National Health and Medical Research Council statement on electronic cigarettes: 2022 update

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Position statement summary

Introduction: Electronic cigarette (e-cigarette) use in Australia has rapidly increased since the 2017 National Health and Medical Research Council (NHMRC) Chief Executive Officer (CEO) statement on e-cigarettes. The type of products available and the demographic characteristics of people using these products have changed. New evidence has been published and there is growing concern among public health professionals about the increased use, particularly among young people who do not currently smoke combustible cigarettes. The combination of these issues led NHMRC to review the current evidence and provide an updated statement on e-cigarettes. In this article, we describe the comprehensive process used to review the evidence and develop the 2022 NHMRC CEO statement on electronic cigarettes.

Main recommendations:

- E-cigarettes can be harmful; all e-cigarette users are exposed to chemicals and toxins that have the potential to cause adverse health effects.
- There are no health benefits of using e-cigarettes if you do not currently smoke tobacco cigarettes.
- Adolescents are more likely to try e-cigarettes if they are exposed to e-cigarettes on social media.
- Short term e-cigarette use may help some smokers to quit who have been previously unsuccessful with other smoking cessation aids. There are other proven safe and effective options available to help smokers to quit.

Changes in management as a result of this statement: The evidence base for the harms of e-cigarette use has strengthened since the previous NHMRC statement. Significant gaps in the evidence base remain, especially about the longer term health harms of using e-cigarettes and the toxicity of many chemicals in e-cigarettes inhaled as an aerosol.

Abstract

The combination of evolving product design, publication of new and emerging evidence, and growing concern among public health professionals about the increased use of e-cigarettes, particularly among young people who do not currently smoke combustible cigarettes, led NHMRC to review the current evidence and provide an updated NHMRC CEO statement on electronic cigarettes on their safety and health impacts.

As noted in the NHMRC Statement, nicotine is well understood to be the major addictive substance in tobacco cigarettes. Evidence for addictiveness of nicotine per se was therefore not under review. The NHMRC Statement also notes e-liquids can contain nicotine, even if labelled “nicotine-free.”

The NHMRC Statement is intended to support the health of all Australians, not just current smokers. The Statement assists consumers and policy makers in understanding the current evidence relevant to the marketing and use of e-cigarettes, their impact on smoking initiation and cessation, uptake among youth, dual use with conventional tobacco products,
and their overall implications on individual and population health.

**Position statement summary**

**Methods**

**Overview of the revision process**

The development of the 2022 NHMRC Statement took two years and followed best practice NHMRC guideline development processes, as outlined in the 2016 NHMRC standards for guidelines\textsuperscript{15} and the NHMRC Guidelines for guidelines handbook\textsuperscript{16} Key stages of the development process are outlined in Box 1. The process drew upon the diverse expertise of the NHMRC Electronic Cigarettes Working Committee\textsuperscript{17} (established at Step 1) to scope outcomes (Step 2), consider evidence reviews (Step 3), and the independent methodological review of those evidence reviews (Step 4). An evidence-to-decision process involved assessment of evidence quality and public health considerations using the

<table>
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<th>Step 1: Committee established</th>
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<tr>
<td>• The Electronic Cigarettes Working Committee (the Committee) was established from 5 June 2020 to 4 September 2022 and reported to the Council of NHMRC.</td>
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<th>Step 2: Project scoped</th>
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<tr>
<td>• NHMRC undertook a scoping activity to help the Committee to determine what should/should not be included in the review and update of the NHMRC Statement, including priority topics and formation of research questions.</td>
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<th>Step 3: Evidence reviews</th>
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<td>• NHMRC commissioned several evidence reviews on the topics of e-cigarette use and smoking behaviour (uptake and cessation), the effects of e-cigarette advertising, promotion and sponsorship, and e-cigarette use and health outcomes. NHMRC undertook a scoping review on the toxicology of e-cigarettes.</td>
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<th>Step 4: Methodological review</th>
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<td>• NHMRC procured methodological reviewers to independently examine the quality of the commissioned evidence reviews and the toxicology scoping review to ensure that the reviews followed the systematic and rigorous approach as documented in the review protocols.</td>
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<th>Step 5: Evidence synthesis</th>
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<td>• GRADE was used to assess the certainty (quality) of the evidence. The WHO–INTEGRATE evidence-to-decision framework was used to develop the updated NHMRC Statement. The Santesso et al (2020) <em>informative statements to communicate the findings of systematic reviews of interventions</em> was used to inform the terminology of the evidence statements.</td>
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<th>Step 6: Targeted consultation</th>
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<td>• The draft NHMRC Statement was circulated to federal, state and territory Chief Health Officers/Chief Medical Officers for targeted consultation over a two-week period in March 2022.</td>
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<th>Step 7: Independent expert review</th>
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<td>• Independent expert review of the NHMRC Statement took place between 14 April and 13 May 2022. The expert reviewers provided their comments on the draft NHMRC Statement to ensure that the evidence on e-cigarettes had been appropriately interpreted and synthesised in the NHMRC Statement.</td>
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<th>Step 8: Launch</th>
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<td>• NHMRC Council considered the NHMRC Statement in June 2022. The NHMRC Statement was launched on 23 June 2022.</td>
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WHO–INTEGRATE framework18 (Step 5), targeted consultation (Step 6), and independent review (Step 7) before launch (Step 8).

The Committee considered a comprehensive mix of evidence when updating the NHMRC Statement. This included evidence statements and advice from other countries, such as the United States National Academies of Sciences, Engineering and Medicine23 and Surgeon General reports,20,21 and from Australia, such as the CSIRO (Commonwealth Scientific and Industrial Research Organisation) review22 and the National Industrial Chemicals Notification and Assessment Scheme review.23 This was combined with evidence from commissioned evidence reviews (Step 3). In the evidence-to-decision process (Steps 5–7), relevant data on e-cigarette usage and sociodemographic and other features of the Australian community were also considered.

### Populations and outcomes of interest (Step 2)

The Committee first established and determined which populations and outcomes to examine when updating the 2022 NHMRC Statement, in line with the intended use for broad public health. Populations considered were:

- never smokers (those who have never smoked a tobacco cigarette);
- former smokers (those who used to smoke tobacco cigarettes but have quit); and
- current smokers (those who currently smoke tobacco cigarettes).

Detailed outcomes were considered under three headings:

- e-cigarette use and tobacco smoking uptake and cessation;
- effects of e-cigarette advertising, promotion and sponsorship; and
- e-cigarette use and health outcomes.

The Committee did not examine or include evidence on the passive exposure to second hand aerosol from e-cigarettes or the appeal of e-cigarettes, including flavours, packaging design and price. The addictiveness of nicotine was not examined as this is well established and widely known.

### Evidence reviews (Step 3)

In addition to considering existing international evidence, NHMRC and the Australian Government Department of Health and Aged Care also commissioned specific evidence reviews from external researchers. The Australian Government Department of Health Department of Health and Aged Care commissioned the following evidence reviews:

- E-cigarette use and combustible tobacco smoking uptake among non-smokers, including relapse of former smokers: umbrella review, systematic review and meta-analysis24;
- Efficacy of e-cigarettes as aids to cessation of combustible tobacco smoking: updated evidence review25; and
- Electronic cigarettes and health outcomes: systematic review of global evidence.26

In addition, NHMRC commissioned the following reviews:

- Effects of e-cigarette advertising, promotion and sponsorship on people’s attitudes, beliefs, perception, intentions and behaviours: a mixed methods systematic review27; and
- Supplementary report one: additional material on the review of evidence on the relationship of e-cigarette use to smoking behaviour, including uptake and cessation28; and
- Supplementary report two: additional material on the review of evidence on the health outcomes of e-cigarette exposure.29

NHMRC also conducted the following scoping review to be included as part of the evidence base: Inhalation toxicity of non-nicotine e-cigarette constituents: risk assessments, scoping review and evidence map (toxicology report).30

### Methodological reviews (Step 4)

The research protocols for the reviews commissioned by NHMRC were reviewed by the Committee and independently methodologically reviewed before the reviews commenced. These protocols outlined the scope, research question and methodology. All evidence reviews, supporting materials and supplementary reports produced were also independently methodologically reviewed to ensure that the methodological quality followed the systematic and rigorous approach documented in the review protocols. The reviews are publicly available from the NHMRC website.13

### Evidence synthesis (Step 5)

The internationally recognised Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology was used to assess certainty of the evidence.31 The GRADE methodology aims to improve transparency and consistency in reporting and decision making by assessing key aspects of the way studies are designed, run and analysed, which affects how certain (or confident) reviewers and committees can be that the results reported in studies are accurate. GRADE certainty ratings for the type of epidemiological evidence typical of broad public health exposures are generally low to very low. More highly rated study designs that are considered necessary for clinical practice guidelines, such as randomised controlled trials, are not appropriate for most public health exposures. This is chiefly because randomisation to many public health exposures of interest, such as smoking, alcohol, or early age at first pregnancy, is often not feasible or ethical. To acknowledge that well designed observational studies are often the best source of evidence on public health issues, Committee members agreed that bodies of evidence that consist of randomised controlled trials would assume an initial level of certainty of “high”, prospective cohort studies would assume an initial level of certainty of “moderate”, and all other observational studies would assume an initial level of certainty of “low”. The certainty of the evidence included in the evidence reviews varied across outcomes from moderate (for outcomes relating to the influence of the media on intention to use e-cigarettes in young people) to low or even very low for many of the other outcomes.

The available evidence had several limitations. E-cigarettes are relatively new products and the design and technology behind the devices and components used in e-cigarettes are constantly evolving. The wide variation of e-cigarettes, including manufacturing quality, setting customisation and variation in e-liquids used, makes it difficult to ascertain their safety and health impacts. Most of the direct evidence of safety and health impacts of e-cigarettes was limited to short term human epidemiological or clinical studies, with long term effects mostly unknown.

Most studies examining the toxicological constituents of e-liquids were in vitro or animal-based studies.30 These study
designs have inherent limitations and are generally considered to provide less direct evidence when compared with human randomised controlled trials or long term epidemiological studies. However, in vitro or animal-based studies are useful when needing to understand the effects of an environmental exposure to a substance or when it is not ethical or possible to conduct human studies due to the toxic nature of the substances being examined or to control for confounding factors present in human populations.\textsuperscript{32,33}

The evidence on the impact of e-cigarette marketing on related behaviours, such as intention to use e-cigarettes or uptake/initiation, and on the impact of e-cigarette use on smoking uptake/initiation was mainly limited to international cross-sectional or cohort studies. Very few studies were conducted in Australia.\textsuperscript{27} Contrastingly, most of the evidence examining the efficacy of e-cigarettes as a tobacco cigarette smoking cessation tool was from randomised controlled trials based on clinical settings with behavioural support, which may not be generalisable to real-world effectiveness of e-cigarettes in settings less supportive of cessation; these studies also had small sample sizes and short follow-up periods.\textsuperscript{25}

The WHO–INTEGRATE evidence-to-decision framework\textsuperscript{18} is designed for decision making at population levels and was used to develop the 2022 NHMRC Statement. The WHO–INTEGRATE framework was used to shape and write the 2022 NHMRC Statement, including what evidence was included and emphasised in the key messages.\textsuperscript{34}

Targeted consultation (Step 6) and independent expert review (Step 7)

Consultation is a core component of the NHMRC’s guideline development process, contributing to accountability of the agency and independence of the advice. The draft 2022 NHMRC Statement and infographics underwent targeted consultation with federal, state and territory Chief Health/Medical Officers over a two-week period in March 2022. Chief Health/Medical Officers were also asked to contribute Poisons Information Centre data on nicotine poisoning for inclusion in the Statement (if available) and to comment on two infographic concepts that summarised the Statement. Overall, Chief Health/Medical Officers were supportive of the Statement. In response to feedback, edits to the Statement were made, including the addition of a plain English summary.

After revisions in response to targeted consultation, the next version of the 2022 NHMRC Statement and associated resources underwent review by three independent experts to ensure the evidence on e-cigarettes was appropriately interpreted and synthesised. No errors of fact or significant omissions of evidence were identified. However, the phrasing of the 2022 NHMRC Statement and accompanying resources was clarified at several points. The final Statement and associated resources were released in June 2022 following consideration by the NHMRC Council.

Comparison with international guidance

The 2022 NHMRC Statement is broadly consistent with reports from a number of international health bodies published from 2020 onwards (Box 2). A significant factor contributing to variations between these statements and advice is the way that the questions have been framed,\textsuperscript{22} with some having a major focus on benefits associated with smoking cessation and others considering a broader range of issues including longer term harms and risks associated with use for purposes other than smoking cessation. The 2022 NHMRC Statement does not compare harms of e-cigarette use with smoking tobacco cigarettes, reflecting the purpose to support the health of all Australians and to avoid normalisation of nicotine. Relative harm from e-cigarette use compared with tobacco cigarettes is also difficult to quantify and varies depending on a number of factors such as conditions of use, e-cigarette device type and setting, e-liquid type and concentration, and frequency of e-cigarette and tobacco cigarette use.

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<th>2 Snapshot summary comparison of international guidance on electronic cigarettes (e-cigarettes)</th>
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- E-cigarettes are considered significantly less harmful than cigarettes. They are a better alternative to cigarettes for smokers and can be used as a smoking cessation aid. |
| World Health Organization | Tobacco: e-cigarettes (2022)\textsuperscript{2} | - Both tobacco products and electronic nicotine devices (ENDS) pose risks to health. The safest approach is not to use either. 
- To date, evidence on the use of ENDS as a cessation aid is inconclusive. In part due to the diversity of ENDS products and the low certainty surrounding many studies, the potential for ENDS to play a role as a population-level tobacco cessation intervention is unclear. |
| Scientific Committee on Health, Environmental and Emerging Risks (SCHEER) | SCHEER scientific opinion on electronic cigarettes (2021)\textsuperscript{16} | - There is moderate evidence that e-cigarettes are a gateway to smoking for young people and strong evidence that flavours have a relevant contribution for attractiveness of use of e-cigarettes and initiation. 
- There is weak evidence for the support of e-cigarettes’ attractiveness in helping smokers to quit and the evidence on smoking reduction is assessed as weak to moderate. |
| United States Preventive Services Task Force | Interventions for tobacco smoking cessation in adults, including pregnant persons (2021)\textsuperscript{27} | - The current evidence is insufficient to assess the balance of benefits and harms of e-cigarettes for tobacco cessation in adults, including pregnant persons. |
| Irish Health Research Board | Electronic cigarette use and tobacco cigarette smoking initiation in adolescents: an evidence review (2020)\textsuperscript{36} | - This review found a fourfold association between ever using e-cigarettes and initiating smoking tobacco cigarettes in adolescents. |
|  | Electronic cigarette and smoking cessation: an evidence review (2020)\textsuperscript{37} | - The systematic review and network meta-analysis of electronic nicotine delivery systems (e-cigarettes) versus therapies usually given for smoking cessation showed that there is no evidence of a difference in effect on incidences of smoking cessation. There is a low level of certainty in these results due to low successful event rates and high rates lost to follow-up in all studies. |
The absolute risks of e-cigarettes cannot be determined at the present time and longer term effects, of importance for young people who become dependent, remain unclear.\(^1\) As such, the 2022 NHMRC Statement can be characterised as supporting a continuation of the precautionary approach.

### Key messages

Following this extensive evidence synthesis, targeted consultation and expert review, a precautionary approach to e-cigarettes, particularly for people who have never smoked, remains appropriate. The key messages in the 2022 NHMRC Statement\(^1\) include:

- E-cigarettes can be harmful; all e-cigarette users are exposed to chemicals and toxins that have the potential to cause adverse health effects.
- E-cigarette-related poisonings have substantially increased over the past five years. E-cigarette-related calls to Australian Poisons Information Centres have more than doubled between 2020 and 2021.
- There are no health benefits of using e-cigarettes if you do not currently smoke tobacco cigarettes.
- People who have never smoked may be more likely to take up tobacco smoking if they use e-cigarettes.
- Adolescents are more likely to try e-cigarettes if they are exposed to e-cigarettes on social media.
- Short term e-cigarette use may benefit smokers if they are able to quit smoking and have been previously unsuccessful with other smoking cessation aids.
- There are other proven safe and effective options available to help smokers quit.

Following the development and publication of the NHMRC Statement, a media release and associated social media content was issued. The 2022 NHMRC Statement is an essential synthesis of all committee member contributions to the development of the National Health and Medical Research Council (NHMRC)’s 2022 CEO statement on electronic cigarettes, including his sound advice and knowledge on the toxicological aspects of e-liquids and e-cigarettes. We also acknowledge the contribution of Jennifer Savenake, Director (Public Health), and the NHMRC project team throughout the development of the NHMRC 2022 CEO statement on electronic cigarettes.

**Key messages**

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- Adolescents are more likely to try e-cigarettes if they are exposed to e-cigarettes on social media.
- Short term e-cigarette use may benefit smokers if they are able to quit smoking and have been previously unsuccessful with other smoking cessation aids.
- There are other proven safe and effective options available to help smokers quit.

### Acknowledgements

We would like to show our gratitude and pay our respects to our colleague, Dr Kerry Nugent, who died on 29 December 2022 after a brief illness. Dr Nugent was a highly valued member of the Electronic Cigarettes Working Committee. We are especially grateful for his contributions to the development of the National Health and Medical Research Council (NHMRC)’s 2022 CEO statement on electronic cigarettes, including his sound advice and knowledge on the toxicological aspects of e-liquids and e-cigarettes. We also acknowledge the contribution of Jennifer Savenake, Director (Public Health), and the NHMRC project team throughout the development of the NHMRC 2022 CEO statement on electronic cigarettes.

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12. HealthStats NSW. E-cigarette use by electronic cigarette use and age (years) [NSW Population Health Survey (SAPHar)], Centre for Epidemiology and Evidence, NSW Ministry of Health]. Sydney: NSW Health, 2022. https://www.healthstats.nsw.gov.au/#/indicator?name=beh-smo-ecig-18&location=NSW&view=Trend&measure=prevalence&group=Age%20(years);Electronic%20cigarette%20use&compare=Electronic%20cigarette%20use&Age%20(years);Filter=Electronic%20cigarette%20use&Current%20use&Ever%20used&Filter=Age%20(years);All%20ages,16-24%20years (viewed Feb 2023).
Position statement summary


