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Commentary

The co-occurrence of smoking and suicide†

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Summary

This article is an invited commentary on a recent article by Harrison et al. investigating the purported causal link between smoking behaviours and suicide attempts.

Keywords

Mendelian randomisation; suicide; smoking; genetics; epidemiology.

For many decades, preventing death from suicide has been an important focus in mental health research. Hence, researchers have aimed to find causal risk factors, which could inspire improvements of suicide intervention strategies. In this issue of the *British Journal of Psychiatry*, Harrison et al[1] examined whether tobacco smoking is a causal risk factor for potentially fatal behaviours such as suicidal ideations or attempts. Their aim was to triangulate the available evidence by testing for observational associations and causality. The latter was done with genetically informed approaches, including Mendelian randomisation and single nucleotide polymorphism (SNP) logistic regression models. Mendelian randomisation is a technique where SNPs are used as instrumental variables to investigate causal directionality of associations, using observed data. There are many important assumptions to consider when conducting Mendelian randomisation, which are explained in the article. Triangulating evidence beyond observational results by using genetic variants decreases the likelihood of residual confounding, reverse causality and thus improving causal inference.

Harrison et al observed cross-sectional associations of all self-reported smoking behaviours with suicide attempts and ideation in 45 825–109 688 UK Biobank participants.[1] Analyses were adjusted for age, gender and socioeconomic status. The strongest association was observed between smoking initiation and suicide attempt (odds ratio, 2.07; 95% CI 1.91–2.26; $P < 0.001$). Various methods of Mendelian randomisation were conducted to further explore the causal direction of this phenotypic cross-sectional relationship. They performed Mendelian randomisation with summary-level data-sets from published genome-wide association studies (using five complementing methods), individual-level data from UK Biobank and single SNP analyses (using an SNP in the CHRNA5-A3-B4 gene cluster, known to be strongly associated with heaviness of smoking). Mendelian randomisation approaches using summary-level results revealed some evidence for a causal effect of smoking initiation on suicide attempts. Subsequently, individual-level Mendelian randomisation or single SNP regression models did not yield any evidence for a causal association.

Although there was support for a phenotypic relationship between smoking behaviours and suicidality, genetically informed methods yielded no strong support for a causal effect of smoking on suicide attempt or suicidal ideation. Furthermore, >50% of the SNPs in the genetic instrument explained more variance in the outcome (i.e. suicide attempts) than in smoking initiation (see Supplementary Table 3 in Harrison et al[1]), which increases the likelihood of reverse causation. Follow-up analyses suggested that risk-taking behaviour, which is well known to affect both substance use and (auto-)aggressive behaviours,[2] might underlie the association between smoking and suicidality. This bidirectional relationship between smoking and risk-taking challenges the value of using this genetic instrument as a proxy for smoking initiation. Several previous Mendelian randomisation studies on smoking behaviours have included similar genetic instruments as the current study.[3] It would be valuable to place more emphasis on variable definition and the validity of a genetic instrument in future Mendelian randomisation studies before drawing firm conclusions on causality. There is a great need for reporting guidelines for Mendelian randomisation studies to improve the quality of the evidence.[4]

Studying causal risk factors for suicide and self-harm is notoriously complex, and treatment trials aimed at modifiable risk factors have been underpowered to unambiguously demonstrate a reduction of the incidence of suicide and self-harm.[2] The present study by Harrison et al is no exception: tobacco smoking had no causal effect on suicidal ideation and self-harm.[1] Instead of focussing on modifiable risk factors, perhaps suicide prevention research should shift from causal frameworks to prediction. Unfortunately, although suicide prediction models have overall very good accuracy, their predictive validity of correctly classifying a suicide death is near zero, i.e. extremely poor.[5] This can largely be explained by the low base rate of suicide death in the general population. Potentially, more common phenotypes across the suicide/self-harm continuum, such as suicidal ideation and (intentional or non-intentional) self-harm, have greater potential to assess in prediction studies. It is, however, important to acknowledge here that there is a clear lack of effective evidence-based interventions to treat patients at risk of suicide and repeated self-harm,[2] raising important ethical questions warranting further exploration.

Although reducing tobacco smoking across the population will probably not result in a reduction of self-harm or suicide, tobacco should nonetheless still be treated and discouraged, to stop the tobacco epidemic causing 8 million deaths a year worldwide. Individuals who survive self-harm are at elevated risk for many poor outcomes later in life, not only death from suicide, including serious psychopathology and repeated self-harm. Future efforts should focus on how to identify vulnerable individuals and offer them the proper mental healthcare. Developing evidence-based interventions following self-harm should be a top priority.

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Author contributions

Both authors contributed equally to the study design and writing of this article.

Declaration of interest

None.

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psychiatry in literature

An almost preventable suicide: Walter Benjamin (15 July 1892–26 September 1940)

George Ikkos

Walter Benjamin was a radically innovative cultural theorist and a German Jewish Marxist, securing refuge in France in 1933. Following the 1940 Nazi invasion he fled France, bound for the USA. However, on the mountainous approach to the French–Spanish border he realised dictator Franco had suddenly blocked transit. Benjamin was in ill health and struggling to carry a briefcase with a heavy manuscript, which he declared more precious than his life. Sadly, he completed suicide: there was family history on his father's side.

Benjamin maintained a fiercely productive focus on his intellectual mission throughout his life, despite repeatedly complaining of 'grand-scale defeats' and lows. After his request for divorce from Dora Pollak was granted in 1932, he suffered 10 paralysing days during which he seriously prepared suicide. Suicidal thoughts endured. He was an elegant, cultivated man who oozed old-world charm, exerting attraction on women but not always enough to marry him. Asja Lacis, the Latvian Communist Director of Children's Theatre in the USSR, twice refused, as did later lover Anna Maria Blaupot ten Cate. Lacis suffered relapsing mental illness and was hospitalised with hallucinations when Benjamin rushed to Moscow in 1926, at the brink of Stalinisation. His luminous *Moscow Diary* records his frustrating two-month experience.

Benjamin's luscious *Berlin Childhood around 1900* recalls his experience of the city's material culture as a boy. His family was commercially successful but relations with his parents and sister were poor, although he had a better relationship with his younger brother, who died in a concentration camp. His bleak verdict on school life contrasted with that of his schoolmate Gershom Scholem, who become Professor of Jewish Mysticism at the newly established Hebrew University of Jerusalem. Benjamin impressed some as reserved, discreet and modest, others as oversensitive and uncompromising.

He maintained a life-long friendship with Scholem. A feature of Benjamin's unorthodox Marxism was his attempt to invest it with the passions of Messianic Jewish mysticism. He was also friends with Theodor Adorno, a critical social theory pioneer who was deeply influenced by Benjamin and helped preserve his legacy. Adorno remarked that Benjamin's work had 'settled at the cross-roads between magic and positivism. That place is bewitched'.

Benjamin revolutionised text, image and film criticism. His essay 'Hashish in Marseilles' confirms that he experimented with drugs ('under medical supervision'). He argued that reawakening the long-forgotten dreams of childhood could help recover the betrayed potential of technological progress, in the service of humanity's 'redemption' in this life. He collected children's books and recorded attentively the development of his son Stefan like his contemporary Piaget, especially sensation, imitation, gestures and spontaneity. This is from his celebrated modernist short pieces collection *One Way Street*:

> 'A child in his nightshirt cannot be prevailed upon to greet a visitor. Those present, invoking a higher moral standpoint, admonish him in vain to overcome his prudery. A few minutes later he reappears, now stark naked, before the visitor. In the meantime, he has washed'.

The precious manuscript was lost together with Benjamin's life. Shortly thereafter, Franco reopened the border and collaborationist Vichy French authorities rescinded deportation orders to Germany. I share this tragic story of almost preventable loss with suicidal patients; and it has made a difference.

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