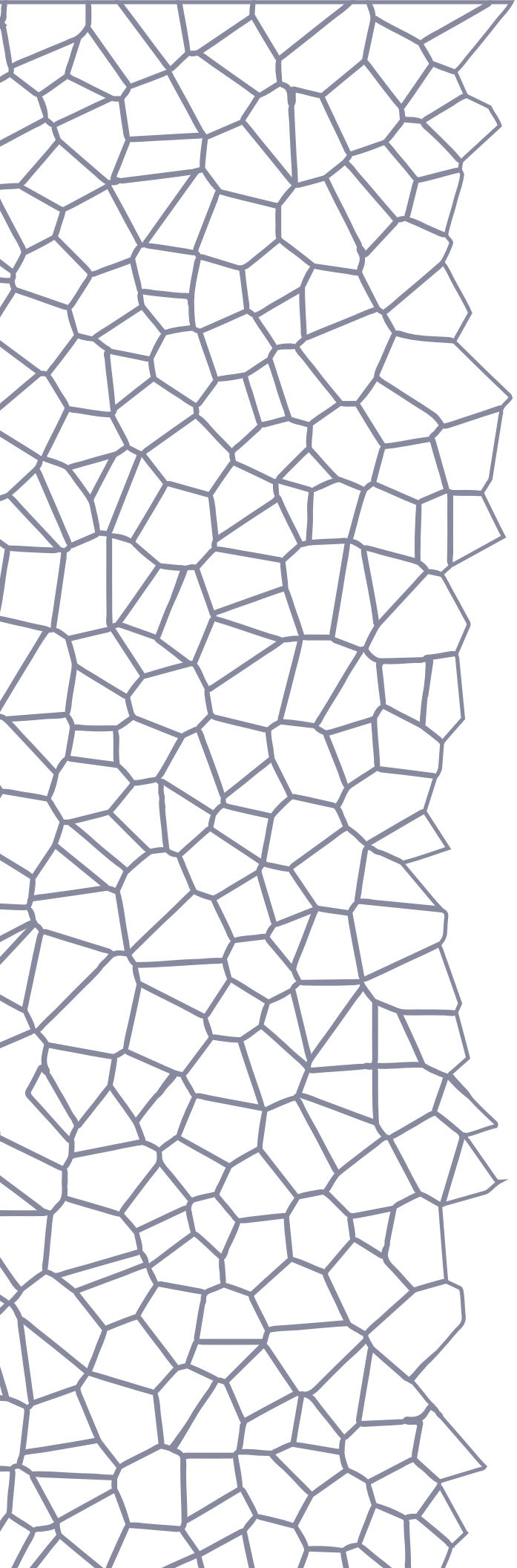
GLOBAL LIVER INSTITUTE

Beyond the Biopsy

MOVING BEYOND THE BIOPSY:

Improving Access and Usage of Non-Invasive Diagnostic Technologies for Liver Disease Screening and Evaluation



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Executive Summary

Liver disease remains underdiagnosed, frequently detected at advanced stages, and unevenly managed across populations and geographies. Despite major scientific advances, liver biopsy continues to function as a gatekeeper for diagnosis, treatment eligibility, clinical trial participation, and payer coverage. This reliance on invasive testing persists even as a broad and rapidly expanding portfolio of validated non-invasive diagnostic technologies (NITs) demonstrates clear clinical utility across the continuum of liver disease.[1]

Convened by Global Liver Institute (GLI), a multi-stakeholder dialogue among clinicians, researchers, technology developers, patient advocates, and policy experts examined the current barriers to adoption of NITs and identified strategies to accelerate their responsible integration into routine care, research, and policy frameworks. Participants consistently emphasized that liver biopsy should no longer serve as the default diagnostic or standard access, particularly given its risks, costs, variability, and limited scalability. This is becoming increasingly relevant as the prevalence of metabolic dysfunction-associated liver disease rises.[2]

This whitepaper synthesizes those discussions and proposes actionable recommendations to advance patient-centered liver care through broader adoption of non-invasive diagnostics. Central themes include the need for regulatory alignment, payer reform, clinician education, ethical deployment of AI, and infrastructure that supports early detection of liver disease, especially in underserved and rural settings.

Introduction

Chronic liver disease, including metabolic dysfunction–associated steatotic liver disease (MASLD), alcohol-associated liver disease, viral hepatitis, cholestatic disorders, and rare genetic conditions affect hundreds of millions of people worldwide.[3] Yet, the liver disease course remains largely silent until advanced stages, such as morbidity, mortality, and health system costs, rise sharply.[4]

Historically, liver biopsy has been considered the reference standard for diagnosis and staging. While biopsy has scientific value, it is curtailed by well-documented limitations, including sampling error, interobserver variability, procedure-associated risk, patient reluctance, and unsuitability for longitudinal monitoring. These challenges are magnified in the context of population-level screening, routine monitoring, and equitable access.

Non-invasive diagnostic technologies—ranging from blood-based biomarkers and functional assays, to imaging-based elastography and emerging home-based tests—offer an opportunity to fundamentally modernize liver disease detection and management. However, their adoption has been uneven, constrained by entrenched clinical habits, outdated policy frameworks, fragmented guidelines, and misaligned incentives.

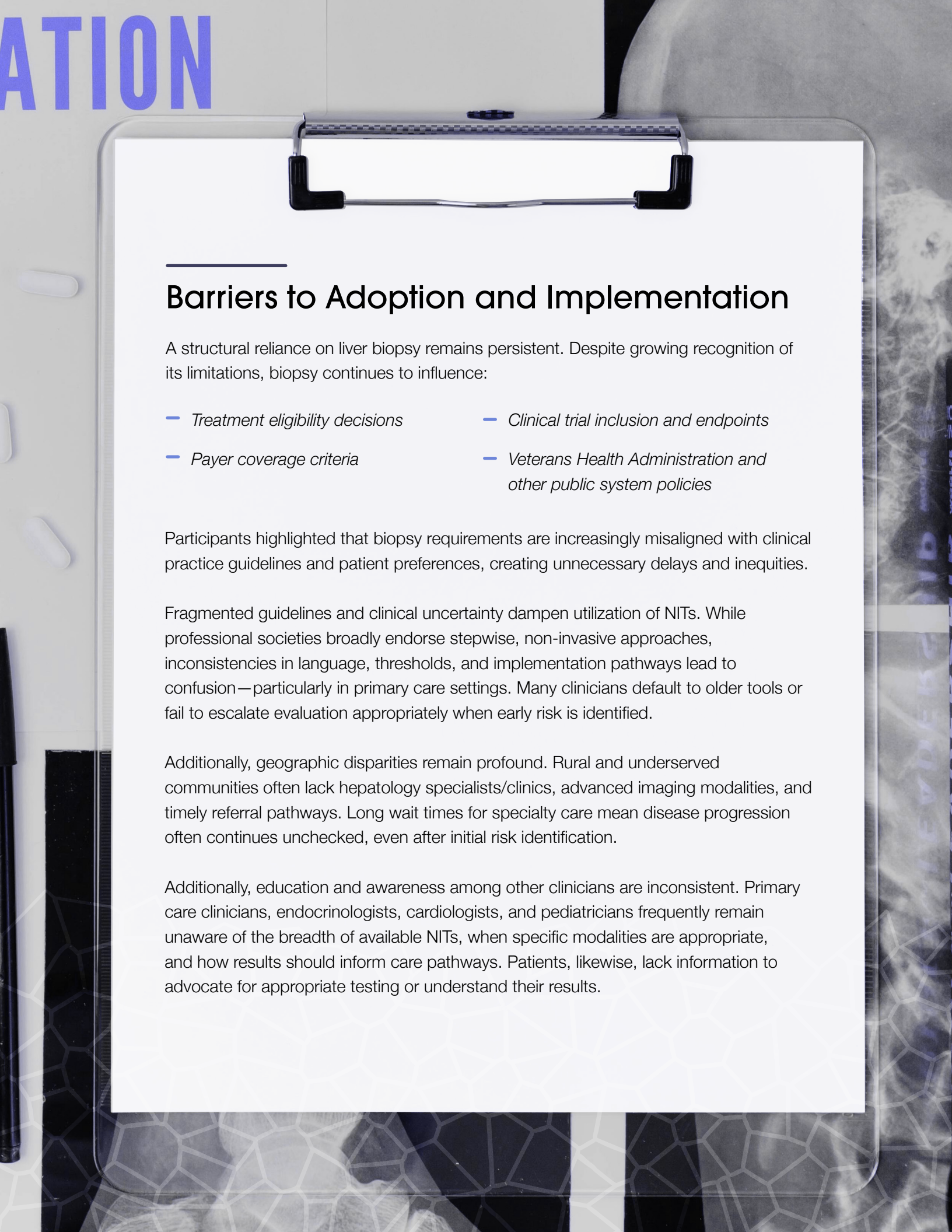
This paper outlines pathways to move beyond biopsy-centered paradigms toward a scalable, patient-centered diagnostic ecosystem.

Methods

This white paper draws on qualitative analysis of proceedings from a closed, in-person multi-stakeholder convening hosted by Global Liver Institute at the NHC offices offices in Washington, DC, in November 2025. Participants included:

- *Board-certified transplant hepatologists and other liver specialists*
- *Diagnostic technology developers across blood, imaging, and functional modalities*
- *Patient advocates and caregivers*
- *Policy and regulatory experts*
- *Representatives from payer-facing, market access, and clinical trial ecosystems*

Discussions were transcribed, anonymized, and thematically analyzed. Key themes were identified through consensus-driven synthesis rather than formal voting or quantitative ranking. Findings were contextualized within existing clinical guidelines, regulatory pathways, and health policy frameworks to produce forward-looking recommendations.



Barriers to Adoption and Implementation

A structural reliance on liver biopsy remains persistent. Despite growing recognition of its limitations, biopsy continues to influence:

- *Treatment eligibility decisions*
- *Payer coverage criteria*
- *Clinical trial inclusion and endpoints*
- *Veterans Health Administration and other public system policies*

Participants highlighted that biopsy requirements are increasingly misaligned with clinical practice guidelines and patient preferences, creating unnecessary delays and inequities.

Fragmented guidelines and clinical uncertainty dampen utilization of NITs. While professional societies broadly endorse stepwise, non-invasive approaches, inconsistencies in language, thresholds, and implementation pathways lead to confusion—particularly in primary care settings. Many clinicians default to older tools or fail to escalate evaluation appropriately when early risk is identified.

Additionally, geographic disparities remain profound. Rural and underserved communities often lack hepatology specialists/clinics, advanced imaging modalities, and timely referral pathways. Long wait times for specialty care mean disease progression often continues unchecked, even after initial risk identification.

Additionally, education and awareness among other clinicians are inconsistent. Primary care clinicians, endocrinologists, cardiologists, and pediatricians frequently remain unaware of the breadth of available NITs, when specific modalities are appropriate, and how results should inform care pathways. Patients, likewise, lack information to advocate for appropriate testing or understand their results.

AI & Noninvasive Technologies

Artificial intelligence is increasingly integrated into non-invasive diagnostics, offering opportunities to improve precision, scalability, and efficiency. Applications include automated imaging interpretation, risk stratification using real-world data, workflow optimization, and clinical decision support.

However, participants emphasized caution. Ethical deployment requires;

1. *High-quality, representative training datasets*
2. *Transparency in algorithm development*
3. *Safeguards against bias, misuse, and data exploitation*

Patients expressed broad willingness to share data when trust, consent, and clear benefit are established; still, concerns remain regarding surveillance, discrimination, and downstream use by payers or third parties. AI should be viewed as an augmenting tool, not a replacement for clinical judgment or patient-centered decision-making.

Policy & Legislative Levers to Drive Adoption

Advocacy efforts are underway to remove biopsy requirements from coverage decisions, most notably within federal systems such as the VA. Legislative engagement has demonstrated that targeted policy action can catalyze broader payer alignment.

While the FDA has expanded acceptance of NITs in early-phase trials and screening, biopsy still dominates as a surrogate endpoint in pivotal approval pathways. Accelerating the qualification of non-invasive endpoints over the next several years is critical to shifting norms.

Additionally, payer policies must be aligned with clear clinical and financial benefits. Clear evidence exists that non-invasive testing can

- *reduce procedural costs*[5]
- *minimize indirect patient burdens like travel, lost work, and caregiving*[6]
- *enable earlier intervention*[7]

Yet reimbursement policies often lag science. Demonstrating real-world cost-effectiveness and cascading system benefits will be essential for reform.

Preparing for the Future

Participants identified several priorities:

- **Integrated Diagnostic Pathways**

  combining multiple NIT modalities based on disease stage and setting

- **Cross-Specialty Engagement**

  particularly with diabetes, obesity, cardiology, nephrology, and pediatrics, and a potential interdisciplinary consensus guidelines

- **Patient-Accessible Tools**

  that explain testing options and empower shared decision-making

- **Community-Based Screening Models**

  including home-based and mobile diagnostics

- **Sustained Investment**

  in validation, implementation science, and data infrastructure

Progress will require coordinated action among advocacy organizations, regulators, industry, clinicians, and patients. Further efforts of this group will aim to prioritize, characterize, and plan joint efforts to achieve and address these goals with the ultimate goal of reducing patient burden and increasing patient access to non-invasive diagnostic technologies in as many situations is clinically appropriate.

Conclusion

The science supporting non-invasive liver disease diagnostics has advanced rapidly. Policy, practice, and payment systems must now catch up. Moving beyond biopsy is not about eliminating a tool, but about ending its inappropriate dominance as a gateway to care.

Non-invasive diagnostics offer a path to earlier detection, more equitable access, better patient experience, and smarter use of health system resources. Achieving this vision will require deliberate alignment across sectors—but the opportunity to transform liver care has never been greater.

Acknowledgements

Global Liver Institute gratefully acknowledges all summit participants for their expertise, candor, and shared commitment to advancing patient-centered liver health. Their insights informed the themes and recommendations presented in this white paper.

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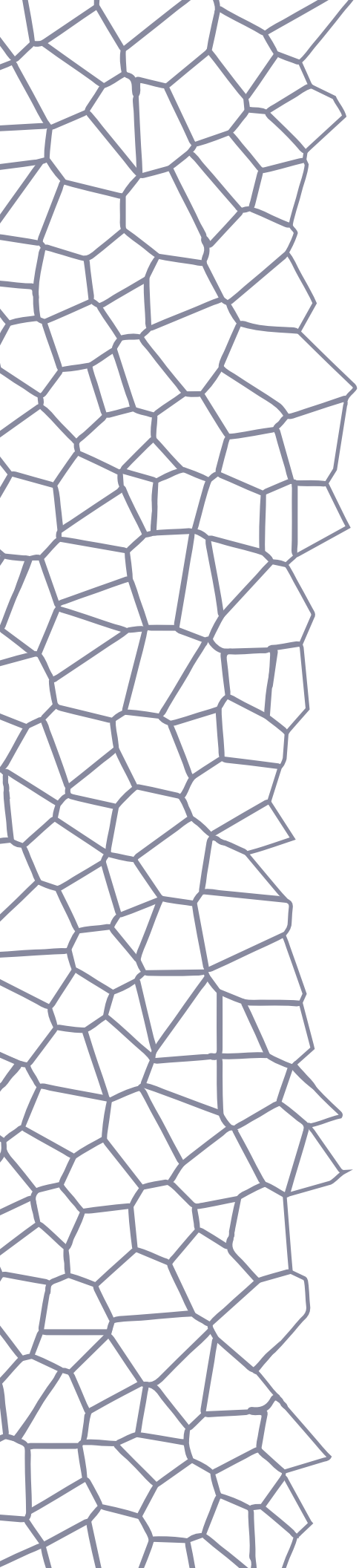

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