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Review Article

Non-Invasive Approaches for Cotinine Detection: Enhancing Accessibility in Tobacco Use Monitoring

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Abstract

Non-invasive approaches for cotinine detection have emerged as vital tools for enhancing access to tobacco use monitoring, addressing the pressing need for reliable, user-friendly methods in public health and clinical settings. This literature review explored various non-invasive testing methods, including saliva, urine, sweat patches, hair analysis, and breath analysis, highlighting their respective detection windows, accuracy, and feasibility. The review emphasizes the role of these methods in public health monitoring, particularly in identifying high-risk populations and facilitating smoking cessation programs. Furthermore, it discusses the implications of non-invasive testing for research on tobacco exposure and secondhand smoke, underscoring the importance of accurate data collection in shaping effective tobacco control policies. Despite the advantages, challenges such as sensitivity, specificity, and environmental factors affecting test results are critically examined. The review identifies areas for future research, including technological innovations and the potential for expanded use in low-resource settings. Ultimately, this review advocates integrating non-invasive cotinine detection methods into routine practice to improve health outcomes and promote informed decision-making about tobacco use.

Keywords: Biomarker, Tobacco use, Nicotine, Public health surveillance

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Introduction

The tobacco situation in India is unique because of a vast spectrum of tobacco products available for smoking as well as smokeless use. The epidemic of harmful substance use, mainly chewing tobacco and smoking, is increasing at an alarming pace. Nearly 1.3 billion people around the world are tobacco users, and 80% of them live in low- and middle-income countries. Tobacco use kills 8 million people every year worldwide.[1]

Non-invasive methods for monitoring tobacco use, particularly through the measurement of cotinine, have gained prominence due to their practicality and reduced burden on participants. Traditional methods, such as self-reported smoking status, are often subject to bias and inaccuracies, as individuals may underreport their tobacco use due to social stigma or health concerns.[2] In contrast, non-invasive sampling techniques, such as urine or saliva collection, provide objective data that can enhance the reliability of tobacco exposure assessments.[3]

Cotinine, the primary metabolite of nicotine, serves as a well-established and reliable biomarker for evaluating tobacco exposure. It is produced in the liver through nicotine metabolism and has an approximate half-life of 20 hours, making it an effective indicator of recent tobacco consumption.[4,5] Cotinine can be measured in various biological specimens such as urine, saliva, and blood, providing flexibility in sampling based on study requirements.[6,7] Its detection in these biological fluids allows for quantitative assessment of nicotine intake, which is essential for determining the extent of tobacco exposure among both active smokers and individuals exposed to secondhand smoke.[8,9] The use of cotinine as a biomarker has been invaluable in epidemiological investigations, public health evaluations, and clinical research, as it facilitates understanding of the health impacts of tobacco use and assessment of smoking cessation interventions.[10,11] Furthermore, cotinine concentrations reflect the intensity of tobacco exposure, which is crucial for estimating the potential risk of developing tobacco-related diseases.[12,13]

The ability to measure cotinine levels non-invasively allows for broader applications in various settings, including clinical trials, public health surveys, and community-based studies.[14] This approach not only facilitates the monitoring of tobacco use patterns but also aids in the evaluation of interventions aimed at reducing tobacco consumption.

The purpose of this literature review was to synthesize current research on the use of cotinine as a biomarker for

nicotine exposure, with a particular focus on non-invasive methods of measurement. This review aimed to examine the effectiveness of cotinine as a biomarker, highlight advancements in non-invasive monitoring techniques, and explore the implications for public health and clinical practice.

Invasive vs. Non-Invasive Approaches

Cotinine, a metabolite of nicotine, is a key biomarker for assessing tobacco exposure. The detection of cotinine can be performed through both invasive and non-invasive methods (Table 1). Invasive methods for nicotine testing typically involve obtaining blood samples (venous or arterial) to measure nicotine and its metabolites using sensitive analytical techniques such as liquid chromatography-tandem mass spectrometry (LC-MS/MS).[15]

Advantages of Non-Invasive Methods in Public Health and Clinical Settings

Non-invasive methods for nicotine testing offer several advantages over traditional invasive procedures. They significantly reduce discomfort and anxiety associated with blood draws, increasing their acceptability among a wider population. These approaches can be conveniently implemented in diverse settings such as community health programs, schools, and workplaces, thereby enabling large-scale screening efforts. Additionally, non-invasive sampling methods lower the costs related to laboratory processing and personnel training, making them a more economical option for extensive studies. They also permit more frequent and timely assessments of cotinine levels, which is particularly beneficial for monitoring the effectiveness of smoking cessation programs and interventions. Furthermore, by eliminating the use of needles, non-invasive methods minimize the risk of infection and other complications that are commonly linked with invasive techniques.[15]

Current Trends in Cotinine Detection Technology

Recent advancements in cotinine detection technology have focused on enhancing the sensitivity, specificity, and practicality of non-invasive methods. Some notable trends include:

Microfluidic Devices[16]

Innovations in microfluidic technology have led to the development of portable devices that can analyze saliva samples for cotinine levels quickly and accurately. These devices integrate sample collection and analysis into a single platform, streamlining the testing process.

Electrochemical Biosensors[17]

Recent studies have explored the use of electrochemical biosensors for the detection of cotinine in saliva. These sensors offer rapid results and can be designed for point-of-care testing, making them suitable for use in various clinical and public health settings.

Wearable Technology[15]

The integration of wearable devices capable of monitoring cotinine levels through sweat or other non-invasive means is an emerging area of research. These technologies aim to provide continuous monitoring of tobacco exposure, which could be particularly useful for individuals in smoking cessation programs.

Machine Learning and Data Analysis[18]

The application of machine learning algorithms to analyze cotinine detection data is gaining traction. These approaches can enhance the accuracy of predictions regarding tobacco exposure and improve the interpretation of results from non-invasive tests.

Environmental Monitoring[19]

Advances in environmental monitoring techniques, such as the use of passive samplers to detect cotinine in air or surface samples, are being explored. This could provide insights into secondhand smoke exposure in various settings.

As technology continues to evolve, these methods are likely to become increasingly integrated into routine assessments of tobacco exposure, enhancing our ability to monitor and address tobacco-related health issues effectively.

Saliva-Based Cotinine Testing Methodology

The steps for saliva-based cotinine testing[20,21] are discussed below.

Preparation

Participants are instructed to avoid eating, drinking, or smoking for a specific period before sample collection to minimize contamination.

Sample Collection

Saliva is collected using specialized devices such as

Table 1. Invasive vs. Non-Invasive Approaches

Approach	Method	Advantages	Challenges
Invasive[15]	Blood sampling	- High accuracy and reliability - Suitable for detailed analysis	- Requires trained personnel - Uncomfortable for patients due to needle insertion - Logistical challenges in blood collection and processing for large-scale studies
Non-Invasive[15]	Urine, Saliva, Sweat, Hair, Breath sampling	- Minimal discomfort for patients - Does not require specialized training - Allows for more frequent sampling - Better suited for large-scale, repeated sampling	- May have lower accuracy than invasive methods - Environmental factors may affect test results - Variability in sensitivity and specificity

Salivette tubes, cotton swabs, or by drooling directly into a collection tube to ensure adequate sample volume and minimize contamination.

Storage and Transport
Samples are stored at approximately 4°C to maintain cotinine stability during transport and storage until analysis, preserving sample integrity.

Analysis
Techniques like high-performance liquid chromatography (HPLC) and mass spectrometry are used to measure cotinine concentration with precision, making the method highly effective for quantifying tobacco exposure.

Urine Cotinine Testing
Urine is widely used as a biological matrix for cotinine testing due to its practical advantages, particularly its longer detection window compared to other matrices like blood or saliva. Cotinine, the primary metabolite of nicotine, has a half-life of approximately 20 hours, allowing it to remain detectable in urine for several days after tobacco exposure. This extended detection window is particularly beneficial for assessing both active smoking and secondhand smoke exposure, making urine a preferred choice for epidemiological studies and public health assessments.[22,23]

Methodology and Accuracy of Urine-Based Cotinine Assays
The methodology for urine cotinine testing typically involves several analytical techniques, including:

Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS)
Considered the gold standard for cotinine detection due to its high sensitivity and specificity. It allows for the simultaneous quantification of cotinine and other nicotine metabolites, providing a comprehensive assessment of tobacco exposure.[24]

Gas Chromatography-Mass Spectrometry (GC-MS)
Another highly accurate method, GC-MS is often used for the analysis of cotinine in urine samples. It involves liquid-liquid extraction or solid-phase extraction to isolate cotinine from urine before analysis.[25]

Immunoassays
Enzyme-linked immunosorbent assays (ELISA) and lateral flow immunoassays (LFIA) are also employed for cotinine detection. These methods are generally simpler and faster but may have lower sensitivity compared to LC-MS/MS and GC-MS.[25,26]

Sweat Patch Testing for Cotinine
Sweat patch testing is an innovative method for monitoring cotinine levels, the primary metabolite of nicotine, in a non-invasive manner. This method involves the application of a sweat patch to the skin, which collects sweat over a specified duration, typically ranging from 24 hours to several days, depending on the design of the patch and the intended monitoring period. The patch is designed to absorb sweat, allowing for the analysis of cotinine and other biomarkers without the need for blood or urine samples.

The sweat patch is typically made of a breathable, adhesive material that adheres to the skin, ensuring that sweat can be collected continuously during the wear period. The duration of wear can vary based on the specific application and the physiological conditions of the individual, with some patches designed for short-term monitoring (1-3 days) and others capable of longer wear (up to 14 days).[15,27]

Benefits of Continuous and Cumulative Exposure Monitoring
One of the primary advantages of sweat patch testing for cotinine is its ability to provide continuous and cumulative exposure monitoring. Unlike traditional methods that rely on single-point measurements (e.g., blood or urine tests), sweat patches can capture fluctuations in cotinine levels over time, offering a more comprehensive view of an individual's tobacco exposure.

Non-Invasive Collection
The sweat patch method is non-invasive, making it more acceptable to users, especially in populations such as children or those who may be uncomfortable with blood draws.[28,29]

Real-Time Monitoring
Continuous monitoring allows for the assessment of cotinine levels in real-time, which can be particularly useful in clinical settings for evaluating the effectiveness of smoking cessation programs or for monitoring exposure to secondhand smoke.[30]

Cumulative Data
The ability to collect data over several days provides insights into long-term exposure patterns, which can be critical for public health assessments and research studies.[31,32]

Sweat patches reliably detect cotinine, showing a strong correlation with urine and blood tests. Some patches can detect concentrations as low as 0.5 ng/mL.[33-35] Continued advancements in sweat patch technology and analytical methods will enhance its utility in public health and clinical applications.

Hair Analysis for Long-Term Cotinine Monitoring
Hair as a Sample for Retrospective Nicotine Exposure Analysis
Hair analysis has emerged as a valuable method for assessing long-term nicotine exposure through the measurement of cotinine, a primary metabolite of nicotine. Unlike other biological matrices such as blood or urine, which reflect short-term exposure, hair can provide

a historical record of nicotine intake over extended periods. This is due to the incorporation of cotinine into the hair shaft as it grows, allowing for the assessment of cumulative exposure to nicotine and tobacco smoke.

The process of hair growth allows cotinine levels to be analyzed in hair segments, providing insights into exposure patterns over time. For instance, a 1 cm segment of hair can represent approximately one month of exposure, making it possible to correlate cotinine levels with specific time frames of smoking behavior or environmental exposure to tobacco smoke.

Advantages of Long-Term Exposure Tracking

Extended Detection Window

Hair can retain cotinine for months, allowing for the assessment of long-term exposure to nicotine. This is particularly useful in studies where understanding chronic exposure is essential, such as in epidemiological research or public health assessments.[36,37]

Non-Invasive Collection

Collecting hair samples is a non-invasive procedure that is generally more acceptable to participants compared to blood draws or urine collection. This can enhance participation rates in studies and make it easier to gather samples from diverse populations.[38,39]

Stability of Samples

Hair samples are stable and can be stored for long periods without significant degradation, making them suitable for retrospective studies. This stability allows researchers to analyze samples long after they have been collected, providing flexibility in study design.[40]

Objective Measurement

Hair analysis provides an objective measure of nicotine exposure, reducing reliance on self-reported smoking status, which can be biased due to social stigma or recall inaccuracies.[41,42]

In other words, hair analysis for cotinine monitoring offers a promising approach for assessing long-term nicotine exposure, with significant implications for public health research and tobacco cessation programs. While challenges such as contamination and variability exist, advancements in analytical techniques and standardization efforts can enhance the reliability and applicability of this method in various contexts.

Breath Cotinine Analysis

Introduction to Breath Testing and Exhaled Breath Condensate (EBC) Methods

Breath testing for cotinine, a metabolite of nicotine, is an emerging non-invasive method for assessing tobacco exposure. This technique primarily utilizes exhaled breath condensate (EBC), which is the aerosolized liquid collected from exhaled air. EBC contains various biomarkers, including cotinine, which can provide insights into an individual's smoking status and exposure to secondhand smoke.

The process of breath testing involves collecting exhaled air, which is then cooled to condense the vapor into a liquid form. This liquid can be analyzed for cotinine levels using various analytical techniques, such as gas chromatography-mass spectrometry (GC-MS) or liquid chromatography-tandem mass spectrometry (LC-MS/MS). The ability to measure cotinine in breath offers a unique advantage, as it reflects recent exposure to tobacco products without the need for invasive sampling methods.[43]

Potential for Non-Invasive, Real-Time Monitoring

One of the most significant advantages of breath cotinine analysis is its non-invasive nature, making it more acceptable to participants compared to blood or urine tests. This method allows for real-time monitoring of cotinine levels, which can be particularly beneficial in various settings:

Future Potential in Point-of-Care and Cessation Programs

Despite the challenges, breath cotinine analysis holds significant potential for future applications:

Integration into Cessation Programs

Breath testing could be incorporated into smoking cessation programs, providing individuals with immediate feedback on their tobacco exposure and progress in reducing nicotine intake. This real-time monitoring could enhance motivation and adherence to cessation efforts.

Development of Portable Devices

Advances in sensor technology could lead to the development of portable breath analyzers that can be used in various settings, including homes, clinics, and public health campaigns. These devices could facilitate widespread screening and monitoring of tobacco exposure.

Research Applications

Breath analysis can contribute to research on the effects of tobacco exposure on health outcomes, helping to establish correlations between cotinine levels and various health conditions.

Personalized Health Monitoring

The ability to monitor cotinine levels in real-time could pave the way for personalized health interventions, allowing individuals to track their exposure and make informed decisions about their health.[44]

In summary, breath cotinine analysis represents a promising non-invasive method for monitoring tobacco exposure, with significant implications for public health, clinical practice, and smoking cessation programs. While there are challenges related to sensitivity and standardization, ongoing research and technological advancements are likely to enhance the utility and accuracy of this method in the future.

Comparative Analysis of Non-Invasive Cotinine Testing Methods

Non-invasive cotinine testing methods include saliva testing, urine testing, sweat patch testing, and breath analysis. Each method has distinct characteristics regarding detection windows, accuracy, feasibility, strengths, limitations and applications are shown in Table 2.

Suitability for Specific Populations

For children, saliva testing is ideal due to its ease of collection. Urine testing is suitable with supervision, while sweat patch testing requires caution to avoid skin irritation. Breath analysis is non-invasive but may need trained personnel for accuracy.

For chronic users, saliva and urine testing are effective for recent exposure but not long-term monitoring. Sweat patch testing is better for long-term tracking, while breath analysis offers immediate feedback but is less suitable for chronic use.

Saliva and urine testing are good for recent exposure, sweat patches for long-term monitoring, and breath analysis for real-time assessments, though it faces sensitivity challenges.[35]

Future Directions and Research Needs

Innovations and Technological Advancements in Non-Invasive Cotinine Testing

The field of non-invasive cotinine testing is rapidly evolving, driven by technological advancements that enhance the accuracy, convenience, and applicability of these methods. Innovations in sensor technology, data analytics, and integration with digital health platforms pave the way for more effective monitoring of tobacco exposure.

Advanced Sensor Technologies

The development of more sensitive and specific sensors for detecting cotinine in various biological matrices (saliva, urine, sweat, and breath) is crucial. Innovations such as microfluidic devices and electrochemical sensors are being explored to improve detection limits and reduce the time required for analysis.[45]

Wearable Devices

The integration of non-invasive cotinine testing into wearable technology could facilitate continuous monitoring of tobacco exposure. These devices could provide real-time feedback to users, promoting awareness and encouraging cessation efforts.[15]

Artificial Intelligence and Machine Learning

The application of AI and machine learning algorithms to analyze cotinine data can enhance predictive capabilities and improve the interpretation of results. These technologies can help identify patterns in tobacco use and exposure, leading to more personalized interventions.[46]

Point-of-Care Testing

The development of portable, point-of-care testing devices for cotinine detection can increase accessibility, particularly in remote or underserved areas. These devices can provide immediate results, facilitating timely interventions.[47]

Areas for Further Research, Including Sensitivity and Specificity Improvements

While non-invasive cotinine testing methods have shown promise, several areas require further research to enhance their effectiveness:

Sensitivity and Specificity

Ongoing research is needed to improve the sensitivity and specificity of non-invasive tests. This includes optimizing

Table 2. Comparison of Cotinine Testing Methods: Characteristics, Applications, and Limitations

Testing Method	Detection Window	Sensitivity	Feasibility	Strengths	Applications	Limitations
Saliva Testing	Up to 3–4 days	High (73%–94%)	Easy, non-invasive	High acceptance; suitable for surveys and trials	Public health studies (children, adolescents); clinical verification of tobacco exposure; home self-monitoring	Affected by hydration, oral hygiene, diet; variability in sensitivity; requires standardized collection; contamination risk
Urine Testing	Up to 3–4 days	Very high (>90% for LC-MS/MS)	Non-invasive, widely accepted	Highly accurate; standard clinical and forensic method	Epidemiological studies; smoking cessation programs; ETS exposure assessment; clinical identification of tobacco use	Sample contamination risk; variability due to hydration/diet; difficulty in cut-off values; ethical/privacy concerns
Sweat Patch Testing	1–14 days	Moderate to high (variable)	Non-invasive, continuous monitoring	Ideal for long-term monitoring; useful in field settings	Clinical and research monitoring; workplace/school-based studies; real-world exposure tracking	Affected by temperature/humidity; variability in sweat composition; possible skin irritation; limited quantitative accuracy
Hair Analysis	Weeks to months (long-term)	High (for chronic exposure)	Non-invasive but requires lab processing	Reflects long-term exposure; useful for retrospective analysis	Public health research; long-term exposure assessment; tobacco cessation monitoring; epidemiological studies	External contamination risk; lag time; variability in hair growth; need for standardization
Breath Analysis	Hours to days	Moderate (variable)	Non-invasive, real-time	Immediate feedback; point-of-care utility	Public health monitoring; clinical screening; rapid assessment and cessation motivation	Lower sensitivity; influenced by diet/metabolism; short detection window; requires standardization

collection methods, refining analytical techniques, and developing standardized protocols to minimize variability in results.[47]

Longitudinal Studies
More longitudinal studies are necessary to assess the long-term reliability and accuracy of non-invasive cotinine testing methods. These studies can help establish the correlation between cotinine levels and health outcomes over time.

Population-Specific Research
Research should focus on the applicability of non-invasive testing methods across diverse populations, including children, pregnant women, and individuals with chronic health conditions. Understanding how factors such as age, gender, and health status affect cotinine levels can inform tailored interventions.

Integration with Other Biomarkers
Exploring the potential of combining cotinine testing with other biomarkers of tobacco exposure or health outcomes could enhance the overall assessment of tobacco-related health risks.

Potential for Expanded Use in Low-Resource Settings
Non-invasive cotinine testing methods hold significant potential for implementation in low-resource settings, where traditional testing methods may be impractical or unavailable:

Cost-Effectiveness
Non-invasive methods are generally less expensive than invasive procedures, making them more accessible for low-resource healthcare systems. Research into cost-effective testing solutions can facilitate broader adoption.

Training and Education
Developing training programs for healthcare providers in low-resource settings can enhance the implementation of non-invasive testing methods. Education on the importance of tobacco monitoring and cessation can empower communities to take charge of their health.

Community Engagement
Engaging communities in the development and implementation of non-invasive testing programs can increase acceptance and participation. Tailoring interventions to meet the specific needs and cultural contexts of communities can enhance their effectiveness.

Quality Control of Cotinine Measurement
High-quality measurement of cotinine requires rigorous validation and ongoing quality control to ensure both precision (reliability) and accuracy (trueness). Several published methods illustrate the components and performance metrics one should consider:

Method Validation Parameters
Many studies validate LC-MS/MS assays for cotinine using control samples at different concentrations (low, medium, high, plus a lower limit of quantification, LLOQ) to assess intra- and inter-run precision (usually expressed as coefficient of variation, CV%) and accuracy (bias from nominal values). For example, Abdullah et. al, 2016 developed a plasma assay with QC samples at 4 concentration levels; mean accuracies for cotinine ranged between ~90.3% to ~102.9%, and intra- and inter-day precision (RSD) were < 15% for all analytes.[48]

Limits of Quantification and Detection
Establishing LOD (Limit of Detection) and LOQ (Limit of Quantification) is essential. A recent method for serum and saliva samples has reported LOQs for cotinine around 0.25 to 1 ng/mL, depending on matrix, with good linearity ($R^2 > 0.995$) over a wide working range.[49]

Accuracy & Bias
True values are assessed via recovery experiments and comparison with reference/control materials. In urine assays (including multiple metabolites), recoveries for cotinine and its metabolites were high (often 76-99%) with bias typically within ± 10%.[49]

Precision (Random Error)
Precision is quantified by repeated measurements. Within-run (repeatability) and between-run (reproducibility) CVs are reported. Good methods report CVs often < 10% for mid- and high-concentration QC samples, somewhat higher (e.g., up to ~15-20%), acceptable at LLOQ levels.[50]

Conclusion
In summary, non-invasive cotinine testing methods represent a significant advancement in tobacco exposure monitoring, offering numerous benefits in terms of accessibility, convenience, and patient comfort. Key findings from the literature highlight the effectiveness of these methods in various settings, including public health monitoring, clinical practice, and research.

The importance of non-invasive methods lies in their ability to enhance accessibility for tobacco monitoring, particularly in populations that may be reluctant to engage in traditional testing methods. As research continues to advance, the integration of innovative technologies and the focus on improving sensitivity and specificity will further solidify the role of non-invasive cotinine testing in public health initiatives.

Ultimately, the impact of these methods on public health initiatives and research is profound, as they provide valuable data that can inform tobacco control policies, enhance smoking cessation efforts, and improve health outcomes for individuals and communities affected by tobacco use.

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References

1. World Health Organization (WHO). Tobacco: Factsheet. Geneva: WHO; 2018.
2. Akiyama Y, Arashidani K, Kawano W, Kunugita N. Urinary nicotine and its metabolites as a biomarker of exposure to environmental tobacco smoke. J UOEH 2006;28(3):245-52. doi:10.7888/juoeh.28.245
3. Coleman T. Commentary on Taghavi et al. (2018): accurate measurement of tobacco smoke exposure and smoking behaviour matters. Addiction 2018;113(11):2097-8. doi:10.1111/add.14389
4. Dai HD, Michaud T, Guenzel N, Morgan M, Cohen SM. Biomarker assessment of nicotine exposure among adolescent e-cigarette users: 2018-2019. Pediatrics 2024;153(4):e2023062424. doi:10.1542/peds.2023-062424
5. Merianos AL, Jandarov RA, Mahabee-Gittens EM. Carcinogenic and tobacco smoke-derived particulate matter biomarker uptake and associated healthcare patterns among children. Pediatr Res 2023;93(1):143-53. doi:10.1038/s41390-022-02031-w
6. Kim H, Lim Y, Lee S, Park S, Kim C, Hong C, et al. Relationship between environmental tobacco smoke and urinary cotinine levels in passive smokers at their residence. J Expo Anal Environ Epidemiol 2004;14 Suppl 1:S65-70. doi:10.1038/sj.jea.7500360
7. Oh S, Kim S, Sung E, Kim CH, Kang JH, Shin H, et al. The association between cotinine-measured smoking intensity and sleep quality. Tob Induc Dis 2022;20:77. doi:10.18332/tid/152221
8. Groppetti D, Pizzi G, Pecile A, Bronzo V, Mazzola SM. Cotinine as a sentinel of canine exposure to tobacco smoke. Animals (Basel) 2023;13(4):693. doi:10.3390/ani13040693
9. Mazumder S, Shia W, Bendik PB, Achilihu H, Sosnoff CS, Alexander JR, et al. Nicotine exposure in the US population: total urinary nicotine biomarkers in NHANES 2015-2016. Int J Environ Res Public Health 2022;19(6):3660. doi:10.3390/ijerph19063660
10. Hajat C, Stein E, Ramstrom L, Shantikumar S, Polosa R. The health impact of smokeless tobacco products: a systematic review. Harm Reduct J 2021;18(1):123. doi:10.1186/s12954-021-00557-6
11. Hersi M, Beck A, Hamel C, Esmaeilisaraji L, Pussegoda K, Austin B, et al. Effectiveness of smoking cessation interventions among adults: an overview of systematic reviews. Syst Rev 2024;13(1):179. doi:10.1186/s13643-024-02570-9
12. Le Foll B, Piper ME, Fowler CD, Tonstad S, Bierut L, Lu L, et al. Tobacco and nicotine use. Nat Rev Dis Primers 2022;8(1):19. doi:10.1038/s41572-022-00346-w
13. Ebbert JO, Dale LC, Nirelli LM, Schroeder DR, Moyer TP, Hurt RD. Cotinine as a biomarker of systemic nicotine exposure in spit tobacco users. Addict Behav 2004;29(2):349-55. doi:10.1016/j.addbeh.2003.08.046
14. Avila-Tang E, Al-Delaimy WK, Ashley DL, Benowitz N, Bernert JT, Kim S, et al. Assessing secondhand smoke using biological markers. Tob Control 2013;22(3):164-71. doi:10.1136/tobaccocontrol-2011-050298
15. Raja M, Garg A, Yadav P, Jha K, Handa S. Diagnostic methods for detection of cotinine level in tobacco users: a review. J Clin Diagn Res 2016;10(3):ZE04-6. doi:10.7860/jcdr/2016/17360.7423
16. Lee K, Yoon T, Yang HS, Cha S, Cheon YP, Kashefi-Kheyrabadi L, et al. All-in-one platform for salivary cotinine detection integrated with a microfluidic channel and an electrochemical biosensor. Lab Chip 2020;20(2):320-31. doi:10.1039/c9lc01024f
17. Mani V, Beduk T, Khushaim W, Ceylan AE, Timur S, Wolfbeis OS, et al. Electrochemical sensors targeting salivary biomarkers: a comprehensive review. Trends Analyt Chem 2021;135:116164. doi:10.1016/j.trac.2020.116164
18. Verma VK, Verma S. Machine learning applications in healthcare sector: an overview. Mater Today Proc 2022;57(Pt 5):2144-7. doi:10.1016/j.matpr.2021.12.101
19. Kot-Wasik A, Zabiegała B, Urbanowicz M, Dominiak E, Wasik A, Namieśnik J. Advances in passive sampling in environmental studies. Anal Chim Acta 2007;602(2):141-63. doi:10.1016/j.aca.2007.09.013
20. Foddai SG, Radin M, Barinotti A, Cecchi I, Rubini E, Arbrile M, et al. New frontiers in autoimmune diagnostics: a systematic review on saliva testing. Int J Environ Res Public Health 2023;20(10):5782. doi:10.3390/ijerph20105782
21. Jung C, Kim M. Direct use of a saliva-collected cotton swab in lateral flow immunoassay for the detection of cotinine. Biosensors (Basel) 2022;12(4):214. doi:10.3390/bios12040214
22. Jain R, Ghosh S, Saifi N. An efficient method for simultaneous detection of pheniramine, pentazocine and cotinine in urine by gas chromatography in de-addiction program. Addict Health 2022;14(2):96-104. doi:10.22122/ahj.2022.196722.1179
23. Purushothama J, Badiger S, Kumar N, Baikunje N, D'souza N, D'Mello M, et al. Validity assessment of self-reported smoking status to detection of urine cotinine levels among patients with tuberculosis undergoing tobacco cessation treatment. Biomedicine 2022;42(2):371-6. doi:10.51248/.v42i2.1412
24. Bartolomé M, Gallego-Picó A, Huetos O, Castaño A. High-performance liquid chromatography with diode-array detection cotinine method adapted for the assessment of tobacco smoke exposure. J Sep Sci 2014;37(12):1404-10. doi:10.1002/jssc.201301259
25. Krokos A, Orfanidis A, Mastrogianni O, Mitsa F, Avgeri M, Eboriadou M, et al. Gas chromatography-mass spectrometry determination of nicotine and cotinine in urine: a study of the effect of passive smoking. Rapid Commun Mass Spectrom 2024;38(18):e9864. doi:10.1002/rcm.9864
26. Terzapulo X, Kassenova A, Bukasov R. Immunoassays: analytical and clinical performance, challenges, and perspectives of SERS detection in comparison with fluorescent spectroscopic detection. Int J Mol Sci 2024;25(4):2080. doi:10.3390/ijms25042080
27. Gluck L. A patch test for chloride in sweat as a simple screening method for detecting cystic fibrosis of the pancreas; preliminary report. Pediatrics 1959;23(4):731-7.
28. Gambelunghe C, Fucci N, Aroni K, Bacci M, Marcelli A, Rossi R. Cannabis use surveillance by sweat analysis. Ther Drug Monit 2016;38(5):634-9. doi:10.1097/ftd.0000000000000327
29. Huestis MA, Scheidweiler KB, Saito T, Fortner N, Abraham T, Gustafson RA, et al. Excretion of Δ9-tetrahydrocannabinol in sweat. Forensic Sci Int 2008;174(2-3):173-7. doi:10.1016/j.forsciint.2007.04.002
30. Kintz P, Tracqui A, Mangin P, Edel Y. Sweat testing in opioid

users with a sweat patch. J Anal Toxicol 1996;20(6):393-7. doi:10.1093/jat/20.6.393
31. Phillips EL, Little RE, Hillman RS, Labbe RF, Campbell C. A field test of the sweat patch. Alcohol Clin Exp Res 1984;8(2):233-7. doi:10.1111/j.1530-0277.1984.tb05846.x
32. Saff RR, Waldron JL. The safety and accuracy of drug patch testing in delayed hypersensitivity reactions. Curr Dermatol Rep 2023;12(4):260-8. doi:10.1007/s13671-023-00405-9
33. Liberty HJ, Johnson BD, Fortner N. Detecting cocaine use through sweat testing: multilevel modeling of sweat patch length-of-wear data. J Anal Toxicol 2004;28(8):667-73. doi:10.1093/jat/28.8.667
34. Servidoni MF, Gomez CC, Marson FA, Toro A, de Oliveira Ribeiro MÂ, Ribeiro JD, et al. Sweat test and cystic fibrosis: overview of test performance at public and private centers in the state of São Paulo, Brazil. J Bras Pneumol 2017;43(2):121-8. doi:10.1590/s1806-37562016000000076
35. Zhao FJ, Bonmarin M, Chen ZC, Larson M, Fay D, Runnoe D, et al. Ultra-simple wearable local sweat volume monitoring patch based on swellable hydrogels. Lab Chip 2020;20(1):168-74. doi:10.1039/c9lc00911f
36. Antunes MV, da Silva CF, Finger MA, Moore C, Linden R. Correlation analysis between cotinine hair concentrations from active smokers and nicotine intake and dependence. Ther Drug Monit 2015;37(3):405-7. doi:10.1097/ftd.0000000000000140
37. Eliopoulos C, Klein J, Koren G. Validation of self-reported smoking by analysis of hair for nicotine and cotinine. Ther Drug Monit 1996;18(5):532-6. doi:10.1097/00007691-199610000-00002
38. Tualeka AR, Jalaludin J, Sopian NA, Aziz MY, Rahmawati P, Ahsan A, et al. The relationship between cotinine levels in the blood with glutathione, and malondialdehyde levels of smokers: a systematic review and meta-analysis. F1000Res 2023;12:1466. doi:10.12688/f1000research.134993.1
39. Kataoka H, Kaji S, Moai M. Risk assessment of passive smoking based on analysis of hair nicotine and cotinine as exposure biomarkers by in-tube solid-phase microextraction coupled on-line to LC-MS/MS. Molecules 2021;26(23):7356. doi:10.3390/molecules26237356
40. Belhadj-Tahar H, Brousse F, Malonga G, Morais S, Sadeg N. Tin hair analysis in poly symptomatic patients with Essure® implant. World J Biol Pharm Res 2023;5(1):28-35. doi:10.53346/wjbpr.2023.5.1.0065
41. Gili A, Bacci M, Aroni K, Nicoletti A, Gambelunghe A, Mercurio I, et al. Changes in drug use patterns during the COVID-19 pandemic in Italy: monitoring a vulnerable group by hair analysis. Int J Environ Res Public Health 2021;18(4):1967. doi:10.3390/ijerph18041967
42. Wang R, Hall JM, Salloum RG, Kates F, Cogle CR, Bruijnzeel AW, et al. Prevalence of underreported nicotine exposure among US nonsmoking adults: a comparison of self-reported exposure and serum cotinine levels from NHANES 2013-2020. Nicotine Tob Res 2024;26(3):298-306. doi:10.1093/ntr/ntad165
43. Oldham MJ, Bailey PC, Castro N, Lang Q, Salehi A, Rostami AA. Prediction of potential passive exposure from commercial electronic nicotine delivery systems using exhaled breath analysis and computational fluid dynamic techniques. J Breath Res 2021;15(4):046006. doi:10.1088/1752-7163/ac2884
44. Paulo BF, Junior LF, Zauli DA. B-205 A simple method for opioids, synthetic opioids and PCP detection in hair samples by LC-MS/MS. Clin Chem 2023;69(Suppl 1):hvad097.534. doi:10.1093/clinchem/hvad097.534
45. Ghosh N, Verma S. Technological advancements in glucose monitoring and artificial pancreas systems for shaping diabetes care. Curr Med Res Opin 2024;40(12):2095-107. doi:10.1080/03007995.2024.2422005
46. Nyiramana Mukamurera P. Advances in non-invasive glucose monitoring: challenges, technologies, and future prospects. Res Output J Public Health Med 2024;3(3):1-5. doi:10.59298/ROJPHM/2024/3315
47. Shukla A. Laser-based ultrasonics for non-destructive material testing: a practical guide. i-manager's Journal on Material Science 2023;11(3):20-5. doi:10.26634/jms.11.3.20522
48. Abdallah IA, Hammell DC, Stinchcomb AL, Hassan HE. A fully validated LC-MS/MS method for simultaneous determination of nicotine and its metabolite cotinine in human serum and its application to a pharmacokinetic study after using nicotine transdermal delivery systems with standard heat application in adult smokers. J Chromatogr B Analyt Technol Biomed Life Sci. 2016;1020:67-77. doi:10.1016/j.jchromb.2016.03.020
49. Kim I, Huestis MA. A validated method for the determination of nicotine, cotinine, trans-3′-hydroxycotinine, and norcotinine in human plasma using solid-phase extraction and liquid chromatography-atmospheric pressure chemical ionization-mass spectrometry. J Mass Spectrom 2006;41(6):815-821. doi:10.1002/jms.1039
50. Kaisar MA, Kallem RR, Sajja RK, Sifat AE, Cucullo L. A convenient UHPLC-MS/MS method for routine monitoring of plasma and brain levels of nicotine and cotinine as a tool to validate newly developed preclinical smoking model in mouse. BMC Neurosci 2017;18(1):71. doi:10.1186/s12868-017-0389-5