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Waterpipe smoking and health outcomes: review of evidence and road map for an international consortium

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► Additional supplemental material is published online only. To view, please visit the journal online (<https://doi.org/10.1136/tc-2025-059374>).

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Received 25 February 2025
Accepted 3 February 2026



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To cite: Toorang F, Etemadi A, Dar NA, *et al.* *Tob Control* Epub ahead of print: [please include Day Month Year]. doi:10.1136/tc-2025-059374

ABSTRACT

The prevalence of waterpipe smoking (WPS) is increasingly recognised as a growing global public health concern. Available studies show that WPS exposes users to toxicants at levels similar to or higher than those in cigarette smoke, contributing to respiratory disease, cardiovascular damage and cancer. The WHO has flagged WPS as a growing threat, especially among adolescents and young adults, where use is rapidly increasing. Yet research progress is constrained by small samples, inconsistent exposure measures and inadequate adjustment for confounders. These limitations highlight the need for more rigorous epidemiological, clinical and toxicological studies. Importantly, the persistence and expansion of WPS cannot be explained solely by individual behaviours or perceptions of health risk. A range of socioeconomic, political and commercial forces—including industry marketing, weak regulatory oversight, cultural acceptance, low cost and the spread of waterpipe cafés—continues to drive WPS and shape patterns of use. These structural factors are likely to undermine the impact of current public health measures but remain under-researched. Expanding the evidence based on these upstream determinants is crucial for developing more effective and context-appropriate policies. In response to these challenges, experts from multiple disciplines convened in June 2024 to examine the evolving WPS epidemic. Participants emphasised the need for comprehensive, multisectoral strategies that integrate robust research, strengthen surveillance systems and target public awareness initiatives. The meeting concluded with a set of recommendations outlining priority research areas and a strategic roadmap aimed at addressing the complex and escalating public health threat posed by WPS.

INTRODUCTION

Waterpipe smoking (WPS)—also known as hookah, argileh, narghile, goza, chicha, kalyan and shisha—is very popular in the Eastern Mediterranean Region (EMR) but has emerged over recent decades as a growing global public health concern.^{1–4} WPS has gained substantial popularity among youth

WHAT IS ALREADY KNOWN ON THIS SUBJECT

⇒ Waterpipe smoking (WPS), once primarily confined to the Eastern Mediterranean region, has experienced a marked global surge in popularity. It poses significant health risks due to the presence of toxic substances comparable to those found in cigarette smoke, in addition to the added health risk posed by the charcoal factor. Despite being recognised by the WHO as a major public health concern—particularly among youth—comprehensive and robust evidence on the determinants of use and health hazards of WPS, as well as successful strategies for its control, remains limited.

WHAT THIS STUDY ADDS

⇒ This study highlights several critical gaps in the field, including:
⇒ Limitation on rigorous epidemiological, clinical and molecular evidence—particularly the scarcity of data on behavioural determinants and effective policymaking approaches related to WPS and its associated health effects—significantly constrains the development, implementation and enforcement of evidence-based public health policies.
⇒ The persistence of deeply rooted social and cultural acceptance of waterpipe use underscores the importance of culturally sensitive research and tailored interventions.
⇒ The development of more comprehensive global surveillance systems—coupled with systematic policy tracking and robust impact evaluation frameworks—is essential for informing, guiding and strengthening regulatory measures.
⇒ Inadequate implementation of the WHO Framework Convention on Tobacco Control (FCTC) articles, particularly those related to taxation, advertising bans, packaging and labelling, and indoor smoke-free policies, especially in high-prevalence countries of the Eastern Mediterranean region

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ The Global Research on WPS and Health consortium has the potential to generate high-quality, standardised data and evidence that can inform evidence-based policy and regulatory frameworks aligned with WHO Framework Convention on Tobacco Control Articles. The consortium will play a crucial role in addressing these knowledge gaps, enhancing regulatory effectiveness and ultimately reducing the global health burden of WPS.

worldwide, spreading since the early 1990s to the USA, Europe and South America.^{4 5} According to the most recent Global Youth Tobacco Surveys conducted between 2010 and 2019 across 73 countries, approximately 7% of adolescents aged 12–16 reported using waterpipe tobacco in the past month, with the highest prevalence in Europe and the EMR.⁴ Moreover, the prevalence of current WPS increased or remained stable in 19 of 38 countries surveyed (50%) during the survey periods. Globally, it is estimated that over 100 million individuals are regular WPS users. This widespread increase underscores an urgent need for comprehensive research and targeted policy interventions.^{6–10}

Although a growing body of evidence links WPS to acute and chronic health effects similar to those from cigarette smoking, many studies are constrained by small sample sizes, methodological weaknesses and inadequate adjustment for confounding variables.^{11–16} Research is also geographically concentrated. The full long-term health impacts remain uncertain, especially in Western countries, due to the latency period of tobacco-related diseases. These challenges are further compounded by the unique social and cultural contexts surrounding WPS use, the evolving nature of tobacco products—including electronic waterpipes—and widespread misconceptions regarding their safety. As this epidemic continues to spread globally, addressing these research gaps is essential to inform effective policies and interventions.

In response, international experts from multiple disciplines convened at the University of Bologna in June 2024 to develop a comprehensive research agenda focused on advancing the understanding of WPS and its associated health risks, particularly cancer. A summary of the meeting's discussions is provided in online supplemental table 1.

Biochemical constituents and carcinogenesis

Tobacco smoke contains numerous biologically active and carcinogenic compounds, including nicotine, tobacco-specific nitrosamines, polycyclic aromatic hydrocarbons (PAHs) and volatile organic compounds such as acrolein, crotonaldehyde, acrylonitrile, benzene and propylene oxide.¹⁷ Among PAHs, benzene and benzo[a]pyrene are classified as carcinogenic to humans, whereas acrolein, acrylonitrile, crotonaldehyde and propylene oxide are considered suspected human carcinogens.¹⁸

A key feature of WPS is the use of charcoal to heat tobacco, generating toxicants not typically produced or produced in different amounts in cigarette smoke. Charcoal temperatures can exceed 150 °C, promoting thermal degradation of both tobacco and charcoal and forming unique toxic compounds. This combustion process creates a toxicant profile that differs qualitatively and quantitatively from cigarettes, highlighting the distinct health risks of WPS.¹⁹

Waterpipe smokers typically engage in longer sessions, often in homes or cafés, leading to greater cumulative exposure to certain carcinogens.²⁰ Biomarker evidence supports this: in the Golestan

Cohort Study, urinary nicotine levels in waterpipe users were similar to or slightly lower than those of cigarette smokers, yet several PAH biomarkers and a benzene metabolite were higher in waterpipe users.²¹ These patterns indicate a greater internal dose of specific carcinogens from waterpipe use, with important implications for disease risk.

Laboratory studies provide additional insight into toxicant exposure during WPS sessions. One study found that a single waterpipe session produces 2.5 times the amount of phenanthrene, 8.2 times the amount of fluoranthene and 5 times the amount of chrysene compared with a single cigarette.²² Another study reported that formaldehyde levels were 16.6 times higher during waterpipe use.²³ Measurements of expired air carbon monoxide (CO) have shown increased levels, and ambient CO concentrations in waterpipe cafés range between 34.7 and 58.2 ppm.^{24 25} Despite evidence of extensive environmental pollution in WPS, studies assessing the health risks of secondhand waterpipe smoke exposure remain lacking.

Moreover, WPS affects biological pathways implicated in the development of chronic diseases, including inflammation, oxidative stress, immune dysregulation, tissue injury and repair processes. These alterations contribute to the pathogenesis of chronic obstructive pulmonary disease and cardiovascular diseases (CVDs).²⁶ Additionally, the variety of additives used in waterpipe tobacco products—such as humectants, sugars and flavourings—may exacerbate lung toxicity and inflammatory responses. Given the potential health hazards posed by these additives, further research is essential to fully characterise their impact on pulmonary and systemic toxicity.¹⁷

Health effects of WPS

Previous studies have demonstrated associations between WPS and a wide range of adverse health outcomes, including cancer, CVDs, respiratory diseases, low birth weight, periodontal diseases and some infectious diseases such as hepatitis B and C.^{7 11 12} Multiple factors inherent to WPS contribute to methodological challenges and non-harmonised findings across studies. Nicotine yield is influenced by heating temperature, the chemical composition of the tobacco mixture (including flavours, humectants and additives), user behaviour such as puffing patterns, the dimensions of the waterpipe and the volume of water in the bowl. Additional variability in device types, smoking topography, session duration and tobacco formulations further complicates accurate exposure assessment and hinders direct comparisons with cigarette smoking.^{19 27}

Cancer is among the most extensively studied outcomes associated with WPS. A meta-analysis of 28 studies reported significant associations between WPS and several cancer sites. These included head and neck cancer with a summary relative risk (SRR) of 2.21 (95% CI 1.07 to 4.19), oesophageal cancer (SRR 3.11; 95% CI 1.26 to 7.65) and lung cancer (SRR 3.18; 95% CI 1.87 to 5.42).²⁸ Elevated risks were also found for stomach cancer (SRR 2.21; 95% CI 1.10 to 4.47) and bladder cancer (SRR 1.25; 95% CI 1.14 to 1.51), though the quality of studies on these two sites was generally poor. There were indications of increased risk for colorectal, liver and all cancer sites combined; however, data on these cancers were insufficient to allow for meta-analysis. Notably, a study from EMR estimated that in 2020, 1.7% of cancers in men (n=5568) and 0.4% in women (n=1257) were attributable to current WPS. Despite its prevalence in the EMR, WPS's role in cancer has been underestimated due to limited research across cancer types and underdeveloped population-based cancer registries.^{29 30}

While studies link WPS to acute cardiovascular effects, such as increased heart rate, blood pressure and adverse lipid and glucose changes, a systematic review³¹ and the American Heart Association's Scientific Statement²⁷ highlight limited evidence on clinically verified events due to small samples, poor exposure assessment and lack of clinical validation—underscoring the urgent need for robust research.

More broadly, a recent systematic review analysing 191 published papers reported significant associations between WPS and various health outcomes, including cancer, CVDs, stroke, diabetes, metabolic syndrome, overall mortality, reproductive health issues, lung disease, low birth weight and oral health problems. This review noted a substantial increase in both all-cause and cancer-specific mortality among waterpipe smokers, but emphasised that the overall quality of evidence was generally low.¹⁵

Drivers of popularity and policy gap

Multiple factors underpin the widespread use of WPS, posing significant public health challenges globally. Despite mounting evidence of its harm, WPS-related social and health issues have been largely overlooked at higher decision-making levels. Existing legislation is often outdated, vague and poorly tailored to adolescents. For example, many countries lack clear age restrictions, effective bans on public WPS and standardised regulations on packaging and advertising. These regulatory gaps contribute to fragmented tobacco control efforts that fail to address the unique challenges of WPS's cultural embedding and social acceptability.³² The WHO issued regulatory recommendations on waterpipe tobacco control in 2015; nevertheless, the translation of these guidelines into effective policies remains limited worldwide.³³ A recent policy review by Alaoui *et al* found that only 47 countries had ratified waterpipe-specific regulations, and just 8% of these addressed all seven relevant articles of the WHO Framework Convention on Tobacco Control (FCTC).

Several factors, such as socioeconomic status, age, gender, prior cigarette smoking, alcohol use, opium consumption and secondhand smoke exposure, are important correlates of WPS initiation and continuation, underscoring the need for tailored regulatory approaches.^{32 34–38} While older generations predominantly smoked waterpipes exclusively, recent trends show that younger users prefer flavoured tobacco and often engage in dual or poly use—combining WPS with cigarettes, alcohol, opium or secondhand smoke exposure.^{8 34 39 40} The introduction and rising popularity of electronic waterpipes (e-waterpipes) have further diversified consumer options, complicating regulatory efforts.⁴¹ Although fewer studies exist, a US study found that 4.6% of adults and 7.7% of youth reported ever using e-hookah, showing distinct demographic and substance co-use patterns compared with e-cigarette users.⁴²

Social acceptability and misconceptions play a central role in sustaining WPS. An important concern is the disproportionately higher prevalence of WPS among women and adolescents compared with cigarette smoking—particularly in the EMR—where fewer cultural restrictions may facilitate uptake.^{3 43} Waterpipe smokers enjoy considerable social acceptability, particularly among adolescents and women. Common erroneous beliefs include that WPS is less harmful, less addictive and easier to quit than cigarettes.^{44 45} Moreover, WPS cafés tend to be more accessible to youth, as they face fewer legal restrictions than bars or nightclubs.⁴⁶ These demographic and sociocultural dynamics warrant careful consideration in the development and implementation of policy interventions.^{3 43} Closing these policy gaps

requires integrated tobacco control strategies that also address the social appeal of WPS. Without such measures, misconceptions will persist and related public health risks will remain underestimated.

WPS produces more toxicants than cigarettes but is wrongly seen as less harmful, partly due to the myth that water filters out toxins. In reality, water doesn't effectively remove carbon monoxide, heavy metals or carcinogens—and may cool the smoke, leading to deeper inhalation and greater exposure.^{47 48} Waterpipe use varies across countries due to cultural norms and preparation methods. To ensure effective public health responses, it's crucial to produce context-specific evidence and counter widespread misinformation about WPS.⁴⁹

Research gaps

Despite numerous epidemiological studies on WPS and health outcomes, significant methodological limitations persist. Many studies have small sample sizes, lack well-designed cohort data and do not sufficiently adjust for confounding factors, especially the interaction of WPS with cigarette smoking and other risk factors. There is a notable absence of standardised, validated tools to quantify waterpipe exposure and dose, complicating accurate dose-response analyses and comparative assessment across diverse populations and smoking methods. Recall bias and the predominance of case-control study designs further limit robust data collection and interpretation.^{11 15 16 50} Data on WPS patterns—such as exclusive users, dual users or poly users—and the interaction of WPS with other products like cigarettes, opium or chewing tobacco are scarce. Moreover, studies that include data on WPS often struggle to separate its effects from those of cigarettes or other smoking types. Notably, critical health risks that require further investigation include the effects of waterpipe tobacco smoke on pregnant mothers, birth outcomes, child health and associations with cardiovascular events.

The heterogeneity in waterpipe tobacco types and smoking practices across regions leads to underreporting and difficulty generalising health outcome data among affected populations. Additionally, there is a scarcity of data stratified by sex and age, restricting understanding of differential health effects in vulnerable groups such as women, adolescents and young adults. This gap is critical given the rising prevalence of WPS among youth in both endemic and Western countries, and the decades-long latency before potentially observable health outcomes emerge.

Clinical and molecular research on WPS remains underdeveloped, hindered by limited research infrastructure in high-prevalence regions and overshadowed by cigarette smoking priorities in developed nations, where WPS is more common among adolescents and young adults, suggesting that it may take years, if not decades, to fully observe the health risks associated with this practice in these populations. Epigenomics-based artificial intelligence (AI) shows strong potential for accurately determining WPS status and duration, as epigenetics functions as a molecular sensor of environmental exposures. Specifically, DNA methylation patterns in blood can distinguish waterpipe smokers from cigarette smokers with approximately 90% accuracy using machine learning, reflecting distinct epigenetic markers linked to smoking type and intensity. These methylation markers demonstrate dose-response relationships with smoking extent and can persist or reverse depending on cessation, providing a molecular basis for inferring both smoking status and duration.⁵¹ Advanced approaches such as epigenomics-based AI show promise for improving exposure assessment but are currently constrained

by high costs, technical demands and limited access to suitable biological samples.¹⁵

The perception of WPS as a safer, socially acceptable activity complicates regulation and cessation efforts. However, there is limited research on how social media, peer influence and cultural norms specifically impact young people's waterpipe use. Studies from the USA and EMR indicate that social media promotes WPS among youth by disseminating widespread, often unregulated pro-waterpipe messages. Much of this content—across platforms such as Facebook, Twitter, Pinterest, YouTube, Instagram and Tumblr—links waterpipe use to social venues like bars and clubs, normalising and glamorising the behaviour by emphasising its social and enjoyable aspects. Additionally, cross-promotion with alcohol and portrayals of polysubstance use further enhance its appeal.^{27 52} Additionally, existing regulations often fail to address the unique characteristics of WPS, resulting in regulatory gaps where establishments serving these products are not subject to the same stringent standards as those for cigarette smoking, such as restrictions on indoor smoking, health warning displays and taxation policies. This regulatory disparity stems partly from the different composition and consumption patterns of waterpipe tobacco, as well as inconsistent classification under tobacco control laws.

A critical research gap exists in systematically evaluating how regulatory differences affect WPS prevalence, exposure risks and public health outcomes. Furthermore, tobacco cessation interventions specifically tailored to waterpipe smokers remain critically underexplored. Waterpipe users often differ from cigarette smokers in behaviours, social contexts, perceptions of harm and motivation to quit smoking, indicating that cessation strategies effective for cigarette smoking may not be as successful for waterpipe users. Targeted research is urgently required to develop, test and implement cessation approaches that address the distinct motivations and patterns of WPS to enhance quit rates in this population.^{33 53 54}

Several significant barriers have hindered the advancement of research on WPS. In regions where waterpipe use is culturally entrenched, insufficient research infrastructure, limited funding and a lack of trained personnel have constrained study capacities. In contrast, in areas with stronger research systems, the focus on cigarette smoking often overshadows waterpipe-related investigations, while the long latency period for health outcomes delays observable impacts. Furthermore, social and cultural diversity in waterpipe practices and the widespread misinformation about its safety impede the development of context-specific research tools and public health interventions.

ROADMAP

Consortium development: We are forming an international research consortium dedicated to advancing the scientific understanding of WPS and its associated health risks, including cancer, cardiovascular disease, respiratory outcomes and additional adverse health effects. In addition to the initial meeting participants, the consortium will integrate a broad multidisciplinary network of experts spanning epidemiology, clinical sciences, molecular biology, toxicology, social sciences, data science, engineering and public policy. Leveraging the collective global evidence base and diverse expertise within this collaborative platform, the consortium's overarching roadmap for future priorities includes: (1) conducting large and well-designed epidemiological and clinical studies to investigate the effects of WPS on human health, (2) identifying biomarkers and establishing mechanistic evidence that can provide a biological basis for identified

associations, enhance exposure assessment, and appraise the causal relevance of WPS in disease aetiology, (3) triangulating evidence from multiple resources such as cohort studies, case-control datasets and clinical and experimental models and (4) contributing with reliable evidence for educational purposes, raising awareness and guiding tobacco control programmes. This roadmap will necessitate coordinated contributions from a wide range of disciplines, including epidemiology, clinical medicine, data science, biology, mechanical engineering, sociobehavioural science, exposure science, toxicology, public health and policy.

Address the research barriers: Progress in WPS research has been hindered by several major barriers, including insufficient funding, methodological and measurement challenges, difficulties in accurately characterising exposure, and the cultural and social normalisation of waterpipe use that complicates participant recruitment. Additionally, research efforts remain fragmented, with limited global coordination, restricting opportunities for data sharing, large-scale harmonised analyses and capacity building—particularly in regions with high WPS prevalence and limited resources. To address these challenges, our consortium is committed to establishing a unified international research network that will (1) develop and implement standardised study protocols, validated exposure assessment tools and centralised secure data repositories to facilitate data harmonisation and sharing. This infrastructure will enable pooled analyses and meta-analyses across multiple populations and geographic regions, enhancing statistical power, comparability and generalisability of findings; (2) integrate epidemiological cohorts and biobank resources, particularly from high-prevalence countries in EMR, while promoting the development of new longitudinal studies and clinical investigations specifically designed to evaluate WPS and its health impacts; (3) foster interdisciplinary collaboration across epidemiology, clinical sciences, molecular biology, toxicology, social sciences and policy evaluation. This will include biomarker discovery, mechanistic studies and assessment of tobacco control policies, generating robust evidence on causal relationships and effective interventions; (4) implementing targeted training and mentorship programmes in epidemiological methods, molecular techniques, exposure assessment, data science and culturally competent participant engagement, with a focus on empowering researchers in resource-limited settings and (5) collaborating with global health organisations such as the WHO to raise awareness, advocate for sustainable funding and support infrastructure development.

By uniting these strategic efforts within a cohesive global network, the consortium will generate high-quality, actionable evidence. This evidence base will be essential to inform and strengthen global tobacco control policies and public health strategies aimed at reducing the burden of WPS worldwide. Resources for constructing this roadmap should likely include the following:

1) Cohort studies: Assembling large, well-designed cohorts with comprehensive exposure assessment remains a critical priority. However, these studies are resource-intensive and require long follow-up periods before yielding robust evidence. In the absence of such data, tobacco control efforts remain constrained, and preventable tobacco-related deaths will continue to occur. Although establishing new cohorts specifically tailored to WPS is challenging, it becomes feasible when adequate funding is available. In the interim, it is essential to leverage existing cohorts that already capture WPS exposure and to integrate multiple such cohorts globally through pooled or meta-analytic approaches. Promising starting points exist in several Middle Eastern countries (eg, Lebanon, Iran and Saudi

Table 1 Summary of WPS research gap and GLOW's roadmap to address the research gap

Research gap area	Specific challenges	GLOW's strategic roadmap
Methodological limitations	▶ Small sample sizes and limited statistical power ▶ Recall bias and overreliance on case-control designs ▶ Lack of adjustment for confounding factors (eg, dual/poly use) in previous studies ▶ Absence of standardised, validated tools for exposure (dose, frequency, duration) ▶ Limited stratification by age, sex and user type (exclusive/dual/poly)	▶ Develop standardised protocols, validated questionnaires and exposure assessment tools ▶ Integrate advanced biomarkers (eg, epigenomic signatures) for dose and duration quantification ▶ Launch large, multinational cohort and case-control studies ▶ Promote pooled and federated data analysis to improve generalisability and power
Geographical and practice variability	▶ Heterogeneity in waterpipe products, usage patterns and cultural practices across regions ▶ Under-reporting and poor generalisability due to regional data gaps	▶ Establish multinational collaborations across diverse populations ▶ Harmonise data collection using centralised repositories ▶ Prioritise research in high-prevalent, under-represented regions (eg, EMR, North Africa, South Asia)
Molecular research	▶ Underdeveloped research infrastructure for molecular research in high-prevalence areas ▶ Limited studies on biomarkers, gene-environment interactions and epigenetic changes ▶ Lack of experimental models replicating real-world WPS exposures	▶ Expand molecular and mechanistic studies to identify WPS-specific biomarkers ▶ Invest in omics-based research (eg, genomic, epigenomic) ▶ Use experimental models (eg, smoking robots, cell/animal studies) to simulate exposure ▶ Study gene-WPS interactions to elucidate disease mechanisms
Clinical research and cessation	▶ Scarcity of clinical data on waterpipe-related diseases ▶ Lack of cessation interventions tailored to waterpipe users' behavioural profiles	▶ Conduct clinical studies assessing WPS-related morbidity across disease types ▶ Develop, test and implement cessation programmes specifically designed for waterpipe users
Health outcomes research	▶ Limited evidence from high-prevalence countries on a wide range of WPS-related outcomes Gaps in research on cancers (liver, cervix, kidney, haematologic) and non-cancer outcomes (CVD, respiratory, reproductive).	▶ Promote comprehensive health outcomes research across multiple systems (oncologic, cardiovascular, respiratory, reproductive, etc) ▶ Include vulnerable and underrepresented populations highly exposed to WPS (eg, women, adolescents, EMR countries)
Behavioural and social factors	▶ Research examining the interplay between adolescent behaviour, social media influence and cultural motivations for WPS adoption is insufficient. ▶ Prevalent misconceptions about WPS safety	▶ Conduct behavioural studies targeting youth, peer influence and social norms ▶ Monitor and analyse social media platforms promoting WPS ▶ Use qualitative and mixed-methods research to inform culturally sensitive interventions
Regulatory and policy gaps	▶ Regulatory frameworks often exclude or inadequately cover WPS ▶ Inconsistent application of WHO FCTC measures ▶ Weak enforcement in waterpipe venues	▶ Evaluate and enhance implementation of FCTC measures specific to WPS (eg, taxation, packaging, smoke-free zones) ▶ Develop and promote WPS-specific policies and enforcement mechanisms ▶ Engage national governments and international bodies in harmonising WPS regulation
Research capacity and coordination	▶ Insufficient funding and infrastructure, especially in high-prevalence regions ▶ Fragmented global efforts, lack of coordination ▶ Limited training opportunities in WPS-specific research	▶ Establish a global WPS research consortium (GLOW) to coordinate and align efforts ▶ Advocate for sustainable funding from global and regional organisations ▶ Provide training, mentorship and capacity-building programmes in research methods, molecular techniques and public health ▶ Organise international conferences and workshops for collaboration, knowledge exchange and dissemination

CVDs, cardiovascular diseases; EMR, Eastern Mediterranean Region; GLOW, Global Research on WPS and Health; WHO FCTC, WHO Framework Convention on Tobacco Control; WPS, waterpipe smoking.

Arabia), where relevant epidemiological data and biobanking resources are already in place.

2) Case-control studies: New case-control studies can be launched in collaboration with researchers from high-prevalence countries, and/or existing control series could be repurposed. Despite limitations of this design, like selection bias, case-control studies can be more feasible and cost-effective, specifically for molecular and genetic epidemiology and biomarker discovery. Conducting pooled and federated analyses across existing case-control studies can reduce the impact of potential study biases and yield more robust results on WPS and health risks. This approach can also provide higher

statistical power and allow for subgroup analyses, such as exclusive waterpipe smokers, dual/poly users, the effect of cessation, etc.

Additionally, case-control studies can allow direct access to clinical data and the study of clinical outcomes related to WPS. Adding molecular and epi/genetic components and clinical data can enhance the study designs and reduce exposure biases by using epigenomics-based exposure assessment and increase the chances of securing international funding.

3) Non-cancer outcomes: Despite the importance of research on all tobacco-related cancers, it is also important to produce more evidence on the association between WPS and other health

outcomes, including cardiovascular and respiratory diseases. The consortium may expand the working groups to involve researchers and associations focused on these health readouts, which could also serve as positive or negative control outcomes for associations investigating cancer development.

4) Experimental systems: Coupling biological models (eg, cell and animal models) to bioengineered smoking robots that mimic the smoking behaviour in humans can offer highly controllable experimental settings that can model smoking exposures and outcomes using well-defined inputs and outputs.⁵⁵ This approach can offer several advantages, such as further limiting exposure assessment bias (as compared with questionnaires), enhancing direct comparisons between WPS and other related exposures (as compared with 'sessions' of waterpipe vs 'numbers' of cigarettes), and reinforcing causality of associations between experimentally controlled exposures and subsequently observed mechanistic effects.

5) Policy research agenda: Addressing the WPS epidemic requires a comprehensive research agenda aligned with the principles of the FCTC. This agenda prioritises assessing public awareness and misconceptions about the health risks to inform targeted educational interventions (FCTC Article 12). Simultaneously, research should evaluate the effectiveness of FCTC measures such as taxation (Article 6), smoke-free environment enforcement (Article 8), packaging and labelling regulations (Article 11), advertising bans (Article 13), public awareness campaigns (Article 12), and tailored cessation support (Article 14)—especially among vulnerable groups such as youth, women and dual/poly tobacco users. Intervention research should encompass behavioural, cessation, policy, regulatory, educational and digital/e-health approaches, utilising randomised controlled trials, observational studies, implementation science and policy evaluation frameworks to generate high-quality evidence on feasibility, acceptability, effectiveness and scalability. Key research questions should address the effectiveness of different intervention strategies in diverse settings. Qualitative and quantitative studies on cultural and social determinants—such as social norms, peer influences and misconceptions driving waterpipe use and affecting research participation—are essential for designing culturally sensitive recruitment strategies and interventions. Longitudinal research is critical to monitor the impact of policies and interventions on smoking prevalence, public attitudes and health outcomes. Table 1 summarises the key research gaps and the corresponding strategic actions proposed by the Global Research on WPS and Health (GLOW) consortium to address them.

CONCLUSIONS

WPS has emerged as a significant global public health concern, driven by its rising prevalence, especially among youth, and fuelled by misconceptions regarding its safety. Despite evidence linking WPS to multiple adverse health outcomes, including cancer and CVDs, existing studies remain limited by methodological weaknesses and geographic gaps. The unique social, cultural and regulatory contexts of WPS, particularly in the EMR, further complicate efforts to fully understand and control its impact. Addressing these challenges requires coordinated international efforts, such as the formation of the GLOW consortium, which aims to advance rigorous, multidisciplinary research and foster collaboration among epidemiologists, clinicians, molecular scientists and policymakers. By implementing the proposed roadmap—including large cohort and case-control studies, mechanistic research and policy-focused investigations, this consortium can generate robust evidence to shed light on the full spectrum of health effects and underlying biological mechanisms associated with WPS and inform effective prevention strategies and regulatory policies. Ultimately, these efforts will contribute

to reducing the burden of WPS and safeguarding public health worldwide.

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Correction notice This article has been corrected since it was first published. Author's name from "Mohammad Muzaffar" to "Mohammad Muzaffar Mir" has been updated.

Acknowledgements The meeting was organised by the University of Bologna (Italy) in collaboration with the Cancer Institute of Iran (Iran), the American University of Beirut (Lebanon) and the National Cancer Institute (USA).

Contributors FT prepared the draft based on the meeting and several consultations with all the authors before and after the meeting. All authors reviewed the draft multiple times and finally approved the report. PB and KZ are guarantors.

Funding The meeting was funded based on a grant from the Italian Association for Research on Cancer (AIRC), Italy (grant number: 24706).

Disclaimer Where authors are identified as personnel of the International Agency for Research on Cancer (IARC)/WHO/National Cancer Institute (NCI), they alone are responsible for the views expressed in this article, and do not necessarily represent the decisions, policies or views of their institution.

Competing interests No, there are no competing interests.

Patient consent for publication Not applicable.

Ethics approval The study is a Review of Evidence and Road Map for an International Consortium and does not contain any information on subjects.

Provenance and peer review Not commissioned; externally peer reviewed.

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