	2131 (90.0%)	260 (9.9%)
	Yes	233 (9.9%)		229 (9.5%)		237 (10.0%)	
AUDIT score at age 17 years, median (IQR)		7 (5)	429 (16.6%)	6 (5)	455 (17.1%)	6 (5)	448 (17.0%)
Regular cannabis use[1] at age 17 years, n (%)	No	2183 (94.1%)	272 (10.5%)	2234 (94.2%)	290 (10.9%)	2200 (94.0%)	288 (11.0%)
	Yes	136 (5.9%)		138 (5.8%)		140 (6.0%)	
In education or employment at age 17 years, n (%)	Yes	2223 (96.7%)	293 (11.3%)	2271 (96.7%)	314 (11.8%)	2271 (96.7%)	311 (11.8%)
	No	75 (3.3%)		77 (3.3%)		77 (3.3%)	
Home ownership status at 8 weeks gestation, n (%)	Own or mortgage	2091 (90.0%)	268 (10.3%)	2154 (89.9%)	267 (10.0%)	2123 (90.1%)	271 (10.3%)
	Rent or other	232 (10.0%)		241 (10.1%)		234 (9.9%)	
Highest parental social class at 32 weeks gestation, n (%)	Non-manual	2073 (89.6%)	278 (10.7%)	2123 (89.3%)	284 (10.7%)	2090 (89.2%)	286 (10.9%)
	Manual	240 (10.4%)		255 (10.7%)		252 (10.8%)	

Highest maternal educational qualification at 32 weeks gestation, n (%)	O-level or higher	2035 (84.9%)	193 (7.4%)	2091 (84.8%)	195 (7.3%)	2054 (84.5%)	196 (7.5%)
	Less than O-level	363 (15.1%)		376 (15.2%)		378 (15.5%)	

Summary statistics in this table relate to participants who: had thoughts of self-harm data available at age 17 years; did not meet criteria for the relevant outcome at 17 years; and had data available for that outcome at age 24 years.

AUDIT: Alcohol Use Disorders Identification Test; BMI: body mass index; IQR: interquartile range; PUFA: polyunsaturated fatty acid; SD: standard deviation; N/A: not applicable.

[1] Regular cannabis use was defined as using cannabis more than once monthly at age 17 and weekly or daily use at age 24.

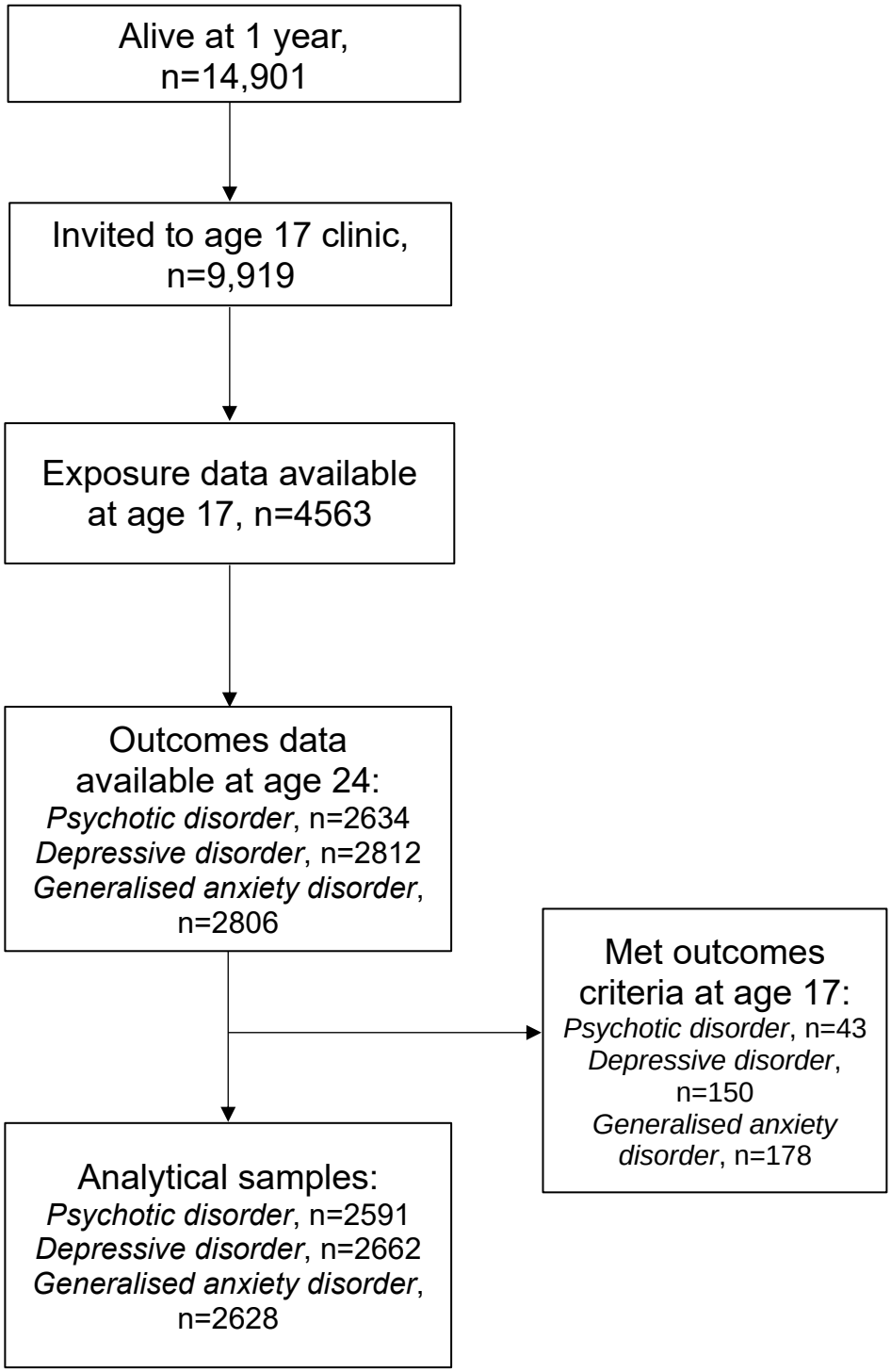
Table 2. Associations between thoughts of self-harm at age 17 years and mental disorders at age 24 years

Sample (total sample size)	***n* (%) with thoughts of self-harm at age 17**	***n* (%) with outcome at age 24**	**Odds ratio (95% confidence interval)**
Psychotic disorder sample (*n*=2591)	267 (10.3%)	18 (0.7%)	7.15 (2.80 – 18.27)
Depressive disorder sample (*n*=2662)	234 (8.8%)	157 (5.9%)	3.19 (2.12 – 4.78)
Generalised anxiety disorder (*n*=2628)	247 (9.4%)	205 (7.8%)	3.64 (2.57 – 5.17)

Table 3. Associations between telling someone about thoughts of self-harm at age 17 years and mental disorders at age 24 years

Outcome	**Exposure**	***n* with outcome**	**Odds ratio (95% confidence interval)**
Psychotic disorder	No thoughts of self-harm	10	[Reference]
	Told no-one	≤5	3.12 (0.68 – 14.35)
	Told someone other than GP	≤5	9.41 (2.54 – 34.91)
	Told GP	≤5	19.34 (5.11 – 73.24)
Depressive disorder	No thoughts of self-harm	123	[Reference]
	Told no-one	17	2.43 (1.42 – 4.16)
	Told someone other than GP	7	2.34 (1.05 – 5.25)
	Told GP	10	14.42 (6.20 – 33.53)
Generalised anxiety disorder	No thoughts of self-harm	155	[Reference]
	Told no-one	26	3.14 (1.99 – 4.94)
	Told someone other than GP	16	4.18 (2.34 – 7.46)
	Told GP	8	5.00 (2.20 – 11.35)

Figure 1: Derivation of study sample



References

1. Cotter D, Healy C, Staines L, Mongan D, Cannon M. Broadening the Parameters of Clinical High Risk for Psychosis. *Am J Psychiatry.* 2022;179(9):593-595.
2. Bolhuis K, Lång U, Gyllenberg D, et al. Hospital Presentation for Self-Harm in Youth as a Risk Marker for Later Psychotic and Bipolar Disorders: A Cohort Study of 59 476 Finns. *Schizophrenia Bulletin.* 2021;47(6):1685-1694.
3. Boyd A, Golding J, Macleod J, et al. Cohort Profile: the 'children of the 90s'--the index offspring of the Avon Longitudinal Study of Parents and Children. *Int J Epidemiol.* 2013;42(1):111-127.
4. Fraser A, Macdonald-Wallis C, Tilling K, et al. Cohort Profile: the Avon Longitudinal Study of Parents and Children: ALSPAC mothers cohort. *Int J Epidemiol.* 2013;42(1):97-110.
5. Northstone K, Lewcock M, Groom A, et al. The Avon Longitudinal Study of Parents and Children (ALSPAC): an update on the enrolled sample of index children in 2019 [version 1; peer review: 2 approved]. *Wellcome Open Research.* 2019;4(51).
6. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics.* 2009;42(2):377-381.
7. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. *Journal of Biomedical Informatics.* 2019;95:103208.
8. Lewis G. Assessing psychiatric disorder with a human interviewer or a computer. *Journal of epidemiology and community health.* 1994;48(2):207-210.
9. Horwood J, Salvi G, Thomas K, et al. IQ and non-clinical psychotic symptoms in 12-year-olds: results from the ALSPAC birth cohort. *The British journal of psychiatry : the journal of mental science.* 2008;193(3):185-191.