Alpha-1 Antitrypsin Deficiency genotype MZ

An overlooked liver condition affecting around 15 million Europeans

Alpha-1 MZ is a relatively common genetic condition in Europe, occurring in around 3.5% of the population. It results in reduced hepatic functional capacity from birth and significantly increases vulnerability to liver injury, inflammation, and metabolic stress. Despite this, Alpha-1 MZ remains one of the most underdiagnosed genetic disorders in Europe, contributing to a substantial and largely unrecognised disease burden.

Some data points:

- Roughly 10% of all liver transplants in Europe are Alpha-1 MZ individuals.
- ~20% of all intrahepatic cholestasis cases during pregnancy are MZs.
- Around 18% of all clinical hospital visits related to cryptogenic liver disease, liver cirrhosis, and COPD-related disease are Alpha-1 MZ individuals.[1]

Economic impact
Although only around 3.5% of Europeans are Alpha-1 MZ, they account for more than 10% of patients in lung and liver diagnostic pathways, as shown in the Irish National AATD Targeted Detection Programme.

Using conservative assumptions, this corresponds to EUR 0.5–1 billion per year in lung and liver specialist consultations, and approximately EUR 10 billion annually when hospitalisations, procedures, and wider disease-related costs are included, not counting productivity losses in Europe.

The European GDP impact is estimated at EUR 20–25 billion per year, based on approximately 3.75 million Alpha-1 MZ individuals with liver involvement, of whom 2.5 million are of working age. Assuming that 5% are entirely out of work and a further 15% experience reduced productivity, the resulting economic loss is substantial.

When lung disease (COPD), pregnancy complications such as intrahepatic cholestasis of pregnancy (ICP), and wider systemic effects are taken into account, the true productivity impact is likely to be even higher.

This reflects a significant and largely unrecognised cost driver within European healthcare and labour systems, one that is not yet incorporated into health-system planning or early diagnostic strategies, despite the potential for substantial savings and reduced pressure on already overstretched services.

Europe can no longer afford to overlook Alpha-1 MZ. With straightforward, low-cost policy measures, the EU could save an estimated EUR 30 billion per year through avoidable healthcare costs, preserved workforce productivity, and improved quality of life.

Your support in addressing this growing burden on patients, society, and the European economy is greatly appreciated.

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[1] Based on data from the Irish National Alpha-1-Antitrypsin Deficiency Targeted Detection Programme.

Alpha-1 genotype MZ; real world morbidities (35 million globally)

↓ Impaired immune system
↑ auto-immune

↓ Endocrine disruption
Hormone dysregulation

31% ↓ Reticulocytes
(precursor of red blood cells)

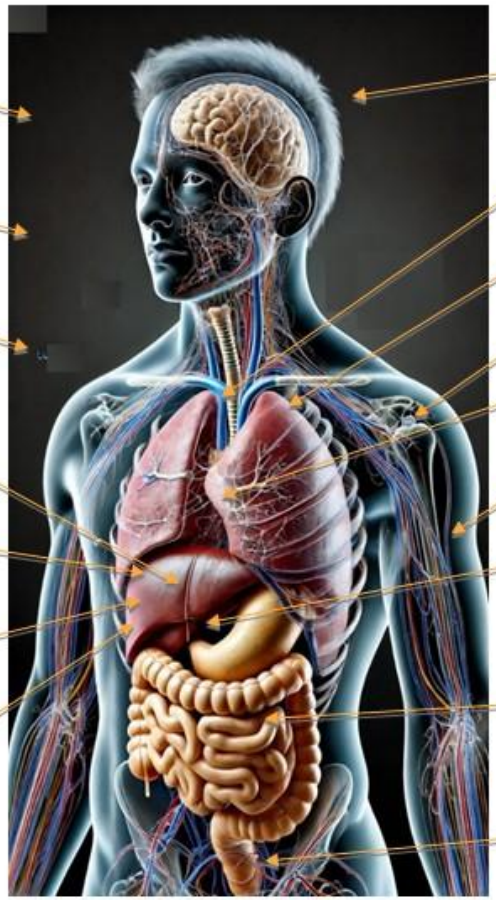
25% ↑ Bile duct disease
50%↑ Gall stones

3x ↑ Liver transplants
(~10% of all transplants)

7x ↑ Intrahepatic cholestasis
during pregnancy
(~20 of all ICP)

1.8x ↑ Faster liver
decompensation

Functional cholestasis
Whole lobule polymer stress



↑ Neuropathy

2.5x ↑ Aneurysm

40%/20% ↑ COPD/bronchitis

3x ↑ Rheumatic arthritis

16% ↓ Coronary atherosclerosis

17% ↑ Osteoporosis

↑ Biomarkers show
mild bilirubin, ALP, GGT

↓ Impaired absorption of
minerals and vitamins SIBO
(A, D, E, K, B12)

26% ↑ Prostatic hyperplasia

Kosinski et al., 2021; Fromme et al., 2021 Strnad et al., 2020 ; Fawcett et al. 2021; Gedde-Dahl et al., 1980; W I Schievink et al., 1996), Callea et al. (2021), Sanders et al. (2019), Nakanishi T, Forgetta V, Handa T, et al. 2020.