HCP SURVEY (164 Q)

A. Epidemiology

1. What is the prevalence of liver disease in AATD for the different protein phenotypes/genotypes?
2. What is the prevalence of lung disease in never smoker MZ individuals?
3. What is the prevalence of lung disease in smoker or ex smoker MZ individuals?
4. What are the general healthcare costs related to AATD?
5. What are the healthcare costs related to augmentation therapy in AATD?
6. What are the healthcare costs related to lung disease in AATD?
7. Who manages patients with AATD across Europe, including pulmonologists, gastroenterologists, internal medicine specialists, pediatricians or general practitioners?
8. What is the real prevalence of rare AAT deficient variants?
9. Are the rare AAT deficient variants more frequent in those countries in which the gene frequency of PiZ is lower?
10. What is the real frequency and type of bronchiectasis in AATD?
11. What is the prevalence of emphysema among never smokers PiZZ?
12. What is the prevalence of coexistent lung and liver disease among AATD individuals?
13. What is the prevalence of liver disease in MMalton individuals?
14. What is the prevalence of other less frequent manifestations, such as panniculitis?
15. How many children with liver diseases have lung and or liver problems later in life?
16. Do children without signs of liver problems develop lung/liver problems just as often later?
17. What are the criteria to consider the rare/ultra-rare SERPINA1 aberration as clinically important?
18. What is the prevalence of patients referred to lung or liver transplant; how many of them actually receive a transplant?
19. What is the survival of AATD patients receiving a lung transplant?
20. How many patients receive surgical or endoscopic LVR?
21. What is the prevalence of never smokers PiZZ without lung disease?

B. Diagnostic and screening

1. Would it be useful to include AAT in the current newborn screening program?
2. Who are the family members of a patient PI*ZZ that should be screened for AATD?
3. Who are the family members of a patient PI*MZ that should be screened for AATD?
4. Who are the family members of a patient PI*SZ that should be screened for AATD?
5. What is the laboratory algorithm that should be used for family screening?
6. When should genetic counseling be offered to AATD patients?
7. What are the mechanisms involved in the initiation, maintenance, and hereditability of the epigenetic changes observed in AATD?
8. Should the laboratory diagnosis algorithm be standardized in Europe?
9. What is the role of European certified laboratories for AATD diagnosis?

10. How can we improve early and accurate diagnosis in AATD?
11. What is the role of the lung microbiome in the pathogenesis of AATD?
12. What is the influence of race, sex and socioeconomic status on the natural history and pathobiology of AATD?
13. What is the psycological effect that the diagnosis might have in asymptomatic individuals?
14. What is the psychological burden of childhood diagnosis for parents and during the individuals development?
15. How relevant are the economic implications after diagnosis for asymptomatic individuals? (health insurance, work environment…)
16. What is the best approach to genetic testing considering the potential negative impacts for AATD patients?
17. What is the role that the electronic cigarrete might have in the development of lung disease in AATD?
18. What is the role that pollution might have in the development of lung disease in AATD?
19. What is the role that work exposures might have in the development of lung disease in AATD?
20. Is there a relation between AATD and cystic fibrosis?
21. How can delay in diagnosis be reduced?
22. Should the AAT activity testing be a part of standard diagnostic algorithm for rare SERPINA 1 mutations?
23. What is the impact that the delay of diagnosis has in the prognosis of the disease?

C. **Awareness and education for HCP and for patients. Registries**

1. How can awareness of AATD, among physicians, be improved?
2. How can awareness of AATD in community care services be improved?
3. How can awareness, and use of peer support forums and social media to exchange information about AATD, be raised?
4. How can we improve communication/quality information from HCP to AATD patients?
5. How can patients have and use equipment at home to monitor their symptoms?
6. How can we improve transition from pediatrics to adult care in AATD patients diagnosed during childhood?
7. What is the awareness of pediatricians regarding AATD manifestations in adult life and how can we improve it?
8. What is the awareness of respiratory specialists regarding non-COPD AATD manifestations (including respiratory) in adults and how can we improve it?
9. What is the level of satisfaction that AATD patients have regarding management and research of AATD within the medical community?
10. Should MZ individuals be included in AATD registries?
11. Should individuals with rare mutations be included in AATD registries?

12. Should Alpha1 guidelines be established for all countries that prescribe testing of Alpha1 in case of COPD, asthma and other indications, or is the European guideline sufficient?
13. What is the awareness of pediatricians regarding AATD manifestations in childhood?

D. **Clinical manifestations**

1. What is the relation between asthma and AATD?
2. Does an early referral to a specialist in AATD change outcome in patients?
3. What is the relation between bronchiectasis and AATD?
4. What is the relation between aneurisms and AATD?
5. What is the relation between AATD and cardiac comorbidities such as cardiac disfunction and aortic dissection?
6. What is the relation between cancer and AATD?
7. What is the relation between fibromyalgia and AATD?
8. What are the causes of fast progression and poor outcome in patients with AATD?
9. How should the severity of an exacerbation, in AATD patients, be assessed and what is its impact on long-term outcomes?
10. Are influenza and/or pneumococcal vaccines effective in preventing exacerbations in patients with AATD?
11. Should influenza and/or pneumococcal vaccines be prescribed to asymptomatic heterozygote patients?
12. What is the efficacy and advisability of vaccination against hepatitis B in AATD patients?
13. Are there pulmonary manifestations in children with AATD?
14. What is the most appropriate AAT blood concentration to consider severe and intermediate AATD?
15. What are the triggers for an exacerbation in AATD patients?
16. What is the relation between AATD and exacerbations?
17. What is the relevance that impaired AAT activity might have in the development of lung disease?
18. Is the prevalence of ACO in AATD the same as in COPD?
19. Do we need the pan-European detailed clinical SOP for AATD patients follow-up? How different would it be for healthy AATDs (PiZZ) or PiMZ patients with COPD?
20. In which proportion does AAT increase during inflammation?
21. What is the relation between p-ANCA vasculitis and AATD?

E. **Outcomes and Monitoring**

1. Should MZ individuals without disease manifestations be followed in a respiratory clinic?
2. How often and for how long should MZ without disease be followed in respiratory clinics?
3. Should SZ individuals without disease manifestations be followed in a respiratory clinic?

4. How often and for how long should SZ without disease be followed in respiratory clinics?
5. Should Mnull individuals without disease manifestations be followed in a respiratory clinic?
6. How often and for how long should Mnull without disease be followed in respiratory clinics?
7. Should Mrare individuals without disease manifestations be followed in a respiratory clinic?
8. How often and for how long should Mrare without disease be followed in respiratory clinics?
9. Which are the best blood markers for the diagnosis and follow-up of liver disease in AATD patients?
10. How frequently should AATD patients undergo a transient elastography for the screening of liver disease?
11. Which are the best lung function tests for the follow-up of pulmonary disease in AATD patients?
12. How often should spirometry be performed during follow-up?
13. How often DLCO should be performed during follow-up?
14. How often a lung CT scan should be performed during follow-up?
15. Do specific patient education packages, self-management plans and patients support groups improve outcomes in patients with AATD?
16. What is the role of pulmonary rehabilitation in patients with AATD?
17. Are current PRO used in COPD suitable for AATD individuals?
18. What are the risk factors, other than cigarette smoking, for the development of lung disease in AATD?
19. What are the risk factors, other than alcohol, for the development of liver disease in AATD?
20. What is the best score to evaluate radiology severity and progression in patients with AATD?
21. How often should lung density be measured during follow up in AATD?
22. Is FeNO useful during follow-up in AATD?
23. How can patients at increase risk of poor outcome or needing urgent treatment be identified?
24. What is the correct threshold of AAT serum level for detecting heterozygous carriers?
25. What is the best health status questionnaire to evaluate AATD patients?
26. What is the best prognostic score in AATD?
27. Which index or indices best stratify AATD patients for the purpose of determining disease severity or recommending treatment?
28. Are there CT findings associated with clinically significant features and differential responses to treatment in AATD?
29. Which outcomes matter most to patients and, therefore, are truly patient-centered outcomes in AATD?
30. What is the optimal CT protocol and quantification method in AATD patients?
31. How often and for how long should deficient individuals without clinical manifestations be followed?
32. What is the role of lung transplant in patients with AATD?

33. Should we follow patients with AATD without lung disease after a liver transplant and for how long?
34. What is the average lung function decline for MZ, SZ and SS patients?
35. How is the microbiome in AATD patients, and it is different among phenotypes and compared to non AATD COPD?
36. What is the impact that viral infections have on the evolution of AATD?
37. What is the role of gene therapy in AATD?
38. What is the clinically valid definition of fast decliner, what is advisable observation period?

F. **Augmentation therapy**

1. Could augmentation therapy be effective in other phenotypes/genotypes with low levels such as SZ?
2. Could augmentation therapy be effective in MZ patients?
3. Could augmentation therapy be effective in rare phenotypes/genotypes with normal levels but low AAT enzymatic activity (PiF?)
4. What is the role of AAT augmentation therapy after lung transplantation?
5. What is the role of AAT augmentation therapy after liver transplantation?
6. What is the role of AAT augmentation therapy for panniculitis, in patients with AATD?
7. What is the role of augmentation therapy for fibromyalgia in patients with AATD?
8. What is the optimal dose regimen (dose and frequency of administration) of augmentation therapy?
9. Should augmentation therapy be considered in PI*ZZ patients with bronchiectasis without emphysema?
10. What is the role of augmentation therapy in AATD asthmatic patients?
11. What is the therapeutic efficacy of aerosol AAT preparation?
12. What is the role of augmentation therapy for reduction of exacerbations frequency and severity?
13. What are the principal barriers for unequal reimbursement policies for AAT augmentation therapy across Europe?
14. How can augmentation therapy be accessible to all patients across Europe?
15. What is the real prevalence of adverse effects of augmentation therapy?
16. What is the role of home intravenous augmentation therapy?
17. Are longer regimes (biweekly and every 3 weeks) really equivalent to weekly augmentation therapy?
18. What is the effect of the discontinuation of augmentation therapy during holidays of hospital admissions?
19. Should augmentation therapy be administered in patients with emphysema with preserved spirometry?
20. Should augmentation therapy be administered in a home setting?
21. What are the side effects of augmentation therapy?
22. When should augmentation therapy be initiated?

23. Do PROs improve (deteriote significantly less) under augmentation therapy?

G. **Other treatments/AATD therapies**

1. What is the role of endoscopic therapy in AATD?
2. What is the role of lung volume reduction surgery in AATD?
3. What is the role of systemic steroids during an exacerbation of AATD?
4. What is the role of inhaled steroids in patients with AATD?
5. What is the role of oral mucolytics in patients with AATD?
6. What is the role of long-term antibiotic therapy in AATD patients?
7. What is the role of inhaled antibiotics in patients with AATD and clinical manifestations?
8. What is the role of biologics for the management of AATD?

H. **Other non pharmacological interventions**

1. When should pulmonary rehabilitation be offered/started in AATD patients?
2. What is the role of pulmonary rehabilitation in AATD?
3. What is the role of environmental and workplace avoidance of exposure, for lung disease in AATD patients?
4. What is the role of environmental avoidance of exposure, for liver disease in AATD patients?
5. What are the risk factors that should be avoided in AATD patients with liver disease?
6. What are the healthcare costs of AATD management across Europe?
7. How can communication between healthcare professionals and each patient be optimized to improve self-management?
8. Is disease management plan agreed with the patient?
9. How can access to healthcare professionals improve AATD management and control of the disease?
10. How can respiratory rehabilitation be accessible to all patients across Europe?
11. What is the impact of diagnosis and treatment of comorbidities in AATD patients?
12. Should psychological support be offered to AATD patients?
13. Are self management interventions effective in AATD patients?
14. Should exacerbation action plans be recommended for all AARD patients?
15. Does lung transplant increase survival in AATD patients?
16. How can a patient organisation/self-help group support the patient?
17. How can patient organisations and professionals network better?
18. Is breathing training/physiotherapy useful for patients with AATD?