Annual Report Stichting Alpha1 MZ Foundation

Year: 2025
Jan 31, 2026

1. Executive Summary

The Alpha1 MZ Foundation, founded in Q1-2024, is a research-driven patient organization dedicated to improving recognition, understanding, and management of health problems associated with the Alpha-1 Antitrypsin deficiency genotype MZ

Alpha-1 Antitrypsin deficiency genotype MZ is caused by a mutation in the SERPINA1 gene (Glu366Lys), which leads to the production of misfolded Alpha-1 Antitrypsin protein in 3.5% of people of European heritage. In individuals with the MZ genotype, this misfolded protein polymerizes and accumulates in liver cells, causing chronic cellular stress, reduced hepatic functional capacity, and 50% less effective Alpha-1 Antitrypsin availability for lung protection.

This disease has long been regarded as a clinically insignificant carrier state. However, new and growing scientific evidence, along with consistent patient experience, show that this view is no longer valid.

The Foundation's work focuses on the liver as the central organ of impact in Alpha-1 MZ individuals and on the downstream systemic consequences. Our role is to connect emerging science, clinical observation, and patient experience into a coherent and credible framework that can be understood and used by patients, clinicians, researchers, and external stakeholders.

Strategic Focus

The Foundation's strategy is based on the observation that health issues associated with the Alpha-1 MZ genotype are insufficiently recognized in clinical practice, despite growing scientific and clinical evidence of a meaningful impact on liver health. Multiple studies and registry-based analyses show that approximately 10% of liver transplant recipients carry the Alpha-1 MZ genotype, that around 20% of patients with intrahepatic cholestasis of pregnancy (ICP) are MZ patients, and that liver disease progression and decompensation occur at a 2x higher rate compared with other populations.

These findings point to a discrepancy between the historical classification of Alpha-1 MZ as a benign carrier state and its observed contribution to liver-related morbidity. Reducing this gap through careful research translation, improved clinical awareness, and support for meaningful assessment and measurement underpins the Foundation's strategic focus.

In 2025, the Foundation focused on three closely connected areas:

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- Reduced functional liver reserve, the observation that Alpha-1 MZ livers may have limited capacity to respond to metabolic, inflammatory, hormonal, or pharmacological stress, even in the absence of advanced fibrosis.
- Functional cholestasis and bile-acid-related dysfunction, impaired bile acid production and handling as a potential upstream driver of metabolic, nutritional, and systemic symptoms.
- Systemic consequences, including medication intolerance, fatigue, metabolic dysregulation, and increased vulnerability under physiological stress.

These areas provide a unifying explanation for many patient-reported patterns and guide the Foundation's research, education, and collaboration activities.

Operational

The Alpha1 MZ Foundation operates at the intersection of patients, science, and clinical practice.

Our activities are structured around:

- Translating emerging research into clear, clinically relevant concepts.
- Collecting and structuring patient-reported outcomes to identify consistent patterns
- Facilitating collaboration between patients, researchers, clinicians, and external organizations
- Providing education and credible information to patients and medical professionals
- The Foundation does not deliver clinical care or develop therapies.
  Its role is to clarify the biology, define the problem space, and support progress through better understanding and measurement.

Year 2025 in Brief

During 2025, the Foundation consolidated its strategic direction and expanded its activities:

- Further development and communication of the root cause, pathways, and mechanics
- Increased focus on functional liver reserve and cholestatic mechanisms
- Active engagement with European and international liver and patient organizations
- Growth of an informed and engaged patient community
- Continued publication of educational and research-translation materials

This Annual Report describes how these activities were carried out in 2025 and how they support the Foundation's long-term mission.

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2. Governance and Organization

2.1 Board composition end 2025

- Frans Frielink; Chairman / Researcher (MZ Patient)
- Reinoud Doeschot; Secretary / Researcher (MZ Wife and children)
- Margaret Millar; Facebook Moderator / Patient Advocate (ZZ Patient)
- Dr. Laura Bonebrake; Obstetrician-gynecologist / ICP Researcher (MZ Patient)
- Natalia Ambridge; Foundation Expansion (Poland) / LinkedIn (MZ Patient)
- Diana Bieniek; Biochemistry and Holistic Nutrition research (MZ Patient)
- Nienke Groenendijk; Treasurer / Website / Substack & PR during 2025
  Replaced by Rob Maier, External Treasurer, early 2026

2.2 Statutory data

Official name: Stichting Alpha1 MZ Foundation
Chamber of Commerce number: 866764586
Postal address: Tjiftjaf 2, 3435BL, Nieuwegein, The Netherlands
Website: www.Alpha1MZ.org
Bank account number (IBAN): NL73SWNB2196162619

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2.3 Policy plan

Main objective: To improve knowledge and stimulate research into Alpha-1 Antitrypsin deficiency, with a specific focus on individuals with the Alpha-1 MZ genotype, addressing both patients and medical professionals.

Long-term vision: To expand the Foundation by establishing groups focused on key Alpha-1 MZ-related topics, supporting research initiatives, and helping to accelerate pathways that lead to the development and approval of relevant diagnostics and therapeutics.

Core pillars: (1) support for research; (2) biomarker and endpoint development; (3) development of a patient database and registry aligned with morbidities and symptom clusters; (4) collaboration with researchers, patient organizations, and industry; and (5) surveys and structured collection of patient-reported outcomes.

3. Activities

3.1 Scientific framework and research translation

In 2025, the Foundation continued to connect emerging medical research with observed clinical patterns in Alpha-1 MZ patients. A key focus is the reduced functional liver reserve, functional cholestasis, and systemic metabolic consequences.

The Foundation's research translation work emphasized practical clinical relevance: identifying which functional impairments may precede overt fibrosis and how these impairments may explain common patient experiences, including medication/supplement intolerance, fatigue, and metabolic dysregulation.

3.2 Biomarkers, datasets, and measurement strategy

A central strategic priority in 2025 was to move from narrative recognition to measurable evidence. The Foundation therefore advanced a biomarker-driven approach aimed at identifying signals of whole-lobule hepatic stress, bile acid handling abnormalities, and altered lipid metabolism in Alpha-1 MZ patients.

Where feasible, this approach integrates genotype-stratified analyses from large datasets (including biobank-type resources) with patient-reported outcomes and real-world laboratory panels, in order to define testable signatures that can support future validation studies, clinical risk stratification, and regulatory-relevant endpoints.

In collaboration contexts, the Foundation contributed input on biomarker concepts and supported survey-based data collection initiatives. Survey results are treated as hypothesis-generating signals that inform subsequent structured validation.

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3.3 Functional liver reserve assessment

Recognizing that current standard laboratory tests and structural imaging are insufficient and fail to capture diffuse or early functional impairment, the Foundation explored functional liver reserve assessment approaches during 2025 and identified various non-invasive tests to capture early functional impairment for further exploration and validation during 2026.

3.4 Communication, education, and community engagement

During 2025, the Foundation published approximately 50 weekly newsletters with research updates and clinical translation content. The number of readers/subscribers grew to over 700 by year-end. In 2025, the number of Facebook members/followers grew from ~500 to ~2000 patients and medical professionals.

The Foundation held a very successful webinar for patients and medical professionals to explain the Alpha-1 MZ morbidities and underlying mechanisms, and hosted guest speakers, including Prof. Gerry McElvaney and representatives from pharmaceutical organizations.

In addition, the Foundation engaged in European-level advocacy by participating in a meeting at the European Parliament (via an ELPA invitation) and by recording a podcast episode to support the broader dissemination of the Alpha-1 MZ liver-focused framework.

3.5 Collaborations and patient representation

Critical Path Institute (C-Path / CPA-1):
The Foundation served as a patient representative stakeholder, providing input on biomarker priorities and supporting the design of patient survey elements relevant to Alpha-1 MZ.

ELPA (European Liver Patients' Association):
The Foundation engaged with ELPA to strengthen patient representation at the European level and to support policy-relevant dialogue on the underrecognized burden of liver disease.

I-Gene:
The Foundation supported expanded access to genetic testing and patient discounts, facilitating broader mutation coverage and awareness.

Made By Daily:
The Foundation promoted an alternative vitamin D formulation (calcifediol) in contexts where reduced hepatic processing capacity may be relevant, and negotiated patient discounts.

Labor Stein:
The Foundation collaborated on the development of accessible AAT serum testing (including finger-prick concepts) and on the exploratory evaluation of polymer testing options.

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3.6 Clinical research programs

A clinical research program to evaluate Alpha-1 MZ prevalence among patients diagnosed with vitamin B12 deficiency was discontinued. Accumulating evidence and emerging clinical observations increasingly support the view that functional cholestasis and reduced functional liver reserve represent upstream drivers of multiple metabolic morbidities in the Alpha-1 MZ population, including disturbances affecting vitamin B12 status.

4. Policy and Future Plans

4.1 Objectives for the Next Year

In the coming year, the Alpha1 MZ Foundation will focus on consolidating and extending the scientific and organizational progress achieved in 2025. A key objective is to further strengthen the Foundation's role as a research-driven patient organization that bridges mechanistic insight, clinical relevance, and stakeholder engagement.

Organizational priorities include continued strengthening of the Foundation's internal structure, recruitment of additional active members and volunteers, and further deepening of collaborations with academic research groups and pharmaceutical and biotechnology companies active in liver disease and diagnostics.

Obtaining ANBI (Algemeen Nut Beogende Instelling) status remains an objective. This designation will enhance transparency, reinforce donor confidence, and support long-term sustainability of the Foundation's activities.

4.2 Scientific and Research Priorities

Building on the scientific advances made in 2025, the Foundation will prioritize further validation and dissemination of emerging evidence related to reduced functional liver reserve and functional cholestasis in the Alpha-1 MZ population.

In addition, the Foundation will work closely with research institutions. to support structured validation, biomarker identification, and future clinical and regulatory relevance.

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5. Financials

Financial overview – 2025

During the 2025 financial year, the Alpha1 MZ Foundation operated with a lean cost structure focused on research support, education, communication, and stakeholder engagement. All income and expenditures during the year were processed via the Foundation's bank account.

Income and result

Total income in 2025 consisted primarily of donations and project-related contributions. After accounting for all operational expenses, the Foundation closed the year with a positive financial result of €773.05.

This positive result reflects prudent financial management and careful alignment of expenditures with the Foundation's mission-driven activities.

Expenses

Expenditures in 2025 were primarily related to:

- Website development and hosting
- Communication and outreach activities (newsletters, webinars, and media)
- Research-related support and preparatory activities
- Administrative and operational costs
- No structural liabilities or long-term financial commitments were incurred during the year.

Balance sheet and liquidity

The balance sheet as of 31 December 2025 closes correctly and reflects a healthy and transparent financial position.

During the year, the founder made a €1,000 deposit on 14 February 2025, recorded as a "current account" for the founder. This amount is accounted for as a liability and does not form part of the Foundation's income. All other 2025 transactions were settled directly via the bank account.

The Foundation ended 2025 with a positive bank balance, a clearly defined and limited R/C Founder position and an equity increased due to the positive annual result

Financial governance

The 2025 bookkeeping follows the same accounting-based structure and principles as the 2024 financials, which are, from time to time, reviewed for structural correctness by an experienced accountant. The board reviewed the financials to ensure that all income and expense bookings were correctly reflected. The Foundation remains financially stable and well-positioned to support its planned activities in the coming year.

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6. Conclusion and acknowledgments

The year 2025 marked an important phase of consolidation and progress for the Alpha1 MZ Foundation. Through the combined efforts of the board, advisors, volunteers, and members, the Foundation strengthened its scientific focus, expanded its activities, and further clarified its role as a research-driven patient organization dedicated to the Alpha-1 MZ population.

Significant steps were taken to advance understanding of Alpha-1 MZ–related liver disease, including refining the functional reserve and functional cholestasis frameworks, engaging international researchers and organizations, and translating emerging insights into patient education and clinical dialogue. These efforts were made possible by the continued commitment of the board and the active involvement of the Foundation's growing community.

The Foundation would like to express its sincere gratitude to all board members, advisors, collaborators, and members for their time, expertise, and support throughout the year. Their contributions, whether scientific, organizational, or community-based, have been essential to the progress achieved.

Looking ahead, the Foundation is well-positioned to build on the momentum of 2025. With a clear strategic direction, a solid organizational foundation, and an expanding network of partners, we look forward to further advancing research, strengthening collaborations, and increasing our impact in the years to come.

7. Attachments

Financial statements 2025

Signatures

Frans Frielink	Reinoud Doeschot	Rob Maier
Chairman	Secretary	Treasurer
Frans Frielink	Reinoud Doeschot	R.T.M. Maier

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Activity

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Frans Frielink IP: 141.135.180.213	sent the document to frans.frielink@alpha1mz.org, reinoud.doeschot@alpha1mz.org, and rob.maier@kpnmail.nl	Apr 27, 2026 19:32:34 UTC
Frans Frielink IP: 141.135.180.213	first viewed document (frans.frielink@alpha1mz.org)	Apr 27, 2026 19:44:14 UTC
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