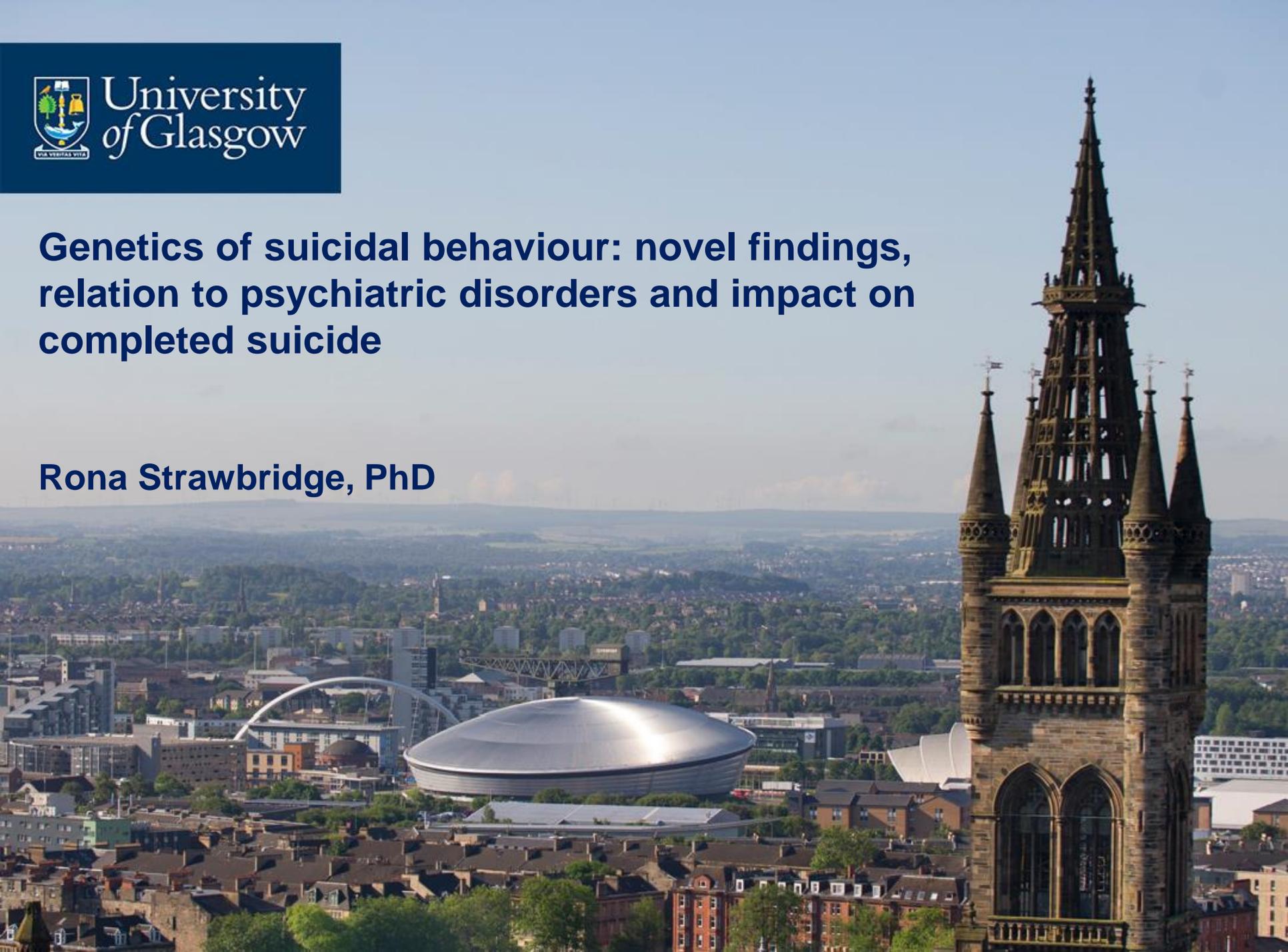


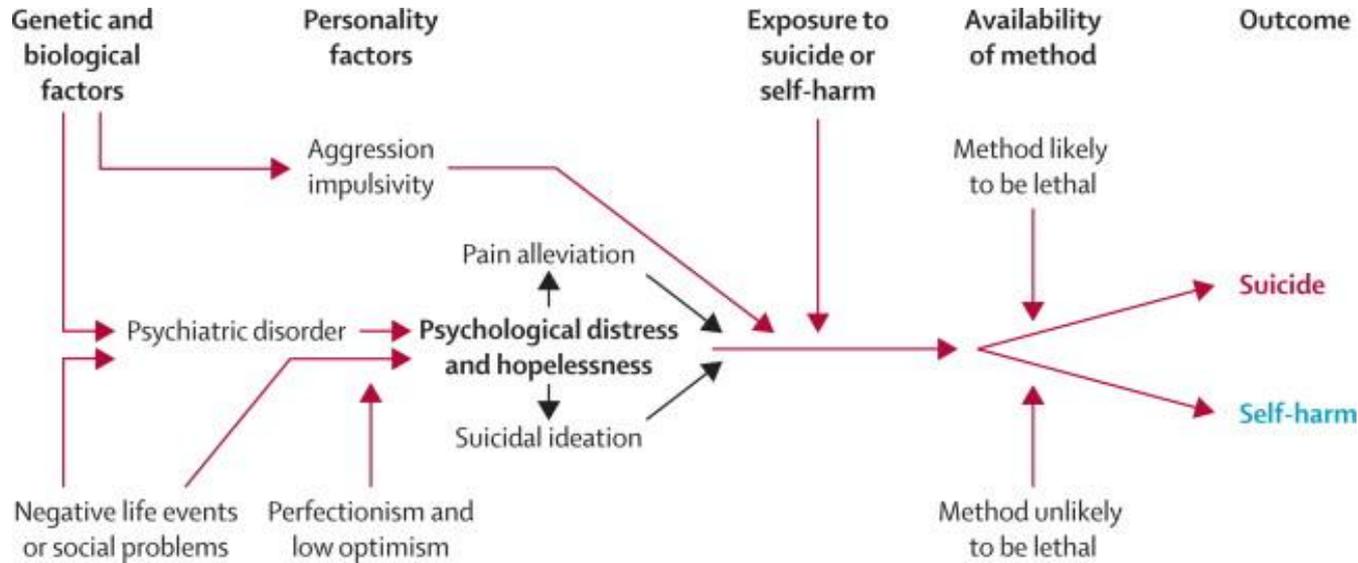
Genetics of suicidal behaviour: novel findings, relation to psychiatric disorders and impact on completed suicide

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Background:

- Suicide is a major (and growing) issue for global health
- ‘Suicidality’ encompasses a broad range of experiences and behaviours
 - features in multiple psychiatric diagnoses
 - Some behaviours occur without psychiatric diagnosis and/or in sub-clinical mental illness
- Heritability estimates for suicidal behaviour: 38–55%



No suicidality

Contemplated self harm

Suicidal ideation
Actual self-harm

Attempted suicide

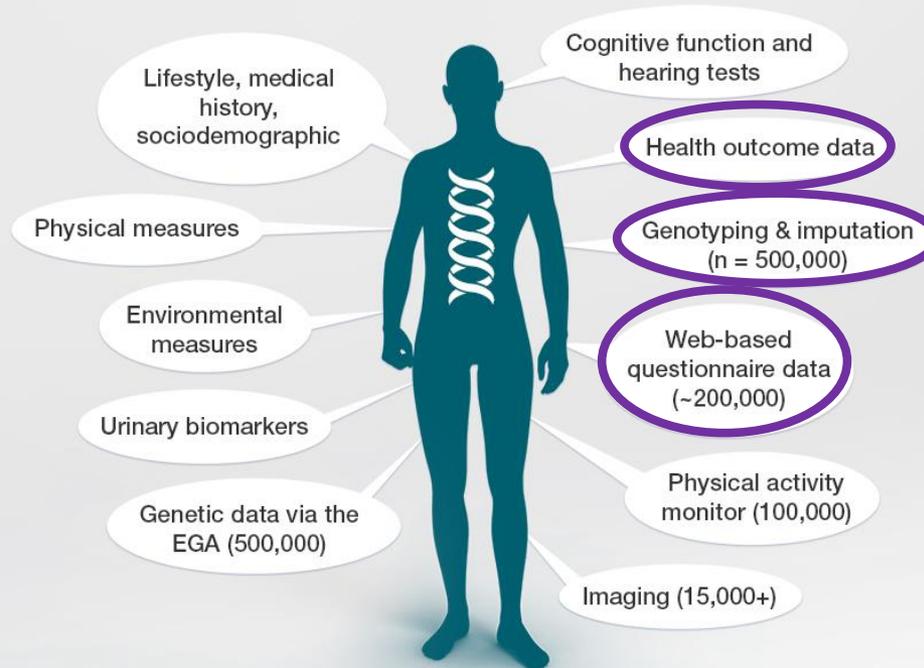
Completed suicide

Our goals:

1. To identify genetic variants associated with suicidality in a general population, specifically UK Biobank
2. To assess overlap between genetic regulation of suicidality and a range of psychiatric disorders
3. To determine whether genetic burden for suicidality associates with completed suicide



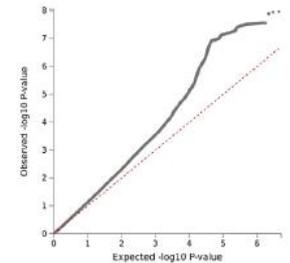
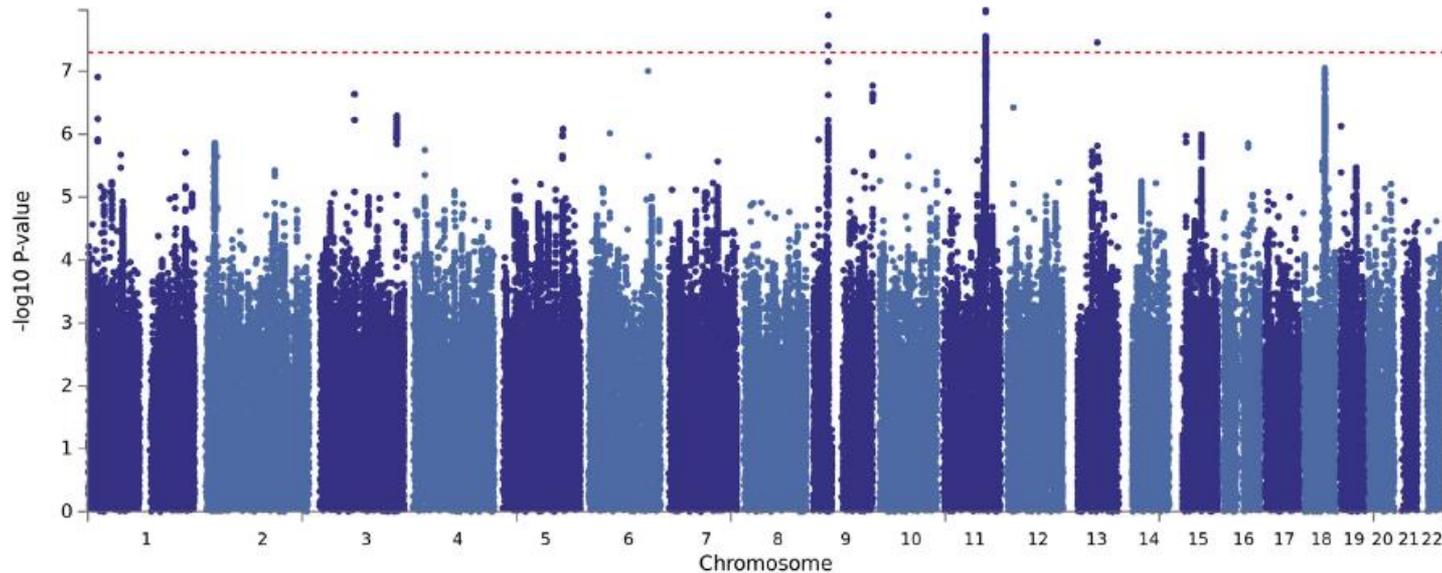
Data on UK Biobank participants



Suicidality phenotypes:

- From the online “*Thoughts and Feelings*” questionnaire:
 - No suicidality controls (N=83,557)
 - Thoughts that ‘life was not worth living’ (N=21,063)
 - Ever contemplated self-harm or suicide (N=13,038)
 - Acts of deliberate self-harm, not including attempted suicide (N=2,498)
 - Ever attempted suicide (N=2,666)
 - Analysis in unrelated individuals of white British ancestry
- From linked death certification records:
 - Completed suicide (N=127)
 - Controls were those excluded from the primary analysis because of relatedness

1. Ordinal GWAS of Suicidality:



Analysis	SNP	CHR	POS	A1	A2	BETA	SE	P	A1F ²
Ordinal suicidality	rs62535711	9	37,174,829	T	C	0.105	0.018	1.29E-08	0.056
	rs598046	11	99,516,468	T	G	0.053	0.009	1.07E-08	0.319
	rs7989250	13	64,900,801	A	C	-0.052	0.009	3.49E-08	0.322

2. Genetic correlation between suicidality and psychiatric disorders and related traits:

Trait	Suicidality				
	r_g	se	z	p	FDR-P
Attempted suicide	0.57	0.096	5.98	2.23E-09	6.24E-09
MDD	0.81	0.04	18.66	1.01E-77	1.41E-76
Neuroticism	0.63	0.04	16.48	5.51E-61	3.86E-60
Mood Instability	0.50	0.03	16.06	4.53E-58	2.11E-57
Schizophrenia	0.32	0.04	8.70	3.19E-18	1.12E-17
Bipolar disorder	0.27	0.05	5.28	1.26E-07	2.94E-07
Risk-taking behaviour	0.20	0.04	5.05	4.44E-07	7.77E-07
Anxiety disorder	0.75	0.17	4.35	1.38E-05	2.15E-05
ADHD	0.21	0.05	4.29	1.79E-05	2.51E-05
PTSD	0.42	0.16	2.70	6.97E-03	8.87E-03

3. Association between PRS for suicidality and completed suicide:

Threshold	OR	L95	U95	<i>P</i>	FDR-adj <i>P</i>
5×10^{-8}	1.07	-0.10	0.24	0.410	0.410
5×10^{-5}	1.20	0.01	0.35	0.041	0.049
0.01	1.22	0.02	0.38	0.026	0.390
0.05	1.26	0.05	0.41	0.011	0.034
0.1	1.27	0.06	0.42	0.008	0.034
0.5	1.25	0.03	0.41	0.021	0.039

Genes of interest within associated loci:

- *CNTN5*: **Contactin 5**, a glycosylphosphatidylinositol-anchored extracellular cell adhesion protein of the immunoglobulin superfamily; may have a role in the formation and maintenance of brain circuitry
- *CEP57*: **Centrosomal protein of 57 kDa**, important for cell division; loss-of-function variants cause a mosaic variegated aneuploidy syndrome, with brain abnormalities and mental retardation
- *DCC*: **Netrin 1 receptor**, has been robustly associated with depression, schizophrenia and related traits

Conclusions:

- Novel approach identified 3 regions of the genome associated with the suicidality spectrum
- Several new candidate genes were identified. Further study of these will aid understanding the biology of suicide
- Demonstrated (incomplete) overlap with genetics of psychiatric disorders
- Association between genetic loading for suicidality and completed suicide

Future work:

- Extend these efforts by including additional datasets
 - Actively seeking collaborations!
- Relevance to suicidal behaviour in adolescents
 - Additional variants involved in suicidal behaviour in early life?
- Can addition of genetics* improve performance of suicide prediction models?
 - *suicidality, risk-taking, neuroticism, mood instability...
- Further investigation of the loci highlighted here

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Thank you



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