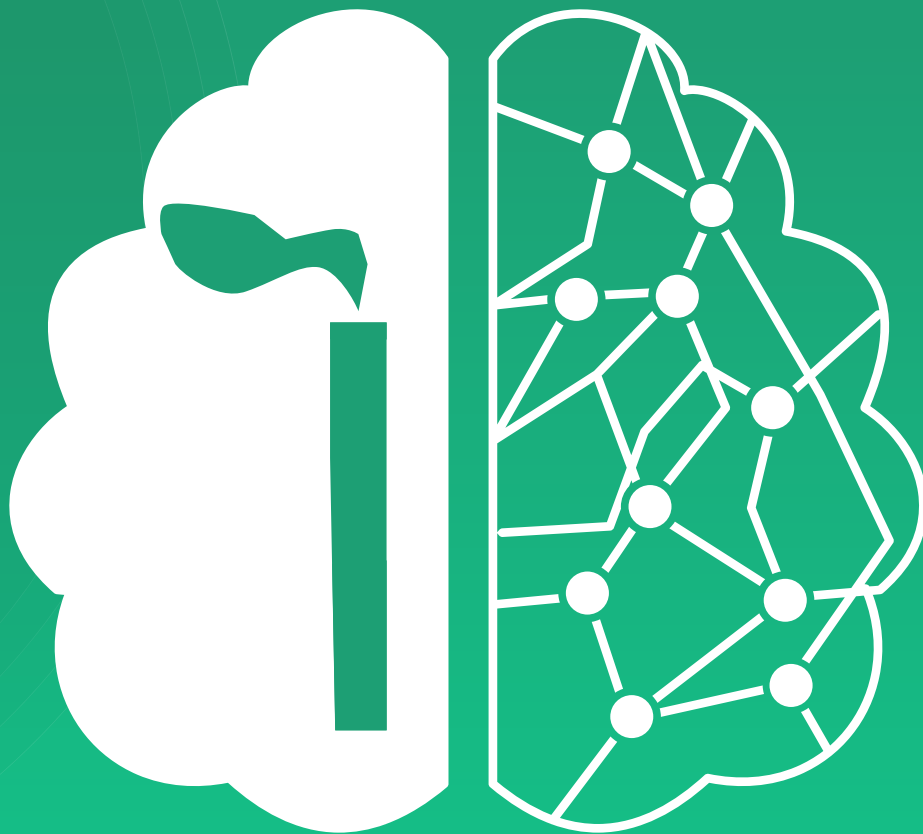# Is there a causal effect of smoking on mental health?

A summary of the evidence

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Executive Summary

In this report, we summarise evidence around two key questions about smoking and mental health: 1) does smoking increase the risk of subsequent mental health problems, and 2) does quitting smoking improve mental health symptoms. Establishing whether or not these are true causal effects will help to better target successful public health policies and to hopefully increase life expectancy and improve health amongst individuals with mental illness.

There is a large body of longitudinal research that finds strong evidence for a prospective association between smoking and mental health, in particular for depression, anxiety and schizophrenia. However observational studies can be biased by residual confounding and reverse causation, and we cannot rule out prodromal symptoms of mental illness leading individuals to start smoking. These studies can be complemented by the method of Mendelian randomisation which has different assumptions and sources of bias (see Box 1). Therefore, consistent evidence across these methods can allow us to draw stronger causal conclusions. Evidence from observational and Mendelian randomisation studies suggest an effect of smoking on both depression and schizophrenia (see section 2.1 and 2.2). However, evidence from co-twin control studies indicates that the association with depression is likely due to shared genetics (see section 2.3). Overall, the evidence seems stronger for an effect of smoking on schizophrenia than for depression or bipolar disorder. Evidence for an association with other mental health conditions (ADHD, anorexia nervosa, suicidal ideation, psychological distress) is weaker still. While these studies show potentially interesting findings, more evidence using alternative study designs is required.

Although Mendelian randomisation studies suggests that smoking behaviours are causal for some mental health outcomes, there is a high degree of bidirectionality in these relationships. This presents the possibility of a vicious cycle of bidirectional effects, whereby having symptoms of mental illness causes individuals to smoke more and to be more susceptible to dependence. At the same time, smoking also increases the risk of subsequent mental illness and exacerbates mental health symptoms.

Overall, there is evidence to suggest a causal effect of smoking on mental illness, in particular for schizophrenia. This body of evidence provides support for public health tobacco control policies, especially those aimed at individuals with a high risk for or with existing mental illness. Smoking cessation interventions for individuals with severe mental illness certainly do not worsen mental health symptoms and may improve them in the long term (see section 3.1).

Key messages

- There is a large body of longitudinal research that finds strong evidence for a prospective association between smoking and mental health, this focuses on depression, anxiety and schizophrenia.

- Much of the evidence from Mendelian randomisation studies suggests that smoking behaviours have a detrimental causal effect on mental health. However, there is a high degree of bidirectionality in these relationships.

- However, evidence from discordant twin studies and negative control studies indicates that smoking and mental health share underlying genetic liability which could be biasing results.

- Smoking cessation interventions for individuals with mental illness do not worsen mental health symptoms and may improve them in the long term.

1.Introduction

Smoking is the leading cause of preventable deaths worldwide,[1] with smokers dying on average 10 years earlier than non-smokers.[2] Smoking is highly prevalent amongst individuals with mental illness.[3–6] In the UK, an estimated 33% of individuals with any mental disorder smoke,[7] compared with around 15% of the general population,[8] and individuals with mental illness make up around one third of adult tobacco consumption.[9] For some severe mental illness, rates are even higher (Figure 1). Recent developments in tobacco control policies have reduced smoking rates in the general population, however, rates remain high among people with mental illness.[7] As a result, these individuals die on average 10-20 years earlier than the general population.[7,9,10]

Figure 1. Smoking rates among individuals with mental illness[7]
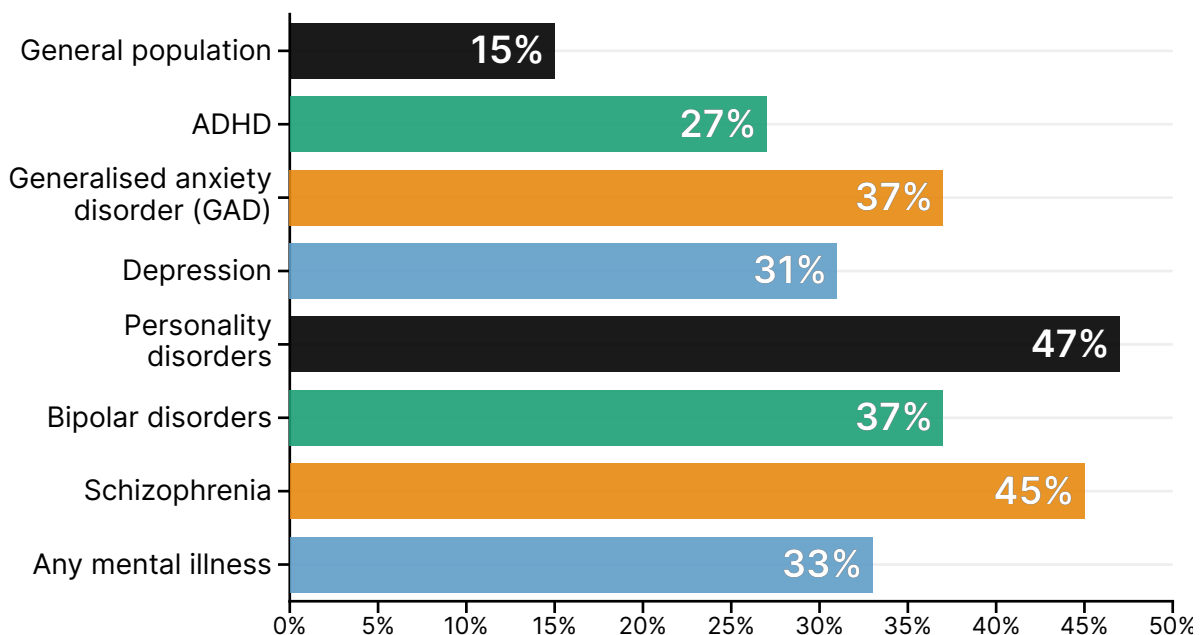
Self-medication is one possible explanation for the high rates of smoking amongst individuals with mental illness. The self-medication hypothesis suggests that symptoms of mental illness, (or side effects of psychiatric medications) are alleviated by the chemical properties of tobacco.[11–14] However, there is a growing body of evidence to suggest that smoking may be a causal risk factor for mental illness and that quitting smoking may be highly beneficial for long term mental health outcomes.

In this report, we synthesise the evidence, in particular drawing upon methodologies that promote stronger causal inference. We consider two aspects:

• Does smoking cause mental illness - we review longitudinal evidence to ensure that smoking preceded mental illness.

We complement this with alternative study designs that use genetic information.[15]

This section of the review considers the potential public health impacts of reducing smoking initiation and heaviness (pages 7-11).

- Does quitting smoking improve mental health – we review randomised controlled trials of smoking cessation.

This section considers the potential public health impacts of helping individuals with mental illness to quit (page 12).

1.

2.Does smoking cause mental illness?

2.1 Longitudinal studies of smoking on the development of mental illness

In observational epidemiology it is not always clear whether smoking or mental illness occurs first. In an attempt to ensure that smoking exposure preceded the diagnosis of mental illness, we only review longitudinal studies which have a clear temporal sequence. We include both cohort and case-control studies of multiple smoking behaviours. All evidence reviewed is from systematic reviews or meta-analyses of multiple other studies, helping to improve the generalisability of results across populations.

2.1.1 Depression and anxiety
We identified two meta-analyses and one systematic review of longitudinal studies of smoking on depression and/or anxiety. The meta-analyses included a combination of depressive symptoms or diagnostic criteria for depression and followed up participants for between 1-6 years.[16,17] Chaiton and colleagues[16] focused on adolescents (aged 13-19 years; N=15,333), while Luger and colleagues[17] included adults (aged 18 years or over; N=52,568). Luger and colleagues[17] compared current smokers to never smokers, while Chaiton and colleagues[16] compared not smoking at baseline to smoking at baseline. Definitions of smoking ranged between one puff to three or more cigarettes per week. Despite the studies having disparate definitions of smoking, they both found evidence for a similar effect of smoking status on subsequent depression. In both studies smokers were found to have around 60-70% increased odds of developing depression compared to non-smokers (OR_{Luger}=1.62, 95% CI: 1.1 to 2.4; $OR_{Chaiton}$=1.73, 95% CI: 1.32 to 2.4).

Fluharty and colleagues[18] conducted a systematic review of smoking on diagnoses of depression and/or anxiety (Depression: 51 studies, Anxiety: 5 studies, Comorbid depression/anxiety: 10 studies), with sample sizes ranging from 59 to 90,627. Smoking behaviours included smoking status, heaviness, tobacco dependence and trajectories of tobacco use. Studies varied in terms of populations sampled which introduced substantial heterogeneity into the review, making a meta-analysis inappropriate. Results were inconsistent across studies, with only a third suggesting evidence of a relationship between smoking behaviour and later depression and anxiety.

However, it is worth noting that both Chaiton and colleagues[16] and Fluharty and colleagues[18] also investigated effects in the opposite direction (from depression and/or anxiety to smoking). Chaiton and colleagues[16] found evidence of an effect in this direction (OR=1.41, 95% CI: 1.21 to 1.63) and nearly half of the studies in Fluharty and colleagues' review[18] suggested that baseline depression or anxiety were associated with later smoking behaviours.

2.1.2 Schizophrenia and non-affective psychosis
We identified two meta-analyses and a systematic review exploring smoking and subsequent schizophrenia and psychosis risk. Both meta-analyses found evidence for a substantial increased risk of schizophrenia or psychosis amongst smokers compared to non-smokers.[19,20]

Hunter and colleagues[20] meta-analysed 5 prospective studies (N=1,783,251) followed up for between 4 and 40 years and found that smokers had around a two-fold increased risk of a diagnosis of schizophrenia (RR = 1.99, 95% CI: 1.10 to 3.61). Gurillo and colleagues[19] meta-analysed 11 case-control and 5 prospective studies (N=287,717) of patients with first episode psychosis comparing smokers with non-smokers. For both case-control (OR=3.22, 95% CI: 1.63 to 6.33) and prospective studies (RR=2.18, 95% CI: 1.23 to 3.85), there was strong evidence of an increased risk of psychosis among smokers.

Scott and colleagues[21] performed a systematic review of 8 studies (7 cohort studies, 1 case-control) to explore the longitudinal association between smoking and schizophrenia spectrum disorders. This review built upon the methodology used by Hunter and colleagues[20] and Gurillo and colleagues[19] and all studies included were rated as high-quality evidence. Estimates ranged from a 1.5 to 6-fold increased risk of schizophrenia spectrum disorders in heavy smokers. They were unable to perform a meta-analysis, however, six studies demonstrated a positive association, one a negative association and the final study (case-control) showed no association.

2.1.3 Other mental illness
To the best of our knowledge, there have not been any meta-analyses of the longitudinal relationship between smoking and subsequent incidence of other mental illness.[22]

2.1.4 Summary of longitudinal observational research
Across these meta-analyses there is evidence that smoking is associated with subsequent mental health problems, in particular depression and schizophrenia. However, we cannot establish causality based on observational findings alone. To ensure public health policies are effective in preventing future cases of depression and schizophrenia, we need to establish whether there is a causal effect of smoking. Findings from traditional observational epidemiological studies may be subject to bias from reverse causation (for example, through unmeasured prodromal symptoms leading individuals to initiate smoking) and residual confounding (for example, through other unmeasured behaviours that influence both smoking and mental health).

In the following section, we review evidence that uses an approach that is more robust to the issues of reverse causation and residual confounding (Mendelian randomisation).

2.2 Mendelian randomisation studies of smoking on mental health

The gold standard approach to determine causality would be to conduct a randomised controlled trial (RCT). However, for smoking behaviours, it is unethical to randomise individuals to smoke given the adverse physical health consequences.[23] Mendelian randomisation (MR) is a popular complementary method which can reduce bias due to reverse causation and residual confounding using genetic variants (Box 1).

Box 1. The Mendelian randomisation method and genetic instruments for smoking

Mendelian randomisation: Through genome-wide association studies, genetic variants have been identified that pre-dispose individuals to certain smoking behaviours.[24,25] These genetic variants can be used as an instrument to test causal effects of the exposure (smoking) on an outcome (e.g., depression), given certain assumptions are satisfied.[26] Genetic variants that alter our average lifetime levels of smoking behaviours are randomised at conception and inherited independently of confounding lifestyle factors. This is akin to a natural experiment, and the genetic variants are less likely to be biased by confounding and reverse causation than observed exposures.[27] Accounting for reverse causation is particularly important when exploring the relationship between smoking and mental health, given the high likelihood of a bidirectional relationship. MR analyses can provide causal estimates, as long as the underlying assumptions are satisfied.[26]

Smoking instruments: Mendelian randomisation studies of smoking use different genetic instruments depending upon the particular smoking behaviour of interest. Earlier studies of smoking heaviness tend to use a single genetic variant in the *CHRNA5-A3-B4* gene cluster which affects nicotine response. Smokers with one version of this genetic variant smoke on average one more cigarette per day than smokers who do not.[28] This genetic instrument is a powerful tool because we understand the underlying biological mechanism, and we can compare the effect of this variant on mental health in smokers and non-smokers. A causal effect of smoking on mental health would be detected only in the smoking group, and not in the never smokers. However, this genetic instrument can lack statistical power and requires knowledge about whether or not the individuals currently smoke. An alternative instrument is to use genetic variants associated with smoking initiation (comparing ever with never smokers) or to use genetic variants associated with lifetime smoking (combined smoking initiation, heaviness, duration and cessation). These latter genetic instruments have high statistical power, but caution must be taken as the biological mechanisms are less well understood.

Limitations: Despite numerous benefits, there are also several limitations to the MR method, some of which are even more pronounced when exploring behavioural and psychological traits like smoking and mental health. These specific limitations have been discussed in detail elsewhere.[23] Here we briefly discuss some important limitations to consider for smoking and mental health. First, the relationship between smoking and mental health is plausibly bidirectional, which can make interpretation of MR results difficult. Second, MR studies predominantly use genetic variants from individuals of European ancestry and therefore, results might lack generalisability to other populations, especially due to geographical differences in smoking behaviours. Third, we do not know the biological mechanisms underlying the genetic instruments associated with smoking initiation and lifetime smoking. Therefore, we cannot rely on these genetic variants alone and the strongest evidence for causal effects will come from comparing results across different research methodologies.[15]

2.2.1 Depression and anxiety

We identified a total of six MR studies that explored possible causal effects of smoking on depression and anxiety. The first four of these studies used the single genetic variant for smoking heaviness located in the *CHRNA5-A3-B4* gene cluster (see Box 1 for details). None of these studies found evidence for a causal effect of smoking on depression.[29–32] Bjørngaard and colleagues[29] found some evidence for an association between smoking and anxiety. However, when stratified into current smokers, former smokers and never smokers, there was stronger evidence for an association in the former and never smokers. This suggests that this association is not due to causal effects of smoking.[29] However, these studies are likely lacking in statistical power due to the use of the single genetic instrument and some small sample sizes. The two most recent MR studies of smoking on depression used the more powerful genetic instruments for smoking initiation and lifetime smoking. Wootton and colleagues[33] found evidence for a causal effect of both smoking behaviours on depression ($OR_{smoking\ initiation}$=1.54,

95% CI: 1.44 to 1.64; $OR_{lifetime\ smoking}$ =1.99, 95% CI: 1.71 to 2.32). Barkhuizen and colleagues[34] also found evidence for an effect of smoking initiation on risk for depression (OR = 1.54, 95% CI: 1.27 to 1.88).

In the reverse direction, Wootton and colleagues[33] found some, although weaker, evidence that genetic risk for major depression was associated with increased smoking behaviours. Barkhuizen and colleagues[34] found no evidence in the reverse direction.

2.2.2 Schizophrenia and non-affective psychosis
We identified a total of five MR studies of smoking on schizophrenia risk. Using the single genetic variant for smoking heaviness located in the *CHRNA5-A3-B4* gene cluster, there was an association with schizophrenia risk in a psychiatric sample (OR=1.60, 95% CI: 0.74 to 3.47) but not in a Danish population sample (OR=1.22, 95% CI: 0.84 to 1.79). However, this Danish sample had a very small number of schizophrenia cases (N=57), and there was evidence for an effect on antipsychotic medication use (N=2,795 cases) (OR=1.16, 95% CI: 1.02 to 1.31).[32] Using an older genetic instrument for smoking initiation, there was no robust evidence for an association with schizophrenia risk, however statistical power was limited.[35] Using more recent genetic instruments for smoking initiation, two studies found evidence for an effect ($OR_{Wootton}$=1.53, 95% CI: 1.35 to 1.74; $OR_{Barkhuzien}$ = 1.94, 95% CI: 1.37 to 2.76). Wootton and colleagues[33] also found evidence for an effect of lifetime smoking on schizophrenia risk (OR=2.27, 95% CI: 1.67 to 3.08). Finally, a study exploring schizophrenia as a risk factor for breast cancer included a sensitivity analysis which explored the effect of smoking heaviness on schizophrenia. They found evidence for a causally increasing effect.[36]

Gage and colleagues[35] found no strong evidence of effects in the reverse direction, from schizophrenia liability to smoking initiation. Two recent studies found evidence for causal effects in this direction, although estimates appeared smaller than for smoking on schizophrenia.[33,34.]

2.2.3 Other mental illness
We identified two MR studies exploring the effect of smoking on risk for bipolar disorder.[34,37] Both found evidence for a causal effect of smoking initiation on bipolar disorder risk ($OR_{Vermeulen}$ = 1.46, 95% CI: 1.28 to 1.66; $OR_{Barkhuizen}$ = 2.46, 95% CI: 1.68 to 3.61). Vermeulen and colleagues[37] additionally explored the effect of lifetime smoking on bipolar risk, again finding evidence for a causal effect (OR = 1.72, 95% CI: 1.29 to 2.28). Neither study found any clear evidence for effects in the opposite direction.

We identified one MR study exploring the effects of smoking on ADHD. This focused on cases of ADHD diagnosed in adulthood, after age 18 years.[38] Using the most recent genetic instruments for smoking initiation they found an increased risk of ADHD (OR=3.72, 95% CI: 3.10 to 4.44), and there was evidence for an effect in the opposite direction. However, the genetic variants for smoking initiation also predicted ADHD diagnosis before the age of 13 years, which is before most individuals initiate smoking. This suggests that the detected effects are unlikely to be the result of a causal effect of child's own smoke exposure.

We identified two MR studies exploring the effect of smoking heaviness on psychological distress.[31,39] Neither study found clear evidence for a causal effect.

We identified one MR study each for the association between smoking and 1) anorexia nervosa[40] and 2) suicidal ideation and attempts.[41] Neither of these studies found clear evidence for a causal effect when combining across multiple genetic instruments for smoking behaviours. Finally, we identified two MR studies investigating the association between smoking behaviours and loneliness. Harrison and colleagues[42] found no clear evidence of an effect, while Wootton and colleagues[43] found strong evidence that smoking initiation increases loneliness (β= 0.30, 95% CI = 0.22 to 0.38). In the reverse direction, there was weak evidence for a causal effect of loneliness on increased smoking initiation and heaviness, and weak evidence for an effect of loneliness on decreased smoking cessation.[43]

2.2.4 Summary of Mendelian randomisation research
Mendelian randomisation results were inconsistent depending on which genetic instrument was used. Findings most strongly indicated a causal effect when using recent instruments for smoking initiation and lifetime smoking. The single genetic variant for smoking heaviness often did not suggest a causal effect. The effect of smoking initiation could be acting via personality and behavioural pathways. Overall, the evidence seems stronger for an effect of smoking on schizophrenia than for depression.

Although MR can be a powerful tool, it is subject to limitations (see Box 1 for details). The strongest evidence for causal effects will come from comparing results across different research methodologies.[15] In the following section, we review studies that use alternative genetically informed designs.

2.3 Other genetically informative studies of smoking on mental health

In this section we focus on two different research designs that can complement observational studies and MR studies: negative control designs and co-twin designs.

2.3.1 Negative control studies
A negative control is a trait that cannot plausibly be causally associated with the outcome. For example, Treur and colleagues[38] used a negative control in their study exploring smoking on adult ADHD diagnosis. The negative control was childhood diagnosis of ADHD (before the age of 13 years). Given that children rarely start smoking before age 13 years, there is no plausible causal pathway from child's own smoking to ADHD risk in childhood. Similarly, a recent exploration of smoking on adolescent outcomes included mental health measures before age 10 years as a negative control. If smoking is associated with mental health in adolescence but not before age 10, this could suggest evidence for a causal effect.[44] However, Schellhas and colleagues[44] found evidence that smoking was associated with externalising disorders in both adolescence and childhood, suggesting that this association is unlikely due to causal effects of child's own smoking. This negative control approach is also used in the analysis of the genetic variant from the *CHRNA5-A3-B4* gene cluster, where evidence for an association within never smokers is inconsistent with causality.[31,32]

2.3.2 Co-twin control designs
Two studies have used a co-twin control design to explore the effects of smoking on schizophrenia[45] and depression.[46] This method uses twin pairs who are discordant for smoking status and compares rates of mental illness diagnoses between the discordant pairs. Twin pairs will share the same in utero environment, and to a large extent their home environments. Therefore, it is unnecessary to adjust for many common risk factors (e.g. parental smoking), as both twins are exposed equally in this design. Smoking twins had significantly higher risk for both schizophrenia[45] and depression.[46] However, by comparing the rates in identical and non-identical twins, Kendler and colleagues[46] conclude that the association for depression is solely due to genes that predispose to both smoking and depression. While in the case of schizophrenia, Kendler and colleagues[45] conclude that the association is only partially explained by shared genes.

2.3.3 Summary of research using alternative designs
Overall, there is a lack of evidence that we have been able to identify which uses alternative study designs to explore effects of smoking on mental health. For example, natural experiments that explore population mental health following a change of tobacco control policies (e.g., raising legal age to purchase cigarettes). We recommend the implementation of more genetically informative designs in the future to increase the strength of causal evidence. As demonstrated here, shared genetic liability between smoking and mental health is an important issue to disentangle, and should not be discounted.

3. Does quitting smoking improve mental health?

3.1 Randomised controlled trials of smoking cessation and mental health

So far, the studies summarised have explored the association between smoking and new incidence of mental illness or subsequent worsening of mental health. However, we cannot conclude from this evidence necessarily that helping individuals with mental illness to quit would improve their mental health. Therefore, here we looked for randomised control trials aimed at promoting successful quit attempts amongst individuals with existing mental illness.

One meta-analysis of randomised control trials included 63 studies and a narrative review of 31 studies (N= over 169,500).[47] Primary outcomes were depression and anxiety symptoms, which both showed an improvement for those who quit compared with those who continued to smoke ($SMD_{anxiety}$ = −0.28, 95% CI −0.43 to −0.13; $SMD_{depressive\ symptoms}$ = −0.30, 95% CI −0.39 to −0.21). However, all studies were at serious risk of bias, leading the authors to rate the evidence as low to moderate quality. Taylor and colleagues[47] conclude that there is low to moderate certainty evidence that mental health improves after quitting compared to those who continue to smoke. These improvements are seen in both unselected samples and amongst people diagnosed with mental health conditions. Despite low quality evidence and risk of bias, there is no strong evidence that quitting worsens mental health.[47] This is supported by evidence from RCTs of smoking cessation interventions amongst individuals with severe mental illness which do not show any worsening of mental health symptoms in those randomised to intervention.[48,49]

3.2 Summary of findings from RCTs of smoking cessation and mental health

Although there are a limited number of studies that look at RCTs of smoking cessation and the impact on mental health, there appears to be evidence that smoking cessation interventions for individuals with mental illness do not worsen mental health symptoms and may improve them in the long term.

4.Discussion and points to consider

In this report, we have summarised evidence around two key questions about smoking and mental health: 1) does smoking increase the risk of subsequent mental health problems and 2) does quitting smoking improve mental health symptoms for those with mental illness. Establishing whether or not these are true causal effects will help to better target successful public health policies and to hopefully increase life expectancy amongst individuals with mental illness.

There is a large body of longitudinal research that finds strong evidence for an association from smoking to mental health, in particular for depression, anxiety and schizophrenia. However observational studies can be biased by residual confounding and reverse causation, and we cannot rule out prodromal symptoms of mental illness leading individuals to start smoking. These studies can be complimented by the method of Mendelian randomisation which has different assumptions and sources of bias. Therefore, consistent evidence across these methods can strengthen our ability to draw causal conclusions.

Whilst overall evidence from both observational and Mendelian randomisation studies suggested an effect of smoking on both depression and schizophrenia, evidence from co-twin studies indicated that the association with depression was likely completely due to shared genetics. This may result in spurious associations in both observational and Mendelian randomisation studies. In the case of Mendelian randomisation, this could mean that genetic variants we believe to be identified for smoking are actually only associated with a shared underlying factor. This is why it is so important to understand the biological mechanisms underpinning the genetic instruments being used and why the single variant instrument from the *CHRNA5-A3-B4* gene cluster is such a powerful tool in these analyses.

In the case of depression, when studies used this instrument, there was either no evidence of an effect of smoking or there was evidence for an association in never smokers, suggesting that there is unlikely to be a causal effect of smoking. Although this is a powerful technique, these studies are subject to small sample sizes and therefore should be explored in large samples in the future.

For schizophrenia, when using this instrument, the *CHRNA5-A3-B4* genetic variant there was some evidence of an effect in smokers compared to never smokers, and alternative genetically informative designs only suggested partial explanation by shared genetic factors. Overall, the evidence seems stronger for an effect of smoking on schizophrenia than for depression. However, we must be cautious of the potential role of cannabis in this relationship. Cannabis is often smoked with tobacco and there is strong evidence to suggest that high potency cannabis is associated with psychosis.[50] Given the high rates of co-use between tobacco and cannabis in many populations, it can be very difficult to disentangle their effects using observational approaches and genetic instruments with unknown biological mechanisms (especially given the high degree of genetic overlap). However, this is again why the *CHRNA5-A3-B4* genetic variant can be so powerful, with a known mechanism specific to nicotine response.

There was evidence from MR studies for a causal effect of smoking on ADHD diagnosis. However, using a negative control outcome of ADHD diagnosis in childhood, it seems highly unlikely that the association is due to the child's own smoking behaviour. It is instead possible that the association might be due to intrauterine effects of maternal smoking during pregnancy

or exposure to passive smoking in childhood, given that parents and children share genetic liability. It was beyond the scope of the current review to summarise the large literature on smoking during pregnancy and offspring mental health. However, taking evidence together from many different genetically informative designs, previous reviews have concluded that causal effects of smoking on ADHD are highly unlikely, and effects are most likely due to underlying genetic liability to impulsivity.[51]

Finally, there are a small number of MR studies exploring bipolar disorder, psychological distress, suicide, loneliness and anorexia nervosa. While these studies show potentially interesting findings (for example, there seems to be evidence to support a causal role of smoking in risk for bipolar disorder), overall there is a need for more evidence using alternative study designs.

Although Mendelian randomisation studies suggests that smoking behaviours have a causal effect on some mental health outcomes, there is a high degree of bidirectionality in these relationships. There was also a strong body of evidence to suggest that this was the case, both from meta-analyses and MR studies. This presents the possibility of a vicious cycle of bidirectional effects, whereby having symptoms of mental illness causes individuals to smoke more and to be more susceptible to dependence. At the same time, smoking also increases the risk of subsequent mental illness and exacerbates mental health symptoms. However, it is important to mention that true bidirectional causal effects can present a problem for MR. We have reviewed these methodological difficulties in more detail elsewhere.[23]

Conclusions

Overall, there is evidence to suggest a detrimental causal effect of smoking on mental illness, in particular for schizophrenia. This body of evidence provides support for public health policies surrounding tobacco control, especially those aimed at individuals with a high risk for or with existing mental illness. Smoking cessation interventions for individuals with severe mental illness certainly do not worsen mental health symptoms and may improve them in the long term.

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