Four years on, what is the SCENTinel screening tool is teaching us about smell disorders?

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SCENTinel test card. Credit: Monell Chemical Senses Center

First, there was SCENTinel 1.0, then 1.1, and now 2.1—the different iterations of the rapid screening tool for detecting new-onset loss of smell developed by scientists at the Monell Chemical Senses Center. Since its launch in late 2020, several studies have validated its accuracy in detecting smell dysfunction and value as a tool for testing in large populations of people.

SCENTinel is now the heart of an international campaign—led by Monell—to make smell testing a routine part of general wellness checks

with primary care physicians, as well as a screening tool for viral outbreaks such as COVID-19 or early smell loss associated with Parkinson's disease and related disorders. In addition, it has been patented and licensed to Ahersla Health for commercial use.

The COVID-19 pandemic showed sensory scientists the need for a quick, inexpensive, easy-to-use way to screen for smell disorders. The SCENTinel test card contains two blank labels and one with an odor. The user detects which label has the odor, rates its intensity, identifies the odor's name from a list of visual choices, and rates its pleasantness. The first three tasks provide an overall pass/fail score for smell function; pleasantness informs the potential of having a distorted sense of smell called parosmia.

The first version (SCENTinel1.0) had only one odor option: flower. SCENTinel 1.1 has four options: flower, coffee, bubblegum, and caramel popcorn, and the current version, SCENTinel 2.1, has nine options: flower, coffee, bubblegum, orange, strawberry, banana, coconut, woody, and lemon.

Even though there are nine odor options, each quick SCENTinel contains only one odor of the nine. For example, if a family of three took the test one evening at home, each could sniff just one type of odor—say, banana, coffee, and bubblegum—on their respective cards.

With each new study using the different versions of SCENTinel, researchers confirmed the advantages of using this rapid smell test. For example, a 2023 all-Monell-authored publication used SCENTinel 1.1 to discriminate between people with normosmia (a normal sense of smell), anosmia (total smell loss), hyposmia (reduced sense of smell), parosmia (distorted odor perception), and phantosmia (odor sensation without a source). The group also determined that SCENTinel 1.1 is the only smell test that can rapidly pick out parosmia from other types of smell

disorders. SCENTinel 2.1 continues to teach sensory scientists about different aspects of how people smell.

Two new papers putting SCENTinel to the test in community settings were published during the first half of 2024. [One study](link) in *Frontiers in Public Health* sought to answer whether SCENTinel could actually screen for COVID infections and if so, how accurately.

Between April 2021 and July 2022, over 1,900 individuals recruited on the campuses of the Northwestern University Hospital System took one SCENTinel test, completed at least one physician-ordered SARS-CoV-2 PCR test, and endorsed a list of self-reported symptoms from a given list. The team found that the self-rated odor intensity score from the SCENTinel test was the strongest predictor of SARS-CoV-2 infection, a feature that many commercial smell tests do not measure.

SCENTinel scored a high specificity and a negative predictive value, indicating that those who passed SCENTinel likely did not have a SARS-CoV-2 infection. SCENTinel also did a better job at screening for COVID-19 during the Delta variant outbreak compared to the omicron variant because smell loss was one of the initial symptoms of COVID during the Delta variant, but not the omicron variant, and prompt testing was reduced and delayed.

"This study showed that SCENTinel, as a rapid assessment tool, could be used for population-level screening to monitor abrupt changes in some participants' ability to smell and to evaluate spread of viral infections like SARS-CoV-2 that often have smell loss as a symptom," said first author Stephanie Hunter Ph.D., a Monell Postdoctoral Fellow.

SCENTinel showed a low sensitivity in this study, meaning that it did not do a great job of identifying whether someone actively had a COVID-19 infection. However, it still performed better at this than the self-reported

symptom list. This is important because self-reported symptoms were relied on early in the pandemic before diagnostic tests were available. If another pandemic occurs, SCENTinel could be rapidly deployed and excel at screening for a smell-loss-associated disorder to better contain the spread versus using self-reported symptoms alone.

"SCENTinel is good at identifying smell loss, irrespective of cause," said Valentina Parma, Ph.D., Monell Assistant Director. "Its power is in longitudinal data: how is one sense of smell changing over time? Hence, the need for routine smell testing."

The second study, published in *Chemical Senses*, assessed SCENTinel in a decidedly different population: twins, triplets, and singletons visiting the annual Twins Days Festival in Twinsburg, Ohio during August 2021 and 2022. Here, the investigators—including Hunter, Parma, Monell Member Pam Dalton, Ph.D., and Chief Science Officer Dani Reed, Ph.D.—probed the effects of genetics on odor perception to determine whether a quick smell test could effectively screen everyone.

For example, some people born with genetic insensitivities to specific odorants—called specific anosmia—may fail a test if they cannot smell a certain odor but otherwise have a normal sense of smell. To better understand whether genetic differences affect test results, the team asked Twins Days Fest participants to complete the SCENTinel test. A subset of twins also provided a saliva sample for genotyping.

The majority of the odors used in SCENTinel2.0 are not affected by genetic-driven perceptual biases, making this test version a good candidate for routine screening. For pleasantness, of the nine odors, banana is the most vulnerable to genetic differences. The team did find that two olfactory receptor gene variants, OR1G1 and OR2T33, were related to the pleasantness rating of the banana odor.

The OR1G1 receptor has been shown in other studies as being responsible in part for the waxy, fatty, and rose notes of a banana smell, as well as fruity and sweet scents. Knowing this genetic connection may contribute to incorrectly indicating that people who rate the banana odor as unpleasant have parosmia. These findings speak to the importance of an increased need to screen for parosmia, which has become more common during the pandemic.

Even though each quick SCENTinel test contains only one odor, it compares favorably in reliability to tests with many odors, with a test -retest correlation of 0.71. The commercial gold-standard tests—more time-consuming and cost intensive—had an almost identical reliability score compared to SCENTinel 2.1.

What's more, age and sex results using SCENTinel track closely with the other types of smell tests, adding to its reliability—this time across demographic groups. The results show that differences in SCENTinel performance on detection, intensity, and identification across age and sex groups match the results of other tests in that women have higher olfactory sensitivity and intensity ratings compared to men, and the sense of smell was better overall in younger people (18–41 years old) compared to older people (64–88 years old).

Importantly, the fact that SCENTinel demonstrates comparable reliability to established smell tests, strongly indicates its potential as a practical, less expensive, and much quicker screening tool for olfactory disorders in a community setting.

"In fact, one of our students in the Monell Science Apprenticeship Program is working on finalizing the validation of SCENTinel's performance compared to other tests," said Parma, also the Director of Academic Affairs at Monell.

"We are in the early stages of sales growth, developing a customer base across medical professionals and researchers with the goal of achieving the evidence and patient care guidelines that will lead to universal smell testing," said Ahersla CEO Patricia Lucas-Schnarre, regarding the commercialization of SCENTinel.

To get to the question in the title, clearly the answers are still pouring in about what SCENTinel has to teach the world.

More information: Hunter, S. R. et al. Using SCENTinel to predict SARS-CoV-2 infection: insights from a community sample during dominance of Delta and Omicron variants. *Frontiers in Public Health*, DOI: 10.3389/fpubh.2024.1322797, www.frontiersin.org/journals/p … bh.2024.1322797/full

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