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SYNTHESIS

Smoke-Free Series: Cessation Maintenance

> **Research Question:** What is the effectiveness of cessation maintenance or relapse prevention interventions on smokers' ability to maintain their status as 'former smokers'?

Key Messages

- One systematic review and meta-analysis, and four narrative reviews were included in this document on cessation maintenance.
- Findings for extended pharmacotherapy to prevent relapse among smokers in the general population were mixed.[1] Extended treatment with Varenicline was found to help prevent relapse, while extended treatment with Buproprion was not shown to have any effect. There was not enough evidence to demonstrate a benefit of nicotine replacement therapy (NRT) in preventing relapse.[1] The evidence did not support the use of behavioural interventions to help smokers in the general population (who recently quit) to avoid relapse.[1]
- Among individuals with schizophrenia, there was some evidence supporting the use of maintenance pharmacotherapy (i.e., Varenicline, NRT, Buproprion),[2-4] and combined pharmacotherapy and behavioural treatment for cessation maintenence.[4]
- There was also some (although limited) evidence to support the use of maintenance pharmacotherapy (particularly Buproprion and Varenicline) among individuals with unipolar depression and bipolar disorder, respectively.
- No significant benefit was identified for behavioural interventions for relapse prevention in pregnant women.
- These findings add to the evidence base regarding the effectiveness of cessation maintenance interventions. The current cessation maintenance evidence is consistent with the key findings summarized by the SFO-SAC (2016) report.

Background

- Relapses from quit attempts are common due to the addictive nature of tobacco. It can take multiple quit attempts to achieve long-term tobacco cessation.[5] Relapse prevention interventions are intended to help a smoker maintain cessation and reduce relapse rates once they have made a quit attempt.[1]
- Interventions designated as relapse prevention interventions are highly heterogeneous; they can include behavioural support, extended use of smoking cessation medications, or both.[1]

These interventions can be administered to abstainers who have quit following a separate cessation intervention or a self-quit attempt. Relapse prevention interventions can be components or extensions, of a cessation intervention that are specifically tailored to relapse prevention and cessation maintenance (e.g., extended treatment with Varenicline, components of a behavioural intervention that target cravings management).[5]

- There is no clear definition of relapse prevention[1] and relapse prevention interventions are generally difficult to separate from cessation interventions; however, the included reviews in this evidence summary focus explicitly on relapse.

- Previous evidence from the Smoke-Free Ontario Scientific Advisory Committee 2016 (SFO-SAC 2016)[5] was mixed regarding the effectiveness of relapse prevention interventions for cessation maintenance. Some of the SFO-SAC (2016) evidence showed that cessation maintenance interventions, such as NRT, Bupropion, Varenicline and self-help materials prevent relapse into smoking; however, there was also evidence that showed no effect for these interventions.

- This synthesis is focused on cessation maintenance evidence published since the SFO-SAC (2016) report.

Methods

- A peer-reviewed literature search was conducted on December 2, 2019 by Public Health Ontario (PHO) Library Services for articles published between 2015 and 2019. The search did not extend earlier than 2015 because a comprehensive summary of evidence on this research question had been completed (see the Cessation Chapter in the Smoke-Free Ontario Scientific Advisory Committee 2016 (SFO-SAC 2016).[5]

- The search involved five databases, including MEDLINE, Embase, CINAHL, Cochrane Database of Systematic Reviews and Cochrane Central Register of Controlled Trials. The following search terms were included, but were not limited to: smoking cessation, secondary prevention, cessation maintenance, stay quit and relapse. The full search strategy is available upon request from PHO.

- Articles were eligible for inclusion if they were review-level articles, published between 2015 and 2019, that examined the effectiveness of cessation maintenance interventions. Articles that did not focus on relapse prevention, or combined relapse prevention with other smoking cessation interventions/programs (e.g., mass media campaigns) were excluded.

- One reviewer screened titles and abstracts, and two reviewers screened full-text versions of all articles for inclusion. For all relevant papers, one PHO staff extracted relevant data and summarized content.

- Quality appraisal was conducted for each included review using the Healthevidence.org Quality Assessment Tool for Review Articles.[6] Two reviewers made independent assessments for each of the 10 quality criteria. Any discrepancies were resolved by discussion.

Findings

- The literature search identified 285 articles and five met the inclusion criteria.[1-4] One paper was a systematic review and meta-analysis[1] and four were narrative reviews[2-4,7] (one of which included both reviews and primary studies).[7] One review was appraised as strong quality,[1] one review was appraised as moderate[2] and three as weak.[3,4,7] The majority of included studies within the reviews were from the US; other jurisdictions included Germany, the UK, Canada, Belgium, Spain, Malaysia, Hong Kong, Netherlands.

- One review examined the general population,[1] two examined cessation maintenance among individuals with schizophrenia,[3,4] one focused on individuals with mental illness (e.g., schizophrenia, depression, bipolar, post-traumatic stress disorder (PTSD),[2] and two reviews examined cessation maintenance among pregnant women.[1,7] The findings below are organized by population.

General Population

- One systematic (Cochrane) review and meta-analysis by Livingstone-Banks et al., (2019) examined the impact of relapse prevention interventions in reducing the proportion of recent quitters who return to smoking.[1] They examined the impact of pharmacotherapy (e.g., Varenicline, Buproprion, NRT), and behavioural interventions (e.g., interventions that help teach individuals skills to cope with the urge to smoke), or additional supports (e.g., leaflets or calls, internet or mobile phone resources, or additional counselling).[1] Participants included smokers who quit on their own, those undergoing enforced abstinence or those participating in treatment programs.[1]

- The findings for extended pharmacotherapy (i.e., using pharmacotherapy for durations longer than what is standard) were mixed.[1] For example, extended treatment with Varenicline was found to help prevent relapse (Varenicline vs. placebo RR= 1.23, 95% CI: 1.08 to 1.41).[1] Extended treatment of Buproprion was not shown to have a benefit in preventing relapse; however, the evidence was limited by imprecision thus the authors did not rule out a clinically important benefit at this time (Buproprion vs placebo: RR=1.15, 95% CI: 0.98 to 1.35; Bupropion plus NRT: RR 1.18, 95% CI: 0.75 to 1.87).[1] Note that imprecision could mean that the included studies had high levels of statistical heterogeneity, small samples (<100) or had confidence intervals that included the possibility of both no effect and clinically significant effect. Lastly, there was not enough evidence to demonstrate a benefit of NRT to prevent relapse (NRT vs. placebo: RR= 1.04, 95% CI: 0.77 to 1.40).[1]

- The systematic review by Livingstone-Banks et al. (2019) found that the evidence did not support the use of behavioural interventions to help smokers (who recently quit) to avoid relapse (RR= 0.99, 95% CI: 0.87 to 1.03).[1]

Individuals with Mental Illness

INDIVIDUALS WITH SCHIZOPHRENIA

- Three reviews examined the impact of relapse prevention interventions (e.g., pharmacotherapy and behavioural) among individuals with schizophrenia. All three reviews reported findings that

support the use of maintenance pharmacotherapy (i.e., Varenicline, NRT, Buproprion)[2-4] and combined pharmacotherapy and behavioural treatment[4] among individuals with schizophrenia.

- For example, Cather et al. (2017) found that maintenance pharmacotherapy appeared to reduce relapse and improve sustained abstinence rates among individuals with schizophrenia.[4] They also reported that maintenance pharmacotherapy combined with behavioural treatment has reduced relapse rates over maintenance behavioural treatment alone among smokers with schizophrenia illness in open, single blind, and double blind trials.[4]

- Similarly, Evins et al., (2015) concluded that maintenance pharmacotherapy for a year improved sustained abstinence rates among individuals with schizophrenia.[3] They found that individuals who received maintenance treatment with Varenicline were more likely to remain abstinent at long-term follow-up compared to those who received a placebo.[3] They also found some evidence from a single study suggesting benefit of NRT.[3]

- Tidey et al., (2015) concluded that maintenance pharmacotherapy using NRT, Varenicline or a combination of NRT and Buproprion reduced rates of relapse among individuals with schizophrenia.[2]

INDIVIDUALS WITH OTHER MENTAL ILLNESS (E.G., BIPOLAR, DEPRESSION, PTSD)

- One review by Tidey et al. (2015) examined the effects of relapse prevention interventions (both pharmacotherapy and behavioural) among individuals with mental illnesses such as unipolar depression, bipolar disorder or PTSD.[2] Based on a single primary study, long-term treatment with bupropion was shown to reduce relapse rates among individuals with unipolar depression who had stopped smoking. Another primary study found that maintenance treatment with Varenicline reduced relapse among individuals with bipolar disorder who had stopped smoking. Lastly, a single primary study examining the effects of combined counselling, NRT and Buproprion among individuals with PTSD did not find any significant effect (compared to a control group); however, it should be noted that sample size for this study was relatively small (n=22).

Pregnant Women

- Two reviews examined the effectiveness of behavioural interventions on relapse prevention among pregnant women.[1,7] Neither review found benefit to behavioural interventions for preventing relapse.

    - For example, the Cochrane review by Livingstone-Banks et al., (2019) examined the effect of behavioural interventions in preventing relapse among pregnant and post-partum women (who had abstained from smoking) and did not find any significant effect (End of pregnancy: RR 1.05, 95% CI 0.99 to 1.11; Post-partum: RR 1.02, 95% CI: 0.94 to 1.09).[1]

    - Similarly, Meernik et al., (2015) reported no significant effects found by two Cochrane reviews of psychosocial interventions to prevent relapse among women who quit smoking during pregnancy.[7]

Limitations

- Most included reviews were appraised at moderate or weak quality. Few reviews assessed the quality of the included primary studies or described the level of evidence of the included studies. Some reviews did not have appropriate inclusion/exclusion criteria (e.g., did not mention any inclusion/exclusion criteria, or criteria were not specific enough).
- Most included reviews focused on a specific population (e.g., individuals with Schizophrenia, or pregnant women), therefore the results may not be generalizable to a broader population.

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