Today's session, »Silent.Strokes?Loud.Consequences? took us deep into a part of stroke medicine that is easy to overlook: the in-fark shun" don't announce themselves, but still matter. These "silent" or "covert" brain in fark shun show up on imaging done for unrelated reasons, and the debates today centered on what—if anything—we should be doing about them.

The first debate asked whether silent infarctions should be treated with aspirin and secondaryprevention–level targets. Eric Smith opened by reminding us that "silent stroke" is a misnomer. These lesions may not produce symptoms recognized by patients or clinicians, but subtle cognitive or gait changes often exist. He showed that covert infarctions behave very much like symptomatic infarctions: in a large Kaiser Permanente dataset, individuals with covert infarctions had a fiveyear stroke risk of 16%, compared to 5% for those without them. After adjustment, the risk remains nearly two to threefold higher. He argued that this risk level is similar to what we see in symptomatic stroke survivors, where secondary prevention is standard. Monthly MRI studies even show that most lacunes start as diffusionpositive ischemic events, reinforcing that these are vascular lesions. Based on these parallels, Smith argued for aspirin, statins, and targeted workup for embolicappearing lesions.-prevention–level targets. Eric Smith opened by reminding us that "silent stroke" is a misnomer. These lesions may not produce symptoms recognized by patients or clinicians, but subtle cognitive or gait changes often exist. He showed that covert infarcts behave very much like symptomatic infarcts: in a large Kaiser Permanente dataset, individuals with covert infarcts had a five-year stroke risk of 16%, compared to 5% for those without them. After adjustment, the risk remains nearly two- to threefold higher. He argued that this risk level is -positive ischemic events, reinforcing that these are vascular lesions. Based on these parallels, Smith argued for aspirin, statins, and targeted workup for embolic-appearing lesions.

But Joanna Wardlaw responded with a clear distinction: silent cortical infarctions and smallvessel lesions are different problems, and lumping them together risks making decisions based on the wrong mechanism. She pointed to multiple contemporary guidelines—AHA/ASA, AHA/ACC, USPSTF—all stating that antiplatelet therapy is not recommended for primary prevention. The ASPREE trial, which enrolled nearly 19,000 healthy older adults, found that aspirin didn't reduce vascular events but did increase bleeding and mortality. When we look specifically at smallvessel disease, the European Stroke Organization's own guideline—led by Wardlaw—recommends against antiplatelets, with no evidence of benefit on cognition or whitematter disease progression. Mechanistically, she noted, smallvessel disease simply doesn't behave like largeartery atherosclerosis: carotid stenosis doesn't localize to lesions, prothrombotic genetics don't track with lacunar stroke, and vascular risk factors explain only about 2% of whitematter

hyperintensity variance. Her conclusion: aspirin is the wrong tool for this problem.-vessel lesions are different -vessel disease, the European Stroke Organization's own guideline—led by Wardlaw—recommends against antiplatelets, with no evidence of benefit on cognition or white-matter disease progression. Mechanistically, she noted, small-vessel disease simply doesn't behave like large-artery atherosclerosis: carotid stenosis doesn't localize to lesions, pro-thrombotic genetics don't track with lacunar stroke, and vascular risk factors explain only about 2% of white-matter hyperintensity variance. Her conclusion: aspirin is the wrong tool for this problem.

The second debate asked whether silent small-vessel disease should prompt genetic testing for monogenic arteriopathies. Guido Falcone argued yes—but only within guideline-supported criteria. He emphasized that young or middle-aged patients, those with heavy small-vessel disease burden, suggestive imaging patterns, family history, or features like neuropathic pain or anterior temporal lobe lesions may have monogenic syndromes worth identifying. Testing costs, he noted, range from $500 to $2500 and are billable, and results can change management—especially in conditions like Fabry disease, where enzyme replacement and chaperone therapy improve outcomes. He highlighted the broader value of cascade testing for families and long-term research contributions through national biobanks.

But Rebecca Gottesman reframed the question: should all silent small-vessel disease prompt testing? Her answer: clearly no. Small-vessel disease is almost universal in older adults—over 90% in some cohorts—while monogenic causes make up only 1–5% of cases. Treating these rare disorders doesn't usually differ from treating sporadic disease, with Fabry being the main exception, and most Fabry patients have systemic manifestations anyway. She walked through the math: if even 20% of the ≥65 population underwent testing at $500–$2500 each, the global cost becomes staggering—$13 to over $100 billion—to find a small minority with actionable findings. And in lower-resource settings, such practices would worsen disparities. The right approach, she argued, is selective testing in atypical cases—not routine screening.

The final debate moved into the territory of PFO closure for silent strokes. David Thaler made the case that silent infarctions—especially those with embolic patterns—may behave similarly to symptomatic embolic strokes. He leaned on the Pascal classification that distinguishes probable, possible, and unlikely PFOrelated events, and showed that in probable cases, PFO closure offers a dramatic 90% relative risk reduction with minimal atrial fibrillation risk. He argued that some socalled silent strokes may simply be forgotten, misinterpreted, or have landed in noneloquent cortex. Since these lesions still predict future stroke, he encourages clinicians to "embrace the gray zone," confirm infarctions

type, assess PFO causality, and engage in shared decisionmaking.-related events, and showed that in probable cases, PFO closure offers a dramatic 90% relative risk reduction with minimal atrial fibrillation risk. He argued that some so-called silent strokes may simply be forgotten, misinterpreted, or have landed in non-eloquent cortex. Since these lesions still predict future stroke, he encourages clinicians to “embrace the gray zone,” confirm infarct type, assess PFO causality, and engage in shared decision-making.

Marco Sposato countered with data showing that only about 4% of silent infarctions in PFO patients are actually attributable to the PFO. The six major PFO closure trials all enrolled patients with symptomatic stroke, and recurrence risk with medical therapy alone was already low—just over 1% per year. In many analyses, silent infarctions weren’t even associated with increased stroke recurrence. Closing a PFO does carry risks—fivefold increased atrial fibrillation, and rare but serious complications like device embolization. And critically, silent infarctions don’t cluster with highrisk PFO anatomy, making a causal link unlikely. The only randomized data to examine silent infarctions found that PFO closure didn’t reduce them anyway. Without evidence of benefit—and with risks upfront—Sposato argued that closure should not be offered.-fold increased atrial fibrillation, and rare but serious complications like device embolization. And critically, silent infarcts don’t cluster with high-risk PFO anatomy, making a causal link unlikely. The only randomized data to examine silent infarcts found that PFO closure didn’t reduce them anyway. Without evidence of benefit—and with risks upfront—Sposato argued that closure should not be offered.

Across all three debates, the evidence strongly favored the more conservative “con” side. Aspirin shouldn’t be used routinely. Genetic testing shouldn’t be applied broadly. And PFO closure shouldn’t be performed for silent infarctions. Silent strokes may be quiet, but today’s discussions made clear that our responses must be thoughtful, selective, and grounded in data—not assumptions.